

5-methoxy-*N*,*N*-dimethyltryptamine:

An ego-dissolving endogenous neurochemical catalyst of creativity

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Abstract

5-Methoxy-N,N-dimethyltryptamine (acronymized as 5-MeO-DMT) is sui generis among the numerous naturally-occurring psychoactive substances due to its unparalleled ego-dissolving effects which can culminate in a state of nondual consciousness that is phenomenologically similar to transformative peak experiences described in various ancient contemplative traditions (e.g., Advaita Vedānta, Mahāyāna Buddhism, inter alia). The enigmatic molecule is endogenous to the human brain and has profound psychological effects which are hitherto only very poorly understood due to the absence of scientifically controlled human experimental trials. Its exact neuronal receptor binding profile is a matter of ongoing research; however, empirical evidence indicates that its remarkable psychoactivity is partially via mediated agonism of the $5-HT_{1A/2A}$ (serotonin) receptor subtypes. Anthropological/ethnopharmacological evidence indicates that various cultures utilized 5-MeO-DMT containing plants for medicinal, psychological, and spiritual purposes for millennia. We propose that this naturally occurring serotonergic compound could be fruitfully utilized as a neurochemical research tool with the potential to significantly advance our understanding of the psychological and neuronal processes which underpin cognition and creativity (e.g., downregulation of the default-mode network, increased global functional connectivity, neuroplasticity, σ_1 receptor interactions, etc.). An eclectic interdisciplinary perspective is adopted, and we present converging evidence from a plurality of sources in support of our that has conjecture. Specifically, we argue 5-MeO-DMT significant neuropsychopharmacological potential due to its incommensurable capacity to completely disintegrate self-referential cognitive/neuronal processes (viz., "ego death"). The importance of unbiased systematic scientific research on naturally occurring endogenous psychoactive compounds is discussed from a Jamesian radical empiricism perspective and potential scenarios of abuse are addressed, particularly in the context of neuroethics, cybernetic manipulation, and military research on torture.

Keywords: 5-MeO-DMT, 5-HT_{2A} agonism, Creativity, Nonduality, Anthropocene, Cognitive liberty, Neuroethics.

Introduction

The following prefatory quotation is adapted from Abraham Maslow's seminal book "Towards a psychology of being" and it provides an apt primer and semantic grounding for the subsequent disquisition.

"An essential aspect of SA [Self-Actualized] creativeness was a special kind of perceptiveness that is exemplified by the child in the fable who saw that the king had no clothes on - this too contradicts the notion of creativity as products. Such people can see the fresh, the raw, the concrete, the ideographic, as well as the generic, the abstract, the rubricized, the categorized and the classified. Consequently, they live far more in the real world of nature than in the verbalized world of concepts, abstractions, expectations, beliefs and stereotypes that most people confuse with the real world. This is well expressed in [Carl] Rogers' phrase 'openness to experience'" (Maslow, 1968, p. 145, content in brackets added).

Humanity is currently *de facto* confronted with an unprecedented existential crisis which could be described as an "anthropogenic planetary emergency". One major acute threat to the survival of the species comes from the military and the constant threat of nuclear annihilation, another from the destruction of the global ecosystem and the significant and extremely worrisome anthropogenic (man-made) reduction of biodiversity which will soon cause a global systemic collapse (Steffen et al., 2018). The term "biological annihilation" has been proposed to describe this ongoing scenario (Ceballos, Ehrlich, & Dirzo, 2017).

In 1798, Thomas Malthus predicted exponential population growth in his "Essay on the Principle of Population" which influenced the ratification of the Census Act 1800 (41 Geo. III c.15) in Great Britain. Malthus foresaw numerous contemporary challenges and the topic of overpopulation has since then been centrally discussed by numerous influential thinkers such as Sir Charles Galton Darwin, Sir Julian Huxley, and Nobel laureate Lord Bertrand Russell, *inter alia*. In 1952, Russel wrote the following in his seminal book entitled "The Impact of Science on Society":

"The danger of a world shortage of food may be averted for a time by improvements in the technique of agriculture. But, if population continues to increase at the present rate, such improvements cannot long suffice. There will then be two groups, one poor with an increasing population, the other rich with a stationary population. Such a situation can hardly fail to lead to world war. If there is not to be an endless succession of wars, population will have to become stationary throughout the world, and this will probably have to be done, in many countries, as a result of governmental measures. This will require an extension of scientific technique into very intimate matters. There are, however, two other possibilities. War may become so destructive that, at any rate for a time, there is no danger of overpopulation; or the scientific nations may be defeated and anarchy may destroy scientific technique." (Russell, 1952, p. 27)

In 1960, Heinz von Förster² et al. published a paper in SCIENCE MAGAZINE which introduced the "Doomsday Equation". Based on mathematical extrapolation of an elongated J-curve, this equation predicts that population growth would become infinite at a specific (finite) point in time, that is, by Friday the 13^{th} of November, A.D. 2026 (von Förster, Mora, & Amiot, 1960). Based on statistical analyses they concluded that the growth of the world population N is most fittingly approximated by the following hyperbolic equation.

$$N = \frac{C}{t_0 - t}$$

where C and t_0 are constants, whereas t_0 corresponds to an absolute upper limit of the increase at which $N \approx \infty$ (for details see also Korotayev & Malkov, 2016).

Obviously, von Förster *et al.* did not actually believe that the world population would become infinite within the doomsday interval $t_0 = \text{A.D.} 2026.87 \pm 5.50$ (op. cit., p.1293)

² The cybernetician Heinz von Förster worked successfully in radar laboratories during the Nazi Germany era and he later immigrated to the USA via the secret operation PAPERCLIP which brought more than 1700 German Nazi scientists to the USA (Jacobsen, 2014). We will return to this topic in a subsequent section.

but rather that the prognosticated longitudinal trend would change into a different direction before the critical calendrical value is reached. Others researchers have propounded an elongated L-shaped curve, i.e., a stabilization at a minimum positive level at ≈ 2050 A.D. (Konar, 2012; cf. Korotayev & Malkov, 2016).

We maintain that there are other factors which are much more important than Malthusian demographic developments per se. The fundamental problems of the 21st century Anthropocene³ (Lewis & Maslin, 2015) are primarily caused by the irrational, short-sighted, reckless, and ego-driven behaviour of the human species, viz., overconsumption and a myopic profit-oriented exploitation of the ecosystem (Fromm, 1962, 1976). In the field of behavioural economics short-sighted thinking has been studied in extenso under the header "temporal discounting" (van den Bos & McClure, 2013). In brevi, immediate rewards are preferred and outcomes in the future are regarded as less important (time-additive discounted utility function), 4 a phenomenon which is also observable in non-human primates (Hwang, Kim, & Lee, 2009). However, there appear to be significant cross-cultural variations in "long versus short-term orientation", a variable which, according to factor analytic computations, constitutes a basic cultural dimension (Minkov & Hofstede, 2012). Since the 1970s countless studies on "delay gratification" (Mischel, Ebbesen, & Raskoff Zeiss, 1972) have been conducted and recent neuroimaging work indicates that neuroanatomical loci associated with self-control (i.c., higher-order prefrontal

³ The present epoch is also termed the 6th mass extinction or "Holocene extinction" (Barnosky et al., 2011; Ceballos & Ehrlich, 2018; Ripple et al., 2017) due to the rapid anthropogenic biodiversity loss which is comparable to other exogenously caused mass extinctions in the history of the planet earth (Régnier et al., 2015; Worm et al., 2006). That is, we are currently witnessing the first mass extinction caused by the behaviour of a species. For comparison, the last Cretaceous–Paleogene extinction event was with a high likelihood caused by the impact of a meteorite or comet.

⁴ Temporally discounted utility refers to the value of a delayed reward multiplied by the discount function F(D), where D signifies the delay. Specifically, the ratio F'(D)/F(D) constitutes the discount rate which signifies how rapidly the discount function decreases as a function of diachronic reward delay (Hwang et al., 2009). In the context of neuroeconomics high discount rates have been associated with various forms of addiction, i.e., substance and behavioral addictions (Monterosso, Piray, & Luo, 2012; Saville, Gisbert, Kopp, & Telesco, 2010). The "impulsivity construct" (e.g., poor self-control) has also been associated with genetic predispositions (Anokhin, Golosheykin, Grant, & Heath, 2011).

executive functions) play a crucial rôle in the top-down regulation of impulsivity/temptation (i.c., nucleus accumbes) (Luerssen, Gyurak, Ayduk, Wendelken, & Bunge, 2014). Sufficient self-control capacity is thus a neurocognitive condicio sine qua non for successful long-term strategies. However, our current capitalistic "economic" system is primarily based on marketing principles which systematically create desires and exploit impulsivity, e.g., methods of "nagging psychology" which explicitly target developing children, and, more recently, highly effective "neuromarketing" techniques which monitor and scrutinise the fine-grained effects of various advertising strategies on neuronal processes in the brain (Stanton, Sinnott-Armstrong, & Huettel, 2017). It could be argued that prefrontal executive control circuitry (which is necessary for reflective rational thought) is systematically compromised by various methods which target and exploit dopaminergic/limbic hedonic processes (cf. Olds & Milner, 1954). According to resource models of selfcontrol (e.g., Baumeister, Vohs, & Tice, 2007) the inherently limited capacity to regulate impulses and desires needs to be practiced (the so called "muscle analogy of self-control", but see Muraven & Baumeister, 2000). By contrast, present Western society is highly seductive (Biehl-Missal & Saren, 2012) and it reinforces a "mindless consumption mindset" 5 (cf. Williams & Grisham, 2012) which is combined with wasteful production principles such as "planned obsolescence" (Guiltinan, 2009) in order to stimulate economic growth (one of the explicit maxims of contemporary macroeconomics). There exists a ubiquitous focus on material externalities which is evidenced by the abundance of consumer objects. This observation is associated with a much more general ascertainment, namely, the widespread dominance of a thoughtpattern which is primarily quantitative, materialistic, outward oriented (extrospective), and egocentric, as opposed to qualitative, inward directed (introspective), and unitive (the psychoanalyst Erich Fromm emphasised the fundamental difference between the "having mode" and the "being mode" of existence

⁵ According to Hofstede's recently updated 6-D model "indulgence versus self-restraint" constitutes the newly added 6th cultural dimension and it would be interesting to examine if this is cross-cultural difference is reflected at the neuronal level (e.g., differences in prefrontal inhibitory control circuitry). "Restrain stands for a society that controls gratification of needs and regulates it by means of strict social norms" (Hofstede, 2011, p. 15).

in much of his work, e.g., op. cit.). We argue that this imbalance is reflective of a "subject versus object" consumption dichotomy and a "separationist Weltanschauung" which conceptualises nature as an objectifiable and exploitable resource which is perceived as entirely detached from the self. This perceptual paradigm is based on a purely materialistic and mechanistic conceptualisation of biology which leaves no room for qualitative aspects like purpose and meaning (i.e., télos & lógos) (cf. "hormic" theoretical approaches to psychology, e.g., McDougall, 1930; Wolman, 1981). It is principally based on utilitarian premises which do not incorporate human values, ethics, and morality. Terms like "sustainability" and "responsibility" are strategically employed by the massive public relations industry as described by Orwell in the context of "newspeak", i.e., psycholinguistic semantic inversion techniques are widely utilised as a façade (see also Chakravartty & Schiller, 2010; Wals & Jickling, 2002). In sum, these psycho-socio-economic factors destroy nature, antagonise rationality and foster egocentrism, irrationality, and short-sighted thinking.

The present *modus operandi* is congruent with the destructive philosophy of neoliberalism ⁶ – a doctrine which is highly influential amongst the "financial power"

⁶ In fact, the neologism "Capitalocene" has been proposed as a more accurate descriptor (Altvater, 2016). Human pressure on the Earth System is primarily caused by the wealthy OECD countries. Their "ecological footprint" (cf. Dietz, Rosa, & York, 2007) is proportionally much larger vis-à-vis the rest of the world, i.e., due to overconsumption (an sheer waste) of resources. Hence, equity significantly factors into the equation of "the great acceleration" (Steffen, Broadgate, Deutsch, Gaffney, & Ludwig, 2015). It is important to emphasize that the problem has interdisciplinary ramifications which cannot be fragmented – a creative transdisciplinary solution is needed.

élite"⁷ (Harvey, 2007; Hill & Kumar, 2009). The continuation of the current irrational course of action will predictably lead to total ecological catastrophe in the foreseeable future (Ceballos et al., 2017) unless humanity comes up with a radical⁸ creative solution.

Due to inherent species-specific cognitive and epistemological limitations prescience is intrinsically bound. Human beings cannot possibly *know* the exact threshold of the "multifactorial nonlinear complex systems equation" which determines the trajectory of our habitat in state-space (which might indeed be a multidimensional Hilbert space). There are simply to many unknown variables and deterministic predictions by a hypothetical omniscient "Laplacian Demon" might be in principle impossible due to the intrinsically stochastic nature of fundamental physics (cf. recent experimental falsifications of local realism, e.g., Gröblacher et al., 2007). However, it is a plausible cautious "Bayesian prior" to assume that once a critical tipping-point is reached the system loses its equilibrium state and a "singularity" ensues (not to be confused with the dystopian AI singularity advertised by prominent advocates of

⁷ The terminology is adopted from sociology, *in casu*, power structure analysis (Domhoff, 1975), where the topic of power concentration has been thoroughly studied (e.g., Froud, Johal, Moran, & Williams, 2017; Harvey, 2007; Hill & Kumar, 2009), for instance, with regard to the "fractional reserve banking system" (Foster & Holleman, 2014) which has been described as "economic parasitism". Currently, financial disparity has reached an extreme climax and statistics indicate that an extremely small ultra-rich segment (>1% of the total population) owns $\approx 50\%$ of the worlds entire wealth (i.e., ≈\$140 trillion are owned by an infinitesimal small minority; but see the "Global Wealth Report" from 2018 published by the Credit Suisse Research Institute). According to Forbes, wealth concentration in the USA has spiked in recent years. For example, "three men own as much as the bottom half of Americans" and the "richest American in 2018 was worth 31 Times as much as in 1982". A recent big-data study conducted at the ETH Zürich provided insightful results. Based on graph-theoretical network topology analysis a "super-entity" consisting of a network of global corporate control was identified (Vitali, Glattfelder, & Battiston, 2011). The researchers concluded that "transnational corporations form a giant bow-tie structure and that a large portion of control flows to a small tightly-knit core of financial institutions", an empirical finding which is indicative of a "richer-get-richer" mechanism.

 $^{^8}$ The term "radical" is etymologically derived from the Latin word "radix" meaning "root" (cf. the radical sign \checkmark in mathematics). That is, a "radical solution" refers to a solution which targets the very roots of the problem, as opposed to peripheral symptomologies (in the case under consideration the roots are primarily psychological).

⁹ See Laplace's "Essai philosophique sur les probabilités" (1814, p. 4).

transhumanism). The grand concept of the fine-tuned universe (Holder, 2002) can be generalised to the Earth System. Human beings can only exist in a very narrow band of fine-tuned environmental parameters (the "Goldilocks" zone of sapient life). Within an evolutionary blink of an eye humankind has changed the natural order (the Humboldtian *Kosmos*) for rather dubious reasons. Irrational primitive psychological motives like cupidity and imperiousness provide the primary impetus for this pervasive development. *Sapientiæ & virtutis* appear to play a subordinate rôle (if any) in this scenario which is often depicted as progress. Our self-image (as a species) is hubristic, unrealistic, and illusionary. To come *vis-à-vis* with the truth about our current condition might be the most difficult task which is prevented by constant distraction and various self-deceptive psychological defence mechanisms (e.g., quasi-Freudian suppression at the level of mass psychology).

In 2018, the figurative "Doomsday Clock" maintained by the BULLETIN OF ATOMIC SCIENTISTS was set to "2 minutes to midnight". ¹⁰ According to this heuristic multicriterial assessment, humanity was never that close to annihilation since 1953 when the USA tested the first hydrogen bomb (Guglielmi, 2018). Ergo, creativity and a fundamentally new way of thinking are of utmost evolutionary importance if the species $Hom\bar{o}$ sapiēns $sapiēns^{11}$ wants to survive this century. A creative solution to this far-reaching existential problem is thus literally a matter of life or death. ¹² As Einstein put it in a New York Times interview: "... a new type of thinking is essential if mankind is to survive and move toward higher levels." ¹³ One of the key components of the solution is a deep first-person emotive comprehension that

¹⁰ URL: https://thebulletin.org/2018-doomsday-clock-statement

¹¹ The binomial taxonomical nomenclature (introduced by Carl Linnæus) is etymologically derived from the Latin "homō" meaning "human being" and "sapiēns" meaning "wise" – thus the "wise human". By contrast, the neologism $Hom\bar{o}$ consumens has been proposed (Fromm, 1976) as a more accurate/realistic designation given the contemporary utilitarian production and consumption orientation of the species (Baudrillard, 1998).

 $^{^{12}}$ Realistic thinkers have argued that the chances of species survival are *de facto* minute (Fromm, 1962). However, classical game theoretical calculi are not applicable to this situation. Even if the chance of success is <1% humanity needs to mobilize all its resources to come up with a solution to the problem of self-destruction.

¹³ Source: New York Times - May 25, 1946, p.13 – "Atomic Education Urged by Einstein" URL: https://nyti.ms/2NpSc8L

the earth is a *single complex system* – an interconnected whole to which we as human beings belong.

Deeply intertwined with socio-political factors, there are systematic psychological barriers which impede rational change. For instance, the "status quo bias" which refers to an unconscious (System 1) preference for the current state of affairs (which is perceived as a comparative baseline level). Any change which deviates from this reference anchor is perceived as a loss (cf. loss-aversion, regret avoidance, existence bias, mere exposure effect, i.a.), despite the fact that an alternative course of action may be objectively advantageous (Kahneman, Knetsch, & Thaler, 1991). From a social group-dynamics perspective, individuals who challenge the perceived dominant status quo (which constitutes an implicit group norm) are socially punished by the ingroup (e.g., loss of reputation, discredititation, ostracism, etc.). In this way, the status quo is socially "cemented" (consolidated), and possible alternatives are prevented. It is noteworthy that norm-defection is socially contagious (for a pertinent historical Nazi Germany case-study see Geerling, Magee, & Brooks, 2015). Based on recent fMRI neuroimaging data it has been concluded that "specific prefrontal-basal ganglia dynamics are involved in rejecting the default, a mechanism that may be important in a range of difficult choice scenarios" (S. M. Fleming, Thomas, & Dolan, 2010, p. 6005). The experimental study documented a selective increase in neuronal activity in the subthalamic nucleus (STN) when the status quo was rejected. Further, statistical analysis indicated that there was a correlative increase in activity in the inferior frontal cortex for difficult decisions (as compared to easy defaults). In line with other conceptually related experimental studies, the results indicated that the frontal cortex has a modulatory top-down influence on the STN during switches away from the status quo (i.e., the non-default option). Such neuropsychophysiological data might provide important insights how to overcome the persistent status quo bias and the results indicate the importance of inhibitory cognitive control mechanisms (cf. studies on self-control/resource models of executive prefrontal functions)... 14 We

¹⁴ The importance of top-down executive control for the functioning of society has already been discussed by Plato in his $Res\ Publica$ (Lat.: Politeia). Plato placed great emphasis on the relation between self-discipline (synonymous with self-control) and justice, at the level of the individual and likewise the city-state (póli), as demonstrated in the following Socratic dialogue:

suggest that social group pressure (e.g., conformity à la Asch) should be systematically investigated as an additional variable in future behavioural and neuroimaging studies along these lines. The problem how to overcome the detrimental *status quo* is of utmost importance and governmental institutions and funding bodies should acknowledge the significance and urgency¹⁵ of this "wicked problem" (DeFries & Nagendra, 2017) which has far-reaching ramifications for the species as a whole. The *status quo* bias relates to the prefatory quotation by Abraham Malow who refers to Hans-Christian Andersons fable entitled "The Emperor's New Clothes" (published in 1837). However, what Anderson and Maslow do not mention is that the child whose innocent veridical perception of reality challenges the *status quo* will by all likelihood be severely punished, verbally abused, and verboten by those who proudly escort the naked emperor and praise the non-existent dress most profusely (i.e., those who benefit from the corrupt *status quo*, who identify with it, whose self-esteem depends on it, and who by no means want to see the truth). Thus,

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Glaucon: 'Rightly so,' he said.

Socrates: 'And the title "wise" because of that small part which acted as an internal ruler and gave those instructions, having within it a corresponding knowledge of what was good both for each part and for the whole community of the three of them together.'

Glaucon: 'Exactly.'

[&]quot;Socrates: 'It is not the same as courage and wisdom. Each of those was located in a particular part, and yet one of them made the whole city wise, and the other made it brave. Self-discipline does not operate in the same way. It extends literally throughout the entire city, over the whole scale, causing those who are weakest - in intelligence, if you like, or in strength, or again in numbers, wealth or anything like that — together with those who are strongest and those in between, to sing in unison. So we would be quite justified in saying that self-discipline is this agreement about which of them should rule — a natural harmony of worse and better, both in the city and in each individual.' [...] 'The title 'brave', I think, is one we give to any individual because of this part of him, when the spirited element in him, though surrounded by pleasures and pains, keeps intact the instructions given to it by reason about what is to be feared and what is not to be feared.'

What about "self-disciplined"? Isn't that the result of the friendship and harmony of these three? The ruling element and the two elements which are ruled agree that what is rational should rule, and do not rebel against it.'

Glaucon: Yes. That's exactly what self-discipline is,' he said, 'both for a city and for an individual.' ¹⁵ In this context another cognitive bias is of pertinence: the "omission bias". *In sensu lato*, omission bias refers to the irrational human tendency to judge omissions that cause harm as less significant compared to actions that cause harm because actions are perceived as more salient and hence consequential than inactions (DeScioli, Christner, & Kurzban, 2011).

the child will painfully learn the consequences of not conforming to fallacious socially shared beliefs (via Bandura-type operant conditioning). Ritualism and orthopraxy (Ellul, 1973) are additional pertinent concepts in this situation. Moreover, this hypothetical punitive scenario does not include the reaction of the royal propagandists and the king himself.

In general, people do not readily give up core beliefs (Weltanschauungen) in the light of new evidence (a quasi-Bayesian epistemological desideratum). Per contrast, humans defend elementary belief tenets which fundamentally (axiomatically) structure their perspective on reality, consciously and/or unconsciously, and one might argue that Hebbian principles of long-term potentiation provide a neuronal "morphometric" explanation for cognitively inflexible "belief networks" 16 (i.e., consolidation/dominance of specific neuronal pathways — any deviation is associated with computational outcome uncertainty). "Belief bias" (Evans, Over, & Manktelow, 1993) is one mechanism which works at the automatic/implicit level, i.e., the syntactical logical validity of a given syllogistic argument is frequently neglected and conclusions are primarily judged based on their semantic congruence with certain apriori beliefs. Around 2000 years ago, Lucius Seneca summarised this irrational human tendency concisely in one sentence: "Every man prefers belief to the exercise of judgment." The elaboration likelihood model (Petty & Cacioppo, 1986) provides a dual-process framework which distinguishes between two modes of information processing — a peripheral (heuristic) mode vs. a central (analytic) mode. The latter constitutes the reflective and rational mode of reasoning while the former is reflexive and belief based. "Rational intelligence" (RQ; Stanovich & West, 2008) is an individual differences variable that refers to people's propensity to utilise critical thinking skills and analytic cognitive processes (note that RQ ≠ IQ). If conditions for rational/analytic processing are not met the status quo is passively adopted as the effortless default (i.e., cognitively economic heuristic decisions which do not engage any elaboration or System 2 intervention and are cost-effective in prefrontal energetic

¹⁶ The Quinan "Web of Beliefs" (Quine & Ullian, 1978) provides an applicable semantic analogy to (Bayesian) neural network connectivity and the process of "belief updating" (i.e., modification of weights between neuronal nodes).

terms). Characterological idiosyncrasies and group conformity propensities are additional significant factors in this regard.

In connection to "herd psychology" the eugenist Sir Francis Galton formulated the following quasi-Darwinian argument on behavioural/cognitive/attitudinal conformity in his book "Inquiries into the Human Faculty" (1983, p. 51 et seq., cap.: "Gregarious and Slavish Instincts"):

"An incapacity of relying on oneself and a faith in others are precisely the conditions that compel brutes to congregate and live in herds; and, again, it is essential to their safety in a country infested by large carnivora, that they should keep closely together in herds. No ox grazing alone could live for many days unless he were protected, far more assiduously and closely than is possible to barbarians. [...] If any brute in a herd makes itself obnoxious to the leader, the leader attacks him, and there is a free fight between the two, the other animals looking on the while. But if a man makes himself obnoxious to his chief, he is attacked, not by the chief single-handed, but by the overpowering force of his executive. The rebellious individual has to brave a disciplined host; there are spies who will report his, doings, a local authority who will send a detachment of soldiers to drag him to trial; there are prisons ready built to hold him, civil authorities wielding legal powers of stripping him of all his possessions, and official executioners prepared to torture or kill him. The tyrannies under which men have lived, whether under rude barbarian chiefs, under the great despotisms of half-civilised Oriental countries, or under some of the more polished but little less severe governments of modern days must have had a frightful influence in eliminating independence of character from the human race."

Much earlier, in 1851, the charismatic German philosopher Arthur Schopenhauer wrote the following on the detrimental effects of conformity and "public opinion":

"When we see that almost everything men devote their lives to attain, sparing no effort and encountering a thousand toils and dangers in the process, has, in the end, no further object than to raise themselves in the estimation of others; when we see that not only offices, titles, decorations, but also wealth, nay, even knowledge and art, are striven for only to obtain, as the ultimate goal of all effort, greater respect from one's fellowmen, — is not this a lamentable proof of the extent to which human folly can go? To set much too high a value on other people's opinion is a common error everywhere; an error, it may be, rooted in human nature itself, or the result of civilization, and social arrangements generally; but, whatever its source, it exercises a very immoderate influence on all we do, and is very prejudicial to our happiness. We can trace it from a timorous and slavish regard for what other people will say, up to the feeling which made Virginius plunge the dagger into his daughter's heart, or induces many a man to sacrifice quiet, riches, health and even life itself, for posthumous glory. Undoubtedly this feeling is a very convenient instrument in the hands of those who have the control or direction of their fellowmen; and accordingly we find that in every scheme for training up humanity in the way it should go, the maintenance and strengthening of the feeling of honor occupies an important place. [...] There was much the same kind of thing in the case of Lecompte, who was executed at Frankfurt, also in 1846, for an attempt on the king's life. At the trial he was very much annoyed that he was not allowed to appear, in decent attire, before the Upper House; and on the day of the execution it was a special grief to him that he was not permitted to shave. It is not only in recent times that this kind of thing has been known to happen. Mateo Aleman tells us, in the Introduction to his celebrated romance, Juzman de Alfarache, that many infatuated criminals, instead of devoting their last hours to the welfare of their souls, as they ought to have done, neglect this duty for the purpose of preparing and committing to memory a speech to be made from the scaffold." (Schopenhauer, 1851, p. 46, et seq., cap. IV "Position, or A Man's Place in the Estimation of Others").

In conclusio, these quotations demonstrate the restrictive impact of public *doxa* (Bourdieu, 1977), impression management, social desirability, and the fundamental

"need to belong" (Baumeister & Leary, 1995) on independent thought which is an essential prerequisite for creativity and modifications of the *status quo*.

The "single-state fallacy" (Roberts, 2006, p. 104) pertains to the widely held naïve belief that worthwhile cognition exclusively takes place in "normal" alert waking consciousness — a superficial assumption which fits into the dominant contemporary materialistic and utilitarian "production habitus" 17 which places great emphasis on "ordinary" states of consciousness and socially discriminates against "altered" states of consciousness as being unimportant, irrational, prejudicial, libidinous, and even infantile (cf. Fromm, 1976). Per contra, there exists copious evidence that important path-breaking creative ideas can emerge from "non-ordinary" states of consciousness (Tart, 1972, 2008). A well-documented paradigmatic historical example is August Kekulés discovery of the benzene structure in 1858, a landmark in the history of science which heralded the birth of the structural theory of organic chemistry (Kekulé, 1866, 1890). Kekulé, a German chemist, had a daydream of the Ouroboros (an ancient symbol of a snake seizing its own tail). This dream-image provided him with the idea of the cyclic structure of benzene (Gillis, 1966; Rocke, 2015), i.e., a symmetrical ring comprised of six carbon atoms with alternating single and double bonds. The farreaching scientific ramifications of Kekulés insight for the rapid development of modern chemistry can hardly be overstated. Interestingly, the Swiss depthpsychologist C.G. Jung assigned particular archetypal and alchemical significance to

¹⁷ The computer analogy (Casey & Moran, 1989) forms the conceptual metaphoric basis of much of contemporary thought (Lakoff & Johnson, 1981). Norbert Wiener wrote the following on *Zeitgeist* in his cybernetics book with the telling title "The human use of human beings" (1950):

[&]quot;... the thought of every age is reflected in its technique. [...] If the seventeenth and early eighteenth centuries are the age of clocks, and the later eighteenth and nineteenth centuries constitute the age of steam engines, the present time is the age of communication and control." A similar argument could be articulate with respect to Cartesian and Freudian "hydraulic" theories.

this ancient symbol¹⁸ which can be found in numerous cultural traditions across various epochs and locations (Jung, 1969). Jung wrote:

"The dream is a little hidden door in the innermost and most secret recesses of the soul, opening into that cosmic night which was psyche long before there was any ego consciousness, and which will remain psyche no matter how far our ego-consciousness extends. For all ego-consciousness is isolated; because it separates and discriminates, it knows only particulars, and it sees only those that can be related to the ego. Its essence is limitation, even though it reach to the farthest nebulae among the stars. All consciousness separates; but in dreams we put on the likeness of that more universal, truer, more eternal man dwelling in the darkness of primordial night. There he is still the whole, and the whole is in him, indistinguishable from nature and bare of all egohood. It is from these all-uniting depths that the dream arises, be it never so childish, grotesque, and immoral." (Jung, 1933, p. 304)

Jung's mentor, Sigmund Freud, famously characterized dreams as "the royal road to the unconscious" (Freud, 1939). However, unbeknownst to early Freudian psychoanalysts, besides dreams, parapraxis, and free-association techniques, there exist other much more effective methods to render unconscious psychic contents more

¹⁸ It is curious to remark that the Ouroboros shares numerous topological similarities with the Möbius band (a paradoxical geometrical object which has been eponymously named after the German mathematician August Ferdinand Möbius who described it in 1885). Interestingly, archaeological excavations demonstrate that the Möbius band has been depicted in artworks across numerous ancient cultures and epochs (Cartwright & González, 2016). The mathematical symbol for the concept of infinity, the lemniscate, shares central defining features with the Möbius band. We submit that the symbolism of the Möbius band can be interpreted as a visual conceptual metaphor, a figure of thought (Lakoff, 1986), for the psychophysical "Pauli-Jung conjecture" of dual-aspect monism (Atmanspacher, 2012). *In abstracto*, the Ouroboros is thus a symbol for second-order cybernetics (von Förster, 2003), i.e., the recursive relationship between the seer and the seen (*psyche* and *physis*).

accessible. ¹⁹ Certain neuroactive chemical substances, colloquially termed "psychedelics", ²⁰ are particularly potent tools in this regard. From a psychoanalytic perspective, it is noteworthy that psychedelics produce dream-like effects and may also be classified as *oneirogenic* substances ²¹ (i.e., substances that produce or enhance

¹⁹ Much later Walter Frederking utilized mescaline and LSD-25 for psychotherapy in order to facilitate "deep relaxation and free ideation" via "drug-induced dream-like states" in order to "shorten the course of psychoanalysis" by facilitation of profound insights (Frederking, 1955, p. 262). Frederking postulated that these psychoactive chemicals could be used to establish a "close connection between the subject and his dreams".

The etymology of the term is derived from the Ancient Greek ψυχή (psukhé, "mind, soul, spirit") + δ ηλος (dêlos, "to manifest, to reveal"), i.e., "psychedelic substances" could be adequately translated as "mind manifesting" or "soul revealing" substances. Similarly decomposed, psychology is "the study of" the "mind, soul, and spirit" — even though most contemporary psychologists would reject this "deep" definition. Previously, psychedelics were also labeled as "psychotomimetics" because they were thought to produce symptoms similar to those of a psychosis. Interestingly, schizophrenia and other psychopathologies involving psychotic symptoms (e.g., bipolar disorder) have been linked to creativity (e.g., Claridge & Blakey, 2009; Power et al., 2015), possibly due to a reduction of latent inhibition (cf. Burch, Hemsley, Pavelis, & Corr, 2006), *inter alia*.

²¹ It is a plausible hypothesis that psychoactive tryptamines are involved in naturally occurring dream-states. Given its central function in biochronological processes, the pineal gland is an important neuroanatomical ROI (cf. Barker, Borjigin, Lomnicka, & Strassman, 2013). Also note the close structural similarity between melatonin (N-acetyl-5-methoxy-tryptamine) and 5-MeO-DMT (5-methoxy-N,N-dimethyltryptamine). There are numerous hypotheses which link dream-states to creativity (e.g., Bob & Louchakova, 2015).

dream-like states of consciousness which is of pertinence for modern oneirology).²² There is a significant amount of anecdotal significant evidence that psychedelics can, *inter alia*, enhance creative ideation (indeed the term "ideagens" has been suggested; Roberts, 2006).

From a purely pragmatic vantage point on creativity the crucial importance of psychedelics in the technological development of the internet and the personal computer should be highlighted (the digital revolution). *Prima vista*, this might appear like a hyperbolic statement. However, there exists considerable historical evidence in support of the claim that psychedelics played a pivotal rôle in the highly creative and innovative 1960s computer-revolution which fundamentally transformed (and interconnected) the world we inhabit (see Markoff, 2005; Nelson, 1975). A similar argument could be made with respect to the development of cybernetics as an interdisciplinary meta-discipline, e.g., the Macy conferences. ²³ Besides the influence of psychedelics on the development of uniting (i.e., boundary

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²² It has been shown that the emotional valence of dreams can be systematically influenced by extraneous (i.c., olfactory) stimuli. It has been experimentally demonstrated that a positive smelling stimulus (rose smell) induced positive dreams while a negative smelling stimulus (the smell of rotten egg) induced negative dreams (Schredl et al., 2009). Similar perceptual/phenomenological interactions may be predicted for the emotional valence of psychedelic states (such techniques might be utilized to foster conditions which are conducive to the unfoldment of creativity or for therapeutic purposes). Furthermore, in relation to dreams and creativity research, "disjunctive cognitions" are another dream-state phenomenon of significant interest. During the perception of "interobjects" the dreamer experiences novel disjunctive phenomena such as objects and geometrical structures that do not occur in general waking consciousness. These objects are self-contradictory and paradoxical, viz., they are incongruent with the axiomatic Aristotelian "laws of thought", i.c., the law of the excluded middle, the law of noncontradiction, and the law of identity. It has been argued that dream events oftentimes feel bizarre but that disjunctive cognitions usually do not. The following example illustrates the point: "I'm sitting in a dream beside a man I don't recognize, but I know in the dream is my father" (Boas, 1994, p. 155). This example could be interpreted as an inversion of the "Capgras' delusion" (Young, 2008), an interpretation which is particularly interesting in view of the fact that Capgras' syndrome has been associated with the alteration of time perception (Aziz & Warner, 2005), a factor which is common to dreams and psychedelic states. Echoing early Freudian theorizing, it has been suggested with regard to the emerging interdisciplinary field of neuropsychoanalysis that by "careful examination of the experiences in dreams, we may gain insight into the workings of our mind/brains" (Blechner, 2001).

²³ Cf.: Glaser, Gilbert (1955). "Neuropharmacology - Transactions of the first conference". *The Yale Journal of Biology and Medicine*. 28(1), 78–79.

dissolving) information-technologies like the *world-wide-web*, innumerable artists across disciplines, epochs, and cultures have been deeply inspired by transcendental experiences occasioned by psychedelics, especially within the branch termed "visionary arts" (e.g., Grey, 2001). Indeed, it has been argued that unconscious processes play a pivotal rôle in artistic expression (e.g., Kandel, 2015). For reasons of space and parsimony we omit a discussion of this extremely rich area.

Eminent contemporary instances of "psychedelically-inspired creativity" include, for example, the entrepreneur Steve Jobs and Nobel laureate Karry Mullis. 24 Jobs famously reported that his experience with Lysergic Acid Diethylamide (LSD) was one of the most important things he did in his whole life, a statement which recently gained experimental empirical support. 25 Biochemist Karry Mullis was even more explicit (Mullis was honoured for his ground-breaking work on the polymerase chain reaction which is currently widely used to replicate DNA). He stated in an interview: "Back in the 1960s and early '70s I took plenty of LSD. A lot of people were doing that in Berkeley back then. And I found it to be a mind-opening experience. It was certainly much more important than any courses I ever took" (Schoch, 1994). Mullis claimed that his ability to "get down with the molecules" was facilitated by LSD (Slattery, 2015). Moreover, he wrote in his autobiography: "The concept that there existed chemicals with the ability to transform the mind, to open up new windows of perception, fascinated me" (Mullis, 2000, p. 62). Mullis articulation reverberates with the title of Aldous Huxley's influential book "The Doors of Perception" (Huxley, 1954) in which Huxley details his extraordinary experiences with the ancient psychedelic compound mescaline (3,4,5-trimethoxyphenethylamine) which was administered to

²⁴ It should be emphasized that these chosen examples should not reinforce the superficial conception that creativity only "matters" if it produces material dividends and has no intrinsic value in itself (Fromm, 1976).

 $^{^{25}}$ In a recent randomized double-blind trial $\approx 70\%$ of participants rated their experimentally induced psychedelic experience as one of their top five spiritually significant lifetime events (Griffiths et al., 2016).

him by the British psychiatrist Humphrey Osmond²⁶ who initially coined the term "psychedelic". Huxley wrote the following couplet in a letter to Osmond:

"To make this mundane world sublime,

Take half a gram of phanerothyme"

Osmond likewise responded to Huxley in poetic rhyme form:

"To fathom Hell or soar angelic,

Just take a pinch of psychedelic"

Huxley²⁷ adopted the title of his mescaline-inspired book from a phrase found in William Blake's 1793 poem "The Marriage of Heaven and Hell". Blake wrote: "If the doors of perception were cleansed every thing would appear to man as it is, Infinite. For man has closed himself up, till he sees all things thro' narrow chinks of his cavern." ²⁸ According to Huxley and Blake, the transcendence of the self-centred perspective which is associated with rigid ego-structures enables the percipient to perceive reality in "new light" and from a more impartial and universal perspective. Likewise, Schopenhauer²⁹ wrote the following in 1831 in a chapter entitled "Genius and Virtue":

²⁶ Osmond first used the term in the scientific literature in 1957 in an article published in the "Annals of the New York Academy of Sciences" entitled "A review of the clinical effects of psychotomimetic agents" (Osmond, 1957).

 $^{^{27}}$ Huxley was a repeated nominee for the Nobel Prize in literature and his genealogy is related to many high-grade British scientists (Berra, Alvarez, & Shannon, 2010). An interesting factoid (especially in the context of ego-dissolution/ego-death) is that Huxley wrote a note to his wife while on his deathbed asking her to inject him with $100\mu g$ of LSD (IM). Huxley died while under the influence of the consciousness expanding substance. Another interesting piece of information is that Huxley was allegedly intimately involved in the illegal CIA MK-ULTRA program (discussed subsequently) which entailed psychological experimentation with psychedelic substances on naïve and nonconsenting subjects (often-times with extremely harmful consequences).

²⁸ A connatural conception can also be found in Plato's "Allegory of the Cave". Plato was very much concerned with eternal forms and most mathematicians can be regarded as implicit Platonists (Burnyeat, 2000; Mueller, 2005) even though they might not be explicitly aware of this philosophical heritage (cf. the importance of Δianoia in Plato's "Theory of Forms" (Cooper, 1966)).

²⁹ Eristische Dialektik: Die Kunst, Recht zu behalten (transl.: Eristic Dialectic: The Art of winning an argument)

"The man who is devoted to knowledge of this character is not employed in the business of the will [ego]. Nay, every man who is devoted to the purely objective contemplation of the world (and it is this that is meant by the knowledge of ideas) completely loses sight of his will and its objects, and pays no further regard to the interests of his own person, but becomes a pure intelligence free of any admixture of will." (Schopenhauer, 1831; content in bracket added).

The transcendence of psychologically conditioned habitual (aprioristic/automatic) self-centred perceptual schemata is crucial with respect to creative cognition. Psychedelics are unique in this regard because they are highly effective neurochemical tools which profoundly change perception and reveal states of consciousness that lie far beyond ordinary waking "states". Moreover, these pharmacological agents possess the ability to catalyse the most "extraordinary" psychological phenomena known to science, e.g., transcendence of experiential spacetime, synesthæsia/somasthæsia/ideasthæsia, spectacular visual hallucinations/illusions, ³⁰ ineffable imaginations/phantasmagoria, indescribable feelings of awe, ³¹ intense emotional catharsis, out-of-body experiences, expansion of consciousness, phenomenological access to higher dimensions of being, experiential

³⁰ There is a crucial distinction between hallucinations and illusions which has been concisely pointed out by Sir Francis Galton": "A convenient distinction is made between hallucinations and illusions. Hallucinations are defined as appearances wholly due to fancy; illusions, as fanciful perceptions of objects actually seen." (Galton, 1883, p. 132). In sum, illusions have an ontologically existent object as a reference while illusions appear seemingly *ex nihilo*.

Hallucinations and illusion can occur in all modalities (e.g., visual, auditory, tactile, olfactory, etc.) and there appear to be interindividual differences. Future studies should address these idiosyncrasies which might help to identify correlated receptor-polymorphism and associated genetic loci of such perceptual predispositions. From an empiricist stance, sensory input forms the foundation of creative ideation (and cognition in general). The classical "Aristotelian Peripatetic Axiom" is of pertinence in this respect. Hence, a deeper understanding of illusions and hallucinations seems to be important for a more detailed understanding of the processes which undergird creativity. This epistemological argument highlights the importance of sensory input in the context of reasoning and knowledge: *Nihil est in intellectu quod non sit prius in sensu* (transl.: nothing is in the intellect that was not first in the senses).

³¹ Interestingly, it has been experimentally demonstrated that the felling of awe expands perception of time, enhances well-being, and makes "life feel more satisfying than it would otherwise" (Rudd, Vohs, & Aaker, 2012).

access to unconscious/archetypal contents, profound noetic insights, enhanced biophilia, amplified empathy and compassion, etc. pp.

In the context at hand, one of the most important qualities of these chemically welldefined compounds is their ability to catalyse novel cognitions and perceptions and their capacity to induce the process of ego-dissolution(Carhart-Harris, Erritzoe, Haijen, Kaelen, & Watts, 2018; J. V. Davis & Canty, 2013; Millière, 2017; Nour, Evans, Nutt, & Carhart-Harris, 2016), viz., the experience of nondual consciousness. 32 In a "state" of nondual consciousness habitual categorical dichotomies which ordinarily structure *all* experience are dissolved. For instance, the duality between subject and object, psyche and physis, epistemology and otology, knower and known, inside and outside, percipient and perceived, self and other, ingroup and outgroup, good and bad, et cetera. With reference to recent neuroimaging research it has been eloquently stated that nondual consciousness is "a background awareness that precedes conceptualization and intention and that can contextualize various perceptual, affective, or cognitive contents without fragmenting the field of experience into habitual dualities" (Josipovic, 2014). The discussion of nondual consciousness has an extensive history in various ancient contemplative knowledge traditions (for example in India where it is associated with sophisticated yogic techniques which place great emphasis on self-control). Nonduality has only very recently become a topic in the neurosciences, and we are unaware of any controlled research which explicitly connects nondual consciousness with creativity. We submit that interdisciplinary research along this line of thought would be both light-bearing and fruitful (in the Baconian sense of *lucifera* & *fructifera*).

³² The concept of nonduality constitutes the *nucleus* of the Indian philosophical system of "Advaita Vedānta" (Sanskrit: अद्वेत वेदान्त, literally, "not-two") which is one of the most ancient spiritual paths to self-realization (cf. Maslow's concept of self-actualisation). Overcoming/dissolving the illusion of the ego or I-ness principle (Ahaṃkāra) plays a crucial rôle in this meditative spiritual tradition which fosters deep insights into the transcendental nature of the Self.

The experience of ego-dissolution is fundamentally ineffable. Hence, the profundity of ego-dissolution will not be fully comprehended by those readers who have not experiences it first-hand. It relates to the problem of noncommunicable quale: One cannot appreciate the taste of sugar by listening to elaborate descriptions or by studying its molecular structure. One must taste it (cf. Nagel, 1974). In philosophy of mind this is known as the "knowledge argument" (Jackson, 1986).

Among numerous experts in the field of psychedelic research, there exists general consensus that psychedelics (i.e., consciousness expanding substances) can augment cognitive processes and enable states of "unconstrained cognition" (Carhart-Harris et al., 2012; cf. Sheldrake, McKenna, Abraham, & Abraham, 2001). Therefore, it is argued that psychedelics are important neurochemical research tools that can significantly broaden our understanding of creativity. However, this idea is not new. An early pilot study from the 1960s (which is by modern research standards methodologically confounded/unsound) indicated that psychedelics can significantly enhance creativity and rational scientific problem solving (Harman, McKim, Mogar, Fadiman, & Stolaroff, 1966). After an initial phase of systematic scientific research, the legal prohibition of psychedelics in the late 1960s put an abrupt halt to the short-lived but very promising research agenda, primarily due to the questionable "War on Drugs" which was initiated by the Nixon administration for evidently perfidious/ominous motives.

After an elongated legally enforced research-hiatus, science is currently witnessing a "psychedelic renaissance", a new rising wave of psychedelic research (Bolstridge, 2013; Cameron & Olson, 2018; Roseman, Demetriou, Wall, Nutt, & Carhart-Harris, 2018; Sessa, 2012) using modern psychological methodologies and advanced neuroimaging technologies (Carhart-Harris et al., 2012; Muthukumaraswamy et al., 2013; Roseman et al., 2016; Tagliazucchi et al., 2016). One can only speculate how far science would have progressed in this domain without the inhibiting effects of the

³³ Psychedelic were not only of interest to academic scientists. After initial studies in German concentration camps (e.g., Auschwitz) the CIA developed its own undercover programs (e.g., Project MK-Ultra) in order to test psychedelics compounds on vulnerable and naïve (non-consenting) populations, e.g., prisoners, homeless people, mental patients. We will briefly discuss these illegal research programs in a subsequent section.

³⁴ John Daniel Ehrlichman who was at this time Assistant to the President (for Domestic Affairs) stated in an interview in 1994 (published in "Harpers" in 2016): "The Nixon campaign in 1968, and the Nixon White House after that, had two enemies: the antiwar left and black people. You understand what I'm saying? We knew we couldn't make it illegal to be either against the war or black, but by getting the public to associate the hippies with marijuana and blacks with heroin, and then criminalizing both heavily, we could disrupt those communities. We could arrest their leaders, raid their homes, break up their meetings, and vilify them night after night on the evening news. Did we know we were lying about the drugs? Of course we did."

judicially imposed interregnum. Hitherto systematic scientific research which focuses specifically on the rôle of psychedelics on creativity is virtually absent ³⁵ and the compound 5-MeO-DMT has to date not been investigated in a rigorous manner. ³⁶ In connection to our previous argument on nonduality and creativity, we predict that future research along these lines will be very probative. Research on psychedelic agents is especially pertinent for our understanding of the neuroscience of creativity because many psychedelics have endogenous counterparts, in other terms, they are structurally similar or identical to neurotransmitters which constitute human physiology/neurochemistry.

Many neuroscientists are unaware that the discovery of LSD-25 led to the idea that neurochemicals might play a central rôle in cognitive processes (Cozzi, 2013). Today the fact that *neurotransmitters* influence cognition is taken for granted. However, before 1952 serotonin was thought to be a vasoconstrictor (hence the composite lexeme "sero-tonin"). In 1952-53 serotonin (5-hydroxtryptamin, 5-HT) was discovered in the brain by Betty Twarog, Irvine Page, and Sir Henry Gaddum (for a historical review see Twarog, 1988). In 1953, Sir Gaddum took LSD in a self-experiment. Shortly afterward he and his colleague published a paper on the antagonistic effects of LSD on 5-HT (Gaddum & Hameed, 1954). Gaddum conjectured a common site of action between both compounds and theorized that the neurocognitive effects of LSD result from its action on 5-HT (Amin, Crawford, & Gaddum, 1954). Because he had experienced the effects of LSD first-hand (self-experiments were quite common), he knew that it produces significant mental changes. Knowing that LSD antagonizes 5-HT, he made the novel theoretical connection for the first time in the documented

³⁵ This is changing while we are writing this article. For instance, sub-threshold microdosing of psychedelics has become a topic of renewed interest in the context of creativity (Anderson et al., 2019). While we were in the process of revising this paper (after initial submission) a first pilot study on 5-MeO-DMT was conducted by researchers in the Netherlands (Uthaug et al., 2019). This study experimentally demonstrated positive effects of 5-MeO-DMT on convergent creative thinking, *inter alia*.

³⁶ In the United Kingdom, the recently ratified "Psychoactive substances act" which reached Royal Assent in January 2016 complicates the matter by creating societal, political, and fiscal impediments to scientific research into the neurobiology of psychedelics. For more information, see:

history of science. That is, Gaddum was the first to postulate that 5-HT might play a rôle in cognition (Cozzi, 2013). This historical example clearly demonstrates that the systematic study of psychedelic compounds is indispensable if science wants to deepen its understanding of various psychological processes (e.g., creativity) and their neuronal correlates. We agree with other creativity researchers that "evidence gleaned from the structure and function of the brain [can] enhance our ability to foster creativity" (Vartanian, 2013, p. 257; content in brackets added). We propound that the systematic scientific exploration of the yet uninvestigated endogenous compound 5-MeO-DMT may provide important novel insight into the neural correlates of its currently only vaguely and anecdotally characterised psychological and phenomenological effects. This type of innovative research has the potential to foster our basic understanding of the evolutionary functions of various tryptamines in human consciousness. Further, this research agenda may lead to novel psychopharmacological interventions and aid in the elucidation of hitherto unidentified neurotransmitter systems (cf. the pathbreaking discovery of the endogenous cannabinoid system which heralded a new and rapidly growing field in medicine). In addition, 5-MeO-DMTs molecular structure could be systematically varied (cf. A. A. Shulgin & Shulgin, 1997) in order to rigorously explore structure activity relationships. Such research might in theory lead to the discovery of "superagonists" (Langmead & Christopoulos, 2013). The exploration of synergistic effects with other naturally occurring psychoactive substances (e.g., Ibogaine (Barsuglia et al., 2018; Glick & Maisonneuve, 1998; Winkelman, 2015)) is another hitherto uncharted and potentially very fruitful research area. In addition, allosteric modulators are of great scientific interest in this respect (cf. Schwartz & Holst, 2007). That is, the agonistic actions of 5-MeO-DMT can in principle be enhanced (>100%) efficacy) by various allosteric modulators (e.g., via allosteric modulators of G proteincoupled receptors; cf. May, Leach, Sexton, & Christopoulos, 2007). Yet another related important research question concerns the "entourage effect" (cf. Sanchez-Ramos, 2015). The appurtenant open research question is: What are the

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³⁷ Supra-physiological describes a level of efficacy which is unseen in organisms which evolved according to the principles of natural evolution.

neuropsychopharmacological and phenomenological differences between the pure compound (5-MeO-DMT synthesised in the laboratory) and the compound as found in nature, i.e., within a whole complex biologism organism (toad venom, tree bark, seed pods, etc.)?

In order to provide corroborating empirical evidence for our hypothesis that psychedelics are important research tools in regard to creativity research, we will now discuss two contemporary experimental studies which are pertinent to the psychology and neuroscience of creativity. Based on the relevant literature (e.g., Nour et al., 2016), we specifically argue that an understanding of the psychological and neurophysiological processes which undergird ego-dissolution (i.e., nonduality) is pivotal for advancing our scientific understanding of creativity. After introducing the corroborating studies, we will provide more detailed information on the underappreciated and virtually unresearched endogenously occurring compound 5-MeO-DMT. Based on this empirical background we will then formulate several empirically falsifiable hypotheses (the main hypothesis is presented in from of a concise and logically valid syllogistic argument).

Psilocybin increases the personality-trait "Openness to Experience"

Psilocybin (O-phosphoryl-4-hydroxy-N,N-dimethyltryptamine) is an indole alkaloid (a structural relative of 5-MeO-DMT) ³⁸ first synthesized and named by the Swiss chemist Albert Hofmann ³⁹ (Hofmann et al., 1959; 1958). After the elucidation of its chemical properties the active principle, psilocin (4-hydroxy-N,N-dimethyltryptamine), was identified (Hofmann & Troxler, 1959). Various experimental chemical modifications were made to both structures (Troxler, Seemann, & Hofmann, 1959). The psilocybin molecule is present in more than 200

³⁸ Even though the chemical structure of both compounds is very similar their psychological effects are incommensurable.

³⁹ Albert Hofmann (1906–2008) also discovered LSD in 1938 but he was unaware of its psychoactivity until 1943 when he conducted the first self-experiment. Hofmann, who later served as a member of the Nobel Prize Committee, stated on his 100th birthday: "It gave me an inner joy, an open mindedness, a gratefulness, open eyes and an internal sensitivity for the miracles of creation. [...] I think that in human evolution it has never been as necessary to have this substance LSD. It is just a tool to turn us into what we are supposed to be."

fungal species which span numerous taxa, some of which are endemic to the USA and Europe, e.g., *Psilocybe semilanceata* (colloquially known as "Liberty Cap"). In crosscultural shamanic contexts, psilocybin has been reportedly utilized for spiritual and healing purposes for millennia (Akers, Ruiz, Piper, & Ruck, 2011; Hofmann, Heim, Brack, & Kobel, 1958). Its molecular structure closely resembles 5-hydroxtryptamine (5-HT, serotonin). In humans, psilocybin functions as a prodrug and is rapidly dephosphorylated to psilocin which acts as a non-selective partial 5-HT receptor agonist. It shows particularly high binding affinity for the 5-HT_{1A}, 5-HT_{2A}, and 5-HT_{2C} receptor subtypes (Kraehenmann et al., 2015; Nichols, 2004).

A landmark study conducted at Johns Hopkins University by MacLean, Johnson, & Griffiths (2011) experimentally demonstrated that a single high-dose of psilocybin can induce long-lasting personality changes in the domain "Openness to Experience", as measured by the widely used NEO-PI (Personality Inventory). Openness to Experience (OTE) is one of the core dimensions of the extensively employed quinquepartite (big five) model of personality (i.e., factor V). OTE is an amalgamation of several interconnected personality traits which include: 1) aesthetic appreciation and sensitivity, 2) fantasy and imagination, 3) awareness of feelings in self and others, and 4) intellectual engagement, *inter alia*. Most relevant for the context at hand is the fact that OTE has a strong and reliable correlation with creativity (Ivcevic & Brackett, 2015; S. B. Kaufman et al., 2016; Silvia, Nusbaum, Berg, Martin, & O'Connor, 2009). Individuals with high scores on the OTE dimension are "permeable to new ideas and experiences" and "motivated to enlarge their experience into novel territory" (DeYoung, Peterson, & Higgins, 2005). Furthermore, OTE is

⁴⁰ Interestingly in the present context, OTE has been correlated with the ability to recall dreams (Watson, 2003).

 $^{^{41}}$ For instance, the Pearson correlation coefficient for "global creativity" and OTE is r=.655 and for "creative achievement" r=.481, By contrast, "Math–science creativity" is not statistically significantly correlated with OTE (r=.059; ns; for further correlation between various facets of creativity and the Big Five factors see Silvia, Nusbaum, Berg, Martin, & O'Connor, 2009). The salient correlation between OTE and creativity has been reported in many studies (a pertinent meta-analysis has been conducted by Feist, 1998; a recent study reporting a strong relationship between OTE and creativity has been conducted by Puryear, Kettler, & Rinn, 2017). Furthermore, a meta-analytical structural equation model of 25 independent studies showed that OTE is the strongest FFM predictor of creative self-beliefs (r=.467; Karwowski & Lebuda, 2016).

associated with personality trait "absorption" (Glisky, Tataryn, Tobias, Kihlstrom, & McConkey, 1991) and we argue that absorption is a state of primordial awareness akin to nondual consciousness. That is, absorption is a type of awareness in which the dichotomy between the sensor and sensed, the percipient and perceived, the seer and seen, transiently dissolves into a state of union which is devoid of any intermediary imagistic, symbolic, or linguistic cognitive preconceptions which usually intercede between the experience and the experienced (i.e., the thing "in itself" and the experienced percept). It is therefore an undistorted state of pure and total awareness without any abstraction and without a Kantian *a priori* space-time interval⁴² which generally mediates between subject and object and therefore prestructures the field of experience in a dualistic format. "Boundaries of the mind" is another conceptually related trait associated with OTE and creativity. It relates to the boundaries between fantasy and reality, sleeping and waking, self and other, and furthermore, the "permeability of ego boundaries" (Hartmann, Rosen, & Rand, 1998; McCrae, 1994).

In the described study by MacLean et al. (op cit.) the psilocybin-induced increase in OTE was mediated by the intensity of the mystical experience. Importantly, egodissolution is a central feature of mystical experiences (see also Griffiths, Richards, McCann, & Jesse, 2006) and we argue that ego-dissolution can culminate in the peak experience of nonduality. Based on this evidence, we hypothesize that the experience of ego-dissolution (viz., nonduality) predicts *post eventum* increases in creativity and we postulate a causal relationship between factors. We term this the "less ego => more creativity hypothesis". Furthermore, we argue that OTE is an important factor relating to the *status quo* bias discussed before. OTE is associated with explorative behaviour, novelty seeking, ⁴³ and cognitive flexibility. From a neuroscientific

⁴² The interposition of the "space-time interval" which divides the percipient from the percept is an idea adopted from Jiddu Krishnamurti mentioned in his book "Freedom from the Known" (Krishnamurti, 1969) while the reference to Kantian apriorism is an annexure. The importance of space-time in duality is especially intriguing given the fact that the effects of psychedelics are associated with phenomenological aspatiality and atemporality.

⁴³ Novelty or sensation seeking is a robust predictor of risk taking and drug use. This might lead to a feedback loop in which those who are open to new experiences are more likely to be exposed to new experiences (such as psilocybin or 5-MeO-DMT) which in turn reinforce their open-mindedness.

perspective the status quo bias may be based on Hebbian principles of long-term potentiation (LTP). That is, repeatedly utilized neural circuits are diachronically strengthened (Hebb, 1949) and become dominant and rigid. 44 The social environment may thus entrain the "Hebbian status quo", i.e., the social milieu consolidates specific neuronal circuitry (via social conditioning, education, enculturation, etc.). Interestingly, complex system theory suggests a bipolar (orthogonal) continuum ranging from rigidity on one end to chaos on the other. Integration lies interjacent between the extremes. Given that the cognitive system can be regarded as a complex system, this generic account might lend itself to conceptualise a "cognitive continuum of information processing states" (Faust & Kenett, 2014) ranging from rigid cognition to chaotic cognition (i.e., closed-mindedness to open-mindedness). In a rigid neural network, nodes are only sparsely interconnected (i.e., cognitive hyper-rigidity). In a chaotic neural network topology, on the other hand, virtually all nodes are interconnected (i.e., cognitive over-flexibility/chaos). According to this schematic, cognitive integration (viz., the linkage of differentiated parts (Siegel, 2010)) is characterised by an intermediate neuronal network connectivity pattern which balances and synchronizes the polar extremes (i.e., adaptive/dynamic cognitive coherence). We argue that the balance between neuronal differentiation and integration is of pertinence with respect to creativity research and the subsequent section provides further details on this proposal, i.e., specifically with respect to the effects of LSD-25 on brain-wide connectivity. In support of this quasi-Lockean "associationist/connectivist" idea, recent neuroimaging work has correlated OTE with increased functional connectivity within mesocortical networks (Passamonti et al., 2014). It would therefore be of great interest to explicitly test the hypothesis that increases in OTE (experimentally induced by psychedelics such as, e.g., psilocybin, LSD, or 5-MeO-DMT) are mediated by increases in functional connectivity in specific

⁴⁴ Using human cerebral organoids and *in silico* analysis it has been demonstrated that 5-MeO-DMT has modulatory effects on proteins associated with the formation of dendritic spines and neurite outgrowth (Dakic et al., 2017) which may influence neuroplasticity and hence ideoplasticity. 5-MeO-DMT has been found to match the σ_1 receptor. Because $\sigma_1 R$ agonism regulates dendritic spine morphology and neurite outgrowth it affects neuroplasticity which form the neural substrate for unconstrained cognition.

networks, i.e., specifically those associated with introspection, self-control, and self-referential processing (cf. Parkinson, Kornelsen, & Smith, 2019; Smigielski, Scheidegger, Kometer, & Vollenweider, 2019).

LSD expands global functional connectivity density in the brain

LSD-25 is one of the most potent psychedelic compounds known to science, producing profound alterations of consciousness after submilligram oral doses ≥20 µg (Nichols, 2018a). A recent multimodal fMRI study by Tagliazucchi et al. (2016) conducted at Imperial College London administered LSD intravenously to healthy volunteers. The researchers found that LSD-induced ego-dissolution was statistically significantly correlated with an increase in global functional connectivity density (FCD) between various brain networks, indicating that the psychedelic enabled novel configurations of brain states. As discussed in the previous study by MacLean et al. (2011), mystical⁴⁵ experience (i.c., ego-dissolution) is correlated with an increase in OTE (which in turn is strongly correlated with creativity). One of the key findings of the LSD/fMRI-study was that high-level cortical regions and the thalamus displayed increased connectivity under the acute influence of the psychedelic. *In concreto*, increased global activity was observed bilaterally in the high-level association cortices and the thalamus (often regarded as the brains "central information hub" which relays information between various subcortical areas and the cerebral cortices). The global activity increase in the higher-level areas partially overlapped with the default-mode, salience, and frontoparietal attention networks. The FCD changes in the defaultmode and salience network were predicted a priori due their association with selfconsciousness. As predicted, a significant correlation between subjectively reported ego-dissolution and an increase in global connectivity between networks was detected. The results of this milestone study demonstrate for the first time that LSD increases global inter-module connectivity (while at the same time decreasing the integrity of individual modules). Specifically, LSD enhanced the connectivity between normally separated brain networks (as quantified by the widely used Φ

⁴⁵ Bertrand Russel discussed the links between mysticism, creative intuition/insight, and logic in great detail in his excellent essay "Mysticism and logic" (Russell, 1981).

connectivity/associativity index). 46 The observed changes in activity significantly correlated with the anatomical distribution of 5-HT_{2A} receptors. We argue that these findings are highly relevant for the identification of the neural correlates of creativity because it is reasonable to postulate that an enhanced communication répertoire between previously disconnected neuronal network modules is crucial for the generation of novel ideas (cf. D. W. Moore et al., 2009). Moreover, associative processes are generally assumed to play a key rôle in creativity (C. S. Lee, Huggins, & Therriault, 2014) and a recent fMRI study provided corroborating evidence for the assumption that greater functional connectivity is related to the capacity to generate novel ideas (Beaty et al., 2018). The researchers argued that "the ability to simultaneously engage the default, executive, and salience brain systems may provide a neurophysiological marker of creative thinking ability". Tagliazucchi et al. concluded that LSD reorganizes the rich-club architecture of brain networks and that this restructuring is accompanied by a shift of the boundaries between self and environment. That is, the ego-based dichotomy (i.e., dualism) between self and other, subject and object, internal and external, dissolves as a function of specific connectivity changes in the modular networks of the brain. 47 In conclusio, Tagliazucchi et al. (2016) demonstrated that LSD induced ego-dissolution is

⁴⁶ The rich-club coefficient Φ is a networks metric which quantifies the degree to which well-connected nodes (beyond a certain richness metric) also connect to each other. Hence, the rich-club coefficient can be regarded as a notation which quantifies associativity. Conceptually related research concluded that "associative abilities represent valid elementary cognitive abilities underlying creativity" (Benedek, Könen, & Neubauer, 2012). We submit that this line of thought connects to the quasi-Newtonian principle of idea formation described by John Locke in his seminal book "An Essay Concerning Human Understanding" (1689), specifically the chapter entitled "On the Associations of Ideas".

⁴⁷ Furthermore, the authors argue convincingly that the notion that LSD (and other psychedelics) "expand" consciousness is quantitatively supported by their data. Specifically, they argue that the neurophysiological changes associated with psychedelic states contrast with states of diminished consciousness (e.g., deep sleep or general anesthesia). The obtained results are congruent with the idea that psychedelic and unconscious states can be conceptualized as polar opposites on a continuous spectrum of conscious states. Furthermore, the authors suggest that the level of consciousness is quantitatively determined by the level of neuronal entropy (in accord with the entropic brain hypothesis formulated by Carhart-Harris et al., 2014). It has been suggested that Aldous Huxley "reduction valve" hypothesis appears to be relevant in this context.

accompanied by significant changes in neuronal rich-club architecture and that egodissolution is accompanied by the downregulation of the default-mode network (DMN). 48 Pertaining to creativity research this finding is particularly intriguing because the DMN may be associated with habitual thought and behaviour patterns (Beucke et al., 2014; Koçak, Kale, & Çiçek, 2012). We suggest that downregulation of the DMN by psychedelics (which is accompanied by the phenomenology of egodissolution) is an important component for understanding the functional connectome which undergirds creativity. Based on these findings, we propose a novel neuropsychopharmacological mechanism for the enhancement of creativity which has, to our best knowledge, never been proposed before. Our hypothesis highlights the importance of ego-dissolution for the enhancement of creativity. That is, a reduction of the influence of self-referential ego structures (ex hypothesi mediated via DMN disintegration) on perception and cognition enables perspectival multiplicity and cognitive flexibility which is crucial for creative ideation. Based on the conjecture that ego-dissolution provides a "cognitive reset" which enables human beings to perceive and conceptualize reality from a more unconstrained (and ultimately nondualistic) perspective, we argue that 5-MeO-DMT is an especially intriguing molecule in this regard because its ego-dissolving effects are much more pronounced than those of psilocybin or LSD (or in fact any other known psychedelic). The "reset theory" is a first primitive attempt to formulate a causal mechanism which could explain why ego dissolution is associated with the hypothesized increase in creativity. Ego-dissolution could enable humans to "see things with new eyes" — i.e., via a reduction of the structuring and organizing influence of perceptual schemata⁴⁹ (i.e., preconception vs.

⁴⁸ Recent evidence focusing on changes in the coupling of electrophysiological brain oscillations by means of transfer entropy suggests that serotonergic psychedelics temporarily change information transfer within neural hierarchies by decreasing frontal of top-down control, thereby releasing posterior bottom-up information transfer from inhibition (Francesc Alonso, Romero, Angel Mañanas, & Riba, 2015).

⁴⁹ A potential explanatory mechanism might be found in the entropic brain hypothesis (Carhart-Harris et al., 2014; Lebedev et al., 2016). Pertinent experimental evidence comes from a recent magnetoencephalographic (MEG) study which showed that classical psychedelics increase signal diversity (Schartner, Carhart-Harris, Barrett, Seth, & Muthukumaraswamy, 2017), a quantitative finding which appears highly relevant in the context of contemporary creativity research.

apperception). Empirical data indicates that ego-dissolution is a unique property of psychedelic substances (Nour et al., 2016). In a web-based study utilizing the "Ego-Dissolution Inventory" (EDI) several psychoactive substances were compared, and the results showed that only psychedelics were significantly correlated with the experience of ego dissolution. *Per contra*, other psychoactive substance like alcohol or cocaine enhance an egoic style of cognition (ego inflation). 50 In the same study, participants also responded to a subset of items from the "Mystical Experiences Questionnaire" (MEQ) (Barrett, Johnson, & Griffiths, 2015). The results indicated a positive correlation between psychedelic dose and the strength of the mystical experience. As discussed, a defining feature of the mystical experience is an egodissolving "unitive" (nondual) experience. In other terms, the noetic insight that human beings are ultimately all connected via consciousness (which is singular and not plural, i.e., the apparent multiplicity is a superficial phenomenon and consciousness is in actuality not dividable). This topic has already been addressed by William James more than a century ago (James, 1985/1902). Unity experience is closely related to the Freudian concept of "oceanic feeling" (oceanic boundlessness) a sensation of being one with universe. In fact, Romain Rolland formulated the phrase in a letter to Freud. Rolland argued that it is this nondual experience which lies at the core of all religious feelings (theistic or nontheistic). Freud utilized this idea in his later writings and hypothesized that this nondual state of consciousness is a psychological residue from the infantile stage in which the egoic schism between self and other (object and subject) has not yet occurred (Freud, 1930). That is, according to Freud, nondual experiences are a relic of the developmental stage in which the infants formation of the self-concept has not yet taken place and has consequently not yet dichotomised experience (perception) into universal "self versus non-self" dichotomies.

 $^{^{50}}$ Interestingly, ego-dissolution was also statistically significantly correlated with enhanced well-being/life-satisfaction ($\rho=0.392$). For alcohol ($\rho=-0.112$) and cocaine ($\rho=-0.083$) this positive effect was absent. However, due to the quasi-experimental nature of this study no solid inferential conclusions are possible. Systematic experimental research is needed to elucidate this important topic which has obvious societal relevance.

5-MeO-DMT: An endogenous neurochemical catalyst of creativity

According to documented history, the intranasal administration of 5-MeO-DMT in form of a snuff preparation called "Cohoba" ⁵¹ by the Taíno people of Hispaniola was first observed around 1496 by Friar Ramón Pané who reported his observation to Christopher Columbus who in 1492 made initial contact with this culture (Nunn & Qian, 2010; Shultes, 1976; Torres & Repke, 2006). As regards contemporary science, 5-MeO-DMT is a relatively unknown member of a group of naturally-occurring psychoactive indolealkylamines (Glennon & Rosecrans, 1982; A. T. Shulgin & Carter, 1980). It was first synthesized by Japanese chemists in 1936 who published their results in German (Hoshino & Shimodaira, 1936). It was later extracted and isolated from *Dictyoloma incanescens* bark (Pachter, Zacharias, & Ribeirol, 1959), a flowering plants that belongs to the family *Rutaceae*. The tryptamine is an analogue of tryptophan and endogenous to human physiology. Research indicates that 5-MeO-

⁵¹ The snuff was administered in a ceremonial setting in which the ground seeds of the cojóbana tree (*Anadenanthera peregrina*) were inhaled via a Y-shaped pipe called Cohoba (Wright & Ortiz, 1941).

DMT may be endogenously synthesized in human pineal and retina. 52 Moreover, it has been detected in blood, urine, and cerebrospinal fluid (H.-W. Shen, Jiang, Winter, & Yu, 2010). Its extremely powerful acute effects are pharmacokinetically short-lived. i.e., ≈ 20 -40 min (Ott, 2001). As many other tryptamine psychedelics, it acts as a nonselective 5-HT agonist and causes a broad spectrum of highly interesting psychological effects. It displays a relatively high binding affinity for the 5-HT_{1A}, 5-HT_{2A}, and 5-HT_{2C} subtypes 53 (Krebs-Thomson, Ruiz, Masten, Buell, & Geyer, 2006), but other mechanism of actions appear to be involved in its psychoactivity (e.g., inhibition of enzymatic monoamine oxidase activity; but see Nagai, Nonaka, & Satoh

⁵² From an evolutionary vantage point it is intriguing to note that the pineal functions as a photoreceptive neuroendocrine organ in numerous vertebrates (Lamb, 2013). Functional and morphological congruencies between photoreceptor cells on the pineal and the retina are indicative of a close evolutionary relationship (Mano & Fukada, 2006). Phylogenetically, the "pineal eye" was a paired organ with a similar structure the lateral eyes. This ontogenetic development and the associated genetic pathway that regulate its development and neurogenesis strongly suggests that "the pineal eye and the lateral eyes share a common genetic and embryologic basis" (Benoit, Abdala, Manger, & Rubidge, 2016) That is, a shared genetic and molecular mechanisms undergirds their similarities (Tosini, 1997). However, the pineal-specific physiological functions remain largely elusive. Note that our knowledge of the photoreceptor system is in general very incomplete, for instance, only recently a new opsin (labelled melanopsin) has been identified (Provencio et al., 2000). We suggest that 5-MeO-DMT might further our understanding of the molecular and neurobiological basis of visual perception (and imagination) — especially with relation to the shared properties of the pineal and the retina. It is furthermore interesting to note that the "visionary" properties of 5-MeO-DMT might not be "merely" metaphorical, but that metaphorical linguistic descriptions convey a biological meaning which is hitherto only poorly understood (e.g., the expression "inner vision" or "introspection" might describe an actual visual process which "focuses" on a domain which is hitherto not sufficiently recognised). According to simulation theories of cognition (Hesslow, 2012) it may be hypothesized that the visual system is intrinsically involved in "DMT-vision" and specifically the function of the pineal is of interest against this adumbrated empirical and theoretical background (cf. Benoit et al., 2016). To put it more poetically, 5-MeO-DMT might shed "new inner light" on molecular and psychological processes associated with vision, visionary power, and imagination. ⁵³ Interestingly, the 5-HT_{1A} receptor appears to be more important for the stimulus effects of 5-MeO-DMT than the 5-HT_{2A} receptor (H.-W. Shen et al., 2010). This has been experimentally demonstrated by various tests of antagonism of stimulus control with the 5-HT_{IA} antagonists pindolol (also a nonselective β-blocker) and the "silent agonist" WAY-100635 (J. . Winter, Filipink, Timineri, Helsley, & Rabin, 2000).

Hisashi Kamimura, 2007).⁵⁴ The 5-HT system is associated with, cognition, emotion, and memory, inter alia. For example, 5-HT receptors are located in the cerebral cortex (cognition), in the amygdala (emotions), and in the raphe nucleus (its projection regulate circadian rhythms, alertness, inhibition of pain, inter alia). The raphe nucleus is located in the phylogenetically most primitive part of the brain, the brainstem, and its serotonergic axons project widely throughout the cortex. The raphe nucleus produces the majority of brain serotonin and it contains $\approx 85\%$ of all the of the serotonin neurons in the brain (Hornung, 2003). Ergo, when it is stimulated by 5-MeO-DMT it causes extensive serotonergic activation throughout many interconnected neural networks. Moreover, 5-HT receptors are present in the hypothalamus which connects the central nervous system to the endocrine system. It can be cogently argued that 5-MeO-DMT causes hypothalamic release of significant amounts of the neuropeptide oxytocin via the pituitary gland. This hypothetical increase in oxytocinergic activity might explain why the qualitative linguistic descriptions of 5-MeO-DMTs phenomenology frequently include words like "love", "unity", and "connectedness" (these semantic descriptors are obviously very imprecise, vague, and ambiguous — a general problem of human language). Accumulating evidence indicates that 5-MeO-DMT is an endogenous ligand of the Trace amine-associated receptors (TAARs), a class of G protein-coupled receptors that were only recently discovered in 2001 (Carbonaro & Gatch, 2016). It has been hypothesized that TAARs are involved in sensory perception (Wallach, 2009). Moreover, TAARs have been associated with pathological neuroadaptations associated with prolonged exposure to addictive drugs (e.g., alcohol, heroin, cocaine, etc.). Consequently, this molecular target might partially explain 5-MeO-DMTs promising neurorestorative and neuroprotective effects (Dakic, 2017). Because 5-MeO-DMT is able to target these receptors it might be able to regulate the

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 $^{^{54}}$ It is important to note that 5-HT agonism does not explain the effects of all psychedelics. For instance, the naturally occurring dissociative hallucinogen salvinorin A (the active principle in the mint plant $Salvia\ divinorum$ which has been utilised by indigenous Mazatec shamans) is not an alkaloid but a terpenoid which agonizes the κ-opioid receptor, but is inactive at the 5-HT receptor (Roth et al., 2002). It is therefore called an $atypical\ psychedelic$. Hofmann and Wasson were the first Westerners to collect a specimen of this extraordinary plant in Oaxaca/Mexico in 1962 (Casselman, Nock, Wohlmuth, Weatherby, & Heinrich, 2014).

pathological neurological adaptions, for example those caused by various substance (and possibly behavioural) addictions (cf. the neuropsychological "reset-hypothesis" (e.g., Carhart-Harris et al., 2017)). Hence 5-MeO-DMT might counteract rigid cognitive and behavioural patterns and facilitate cognitive flexibility (cf. Gruner & Pittenger, 2017). In support of this view, a recent cutting-edge in vivo and in silico study using human cerebral organoids (Dakic et al., 2017) demonstrated that 5-MeO-DMT has modulatory effects on neuroplastic processes, long-term potentiation, cytoskeletal reorganization, and microtubule dynamics (cf. Hameroff & Penrose, 2014). Specifically, it was found that 5-MeO-matches the σ_1 receptor which regulates cytoskeletal dendritic spine morphology and neurite outgrowth. Therefore, σ_1 receptor agonism may potentially mediate neuroplastic processes which are crucial for creativity, cognitive flexibility, and sustained cognitive/behavioural changes (Sun et al., 2016). In addition, agonism of the σ_1 receptor has been shown to have antiinflammatory effects (Szabo, 2015) which may positively influence various creativity related cognitive processes and also genetic/cellular health, e.g., a hypothetical link between creativity, depression, inflammation, and telomeres (via telomerase activity) (see Wolkowitz et al., 2011; Zhang et al., 2016). A related study recently demonstrated that 5-MeO-DMT increases *in vivo* adult hippocampal neurogenesis in mice (Lima da Cruz, Moulin, Petiz, & Leão, 2018). The researchers administered a single dose of 5-MeO-DMT (via intracerebroventricular injection) and measured subsequent quantitative increases in cell proliferation of granule cells (GC) within the dentate gyrus (DG) of the subgranular zone of the hippocampus. Neurogenesis was accompanied by a complexification of GC dendritic morphology, i.e., more complex dendritic tress relative to controls. These findings indicate that 5-MeO-DMT can can increase neuronal survival, stimulate cell proliferation, and accelerate maturation of newborn neurons in the hippocampal DG region. ⁵⁵ Comparable results have previously been obtained with psilocybin (Catlow, Song, Paredes, Kirstein, & Sanchez-Ramos, 2013) which is suggestive of a common serotonergic mechanism of action which is causative for the observed increases in adult hippocampal neurogenesis.

5-MeO-DMT is widespread in the plant kingdom and has been used in shamanic rituals for millennia (Torres et al., 1991). While its structural relative psilocybin is exclusively present in fungi, 5-MeO-DMT is present in various plants, for instance Virola theiodora (Agurell et al., 1969), a tree species belonging to the Myristicaceae (nutmeg) family. In additions to its relatively ubiquitous phytochemical distribution, it is present in high concentrations in the venom of *Incilius alvarius* (known as the Sonoran Desert toad), an Amphibia which produces significant amounts of 5-Meo-DMT in its numerous parotoid glands as a defensive chemical mechanism against predators (Erspamer, Vitali, Roseghini, & Cei, 1965; Hutchinson & Savitzky, 2004). The salience of toad symbolism in Mesoamerican art and mythology is remarkable and well documented by anthropologists, for example, toad effigies (with oftentimes accentuated glands) are prominent in the historical remains of the Mayan and Aztec cultures (Davis & Weil, 1992). 56 Moreover, 5-MeO-DMT is sometime used as an adjunct in certain variations of Ayahuasca (a drinkable plant-based concoction, which is utilized by indigenous tribes in the Amazonian rainforest for divinatory and healing purposes). For instance, the leaves of the plant "Chaliponga" (Diplopterys cabrerana) are occasionally added to the concoction to intensify its psychoactive effects (Callaway et al., 2006; Rätsch, 1998). Therefore, synergistic effects between 5-

⁵⁵ The researchers did not measure neurotrophins such as NGF and BDNF. Various growth factor concentrations would be a factor of great interest (cf. Rossi et al., 2006). Further, we suggest that 5-Meo-DMT effects mitochondrial bioenergetics and that this stipulated mechanism is pertinent in the context of 5-MeO-DMT-induced neurogenesis and neurorestoration (cf. Martorana et al., 2018). To facilitate a deeper understanding of the underlying mechanisms future studies should also examine the expression of associated genes such as BCL2 gene (cf. H. G. Kuhn et al., 2005). Research along this line might provide important insights into the anti-addictive mechanisms of 5-MeO-DMT which are currently mainly hypothetical (Barsuglia et al., 2018; cf. McClintick et al., 2013).

⁵⁶ For example, toad-effigies and iconography (with accentuated glands) are found in archaeological excavation from ancient Mayan and Aztec cultures, e.g., artworks of "Tlaltecuhtli" – the earth or earth mother as a monstrous toad (Furst, 1972).

MeO-DMT and DMT should be systematically examined in future studies. We suggest nonlinear interactions between these compounds, i.e., the effects are not additive but multiplicative and this hypothesis should be testable using various neuroimaging techniques. Furthermore, interactions between compounds may reveal novel insights into the differential phenomenological aspects of 5-Meo-DMT and DMT which would not be possible if each compound would be investigated in isolation.

5-MeO-DMT has been utilized for spiritual purposes as a religious sacrament in the rituals of the Christian "Church of the Tree of Life" and other syncretic churches. Indeed a "bio-psycho-socio-spiritual model" has recently been proposed which is based on the persuasive premise that tryptaminergic psychedelics may have "therapeutic effects against various diseases of civilization" (Frecska, Bokor, & Winkelman, 2016). The unique transcendental phenomenology which is elicited by 5-MeO-DMT has influenced the "visionary arts". Artworks inspired by 5-MeO-DMT experiences are oftentimes geometrically highly complex and depict multidimensional fractal-like symmetric mathematical structures ⁵⁷ an observation which is particularly intriguing from a neuroaesthetics point of view (cf. Ramachandran & Hirstein, 1999). Despite

⁵⁷ See, for example, https://www.fractalimagination.com

Interestingly, under the influence of low doses of LSD spiders spin webs of greater regularity (Witt, 1951). Other researchers applied fractal theory to investigate "the correlation between the fractal structure of spider's web and the fractal dynamics of its brain signal" (Namazi, 2017). Mathematics and particularly its subordinate branch geometry have always been regarded as cognitive activities which enable access to transcendental/metaphysical realms (e.g., Pythagoras's theorem, Plato's transcendent forms) and there is a longstanding well-documented interrelation between geometry, mathematics, and mysticism (e.g., sacred geometry, Fibonacci numbers, etc.), as has been pointed out by eminent mathematicians who argue for the pivotal importance of mystical influences in the history of mathematics (e.g., Abraham, 2015, 2017). For instance, it has been argued that there is a close relation between geometry, space-time, and consciousness (Beutel, 2012), a perspective which can be found in many religions and ancient wisdom traditions, e.g. Yantra (Sanskrit: यन्त्र) and Mandala (मण्डल) in ancient Indian schools of thought (also found in Buddhism, inter alia). Moreover, geometry was pivotal for the progress of the exact sciences like cosmology and astronomy. For example, when the Lutheran astronomer Johannes Keppler's published his "mysterium cosmographicum" at Tübingen in 1596, he based his theory on five Pythagorean polyhedra (Platonic solids) which he conjectured form the basis of the structure of the universe and thus realise God's ideas through geometry (Voelkel, 1999).

its longstanding usage in the course of human evolution 58, controlled human trials are currently lacking, and science knows very little about the psychological effects of 5-MeO-DMT. This research area is thus truly uncharted novel scientific territory (and its exploration required openness to experience on the part of the research community; ibid., p. 27). In line with prior related arguments (Osmond, 1957) it has recently been argued that 5-MeO-DMT is of "potential interest for schizophrenia research owing to its hallucinogenic properties" and that research on this compound can "help to understand the neurobiological basis of hallucinations" (Riga, Soria, Tudela, Artigas, & Celada, 2014). 59 However, it is noteworthy that 5-MeO-DMT induced visual hallucinations are much less commonly reported compared to its structural analogue N,N-Dimethyltryptamine (DMT) which is reliably capable of inducing the most spectacular and vivid visual phenomena possibly imaginable (but see Strassman, 2001). We would like to emphasise that the current research Zeitgeist is very biased towards neuromechanistic explanations and we maintain that the most intriguing effects of psychedelics on the human psyche (i.e., consciousness) cannot be reduced to molecular mechanism and neuronal interactions. The Crickean 60 stipulation that "a person's mental activities are entirely due to the behaviour of nerve cells, glial cells, and the atoms, ions, and molecules that make them up and influence them" is not very plausible. In accordance with our view, Cristof Koch (who collaborated with Crick over several years in an unsuccessful attempt to solve the

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⁵⁸The long history of human usage of this naturally occurring compound in various cultures suggests that it does not convey a significant disadvantage in terms of evolutionary fitness i.e., mutation/natural selection (cf. Martin & Nichols, 2018). Profit-oriented pharmaceutical companies, on the other hand, actively market patented synthetic designer drugs which do not have any evolutionary track record and might cause all kinds of unforeseen neurological, genetic, and epigenetic problems in the long run (cf. Kim et al., 2009), for instance, the widespread prescription of methylphenidate (e.g., Ritalin) in preschool children (Keane, 2008), based on questionable DSM-5 nosology (Phillips et al., 2012b, 2012c, 2012d, 2012a). In contrast to patentable psychopharmacological agents, there is no revenue model for naturally occurring psychedelics in the merely profit-oriented capitalistic paradigm.

⁵⁹ An animal neuroimaging study conducted by Riga et al. (2014) showed that 5-MeO-DMT decreased BOLD responses in the striate cortex (V1) and the medial prefrontal cortex (mPFC).

⁶⁰ Quotation by Francis Crick (*1916;†2004; co-discoverer of the molecular double-helix structure of DNA) from his book "The Astonishing Hypothesis: The Scientific search for the Soul" (published in 1994).

hard problem of consciousness in a materialistic reductionist framework) for some unknown reason changed his mind on this most fundamental topic. He wrote the following in a 2014 Scientific American article entitled "Is Consciousness Universal":

"Yet the mental is too radically different for it to arise gradually from the physical. This emergence of subjective feelings from physical stuff appears inconceivable and is at odds with a basic precept of physical thinking, the Ur-conservation law—ex nihilo nihil fit. So if there is nothing there in the first place, adding a little bit more won't make something. If a small brain won't be able to feel pain, why should a large brain be able to feel the godawfulness of a throbbing toothache? Why should adding some neurons give rise to this ineffable feeling? The phenomenal hails from a kingdom other than the physical and is subject to different laws. I see no way for the divide between unconscious and conscious states to be bridged by bigger brains or more complex neurons."

We propose that 5-MeO-DMT can help to shed new light quanta on the hard problem of consciousness which has engaged philosophers since time immemorial (neuroscience has only very recently joined the debate). Specifically, the tryptamine can provide first-hand (qualitative) insights into the ultimately nondual nature of mind and matter and the universality of consciousness — i.e., a higher perspective on human existence. In contemporary consciousness research the mind is often equated with consciousness. However, mind \neq consciousness. This is easily verifiable because cognition (thought) is an *object* of consciousness (otherwise introspection on mental *events* would be impossible). Thus, the mind is situated *within* consciousness and it needs to be accentuated that science is an activity of the mind. Ergo, science is an activity within the mind which, in turn, is situated within consciousness. The statement that science can *objectively* investigate consciousness is thus a *non sequitur*. This relates to the ancient self-referential (autopoietical/recursive) question about the relationship between the seer and the seen (Sanskrit: *Drg-Drśya*): Can the seer be seen? Can consciousness investigate itself? Thus, the quintessential question is: Who introspects on the mind and its contents (thoughts, feelings, perceptions, etc.). In other words, who is the experiencer, who is the knower, who is the seer? Who is the

ultimate conscious "I"? The 8th century Indian logician Jagadguru Shankaracharya provided the following précis of the timeless nondual philosophy:

"Even in the state of ignorance, when one sees something, through what instrument should one know That owing to which all this is known? For that instrument of knowledge itself falls under the category of objects. The knower may desire to know not about itself, but about objects. As fire does not burn itself, so the self does not know itself, and the knower can have no knowledge of a thing that is not its object. Therefore through what instrument should one know the knower owing to which this universe is known, and who else should know it? And when to the knower of Brahman who has discriminated the Real from the unreal there remains only the subject, absolute and one without a second, through what instrument, O Maitreyī, should one know that Knower?"

Nonduality is first-hand experience. It cannot be objectified. This fact does not exclude it from scientific discourse. Science is an open-ended enterprise and its methods evolve (n.b., there is no "scientific" consensus about what exactly constitutes the scientific method, e.g., the Popperian demarcation problem). By definition, science is concerned with knowledge (lat. scire = "to know") – that is, any kind of knowledge (but see the Jamesian "radical empiricism" argument in the discussion section). Science does not preclude non-objectifiable self-knowledge. In fact, the Greek intellectual tradition (which laid the very groundwork for contemporary thought) placed great emphasis on self-knowledge as exemplified by the aphorism γνῶθι σεαυτόν ("know thyself"). In opposition to the dominant Zeitgeist, science is thus not exclusively concerned with the material aspects of existence. Paradoxically, 5-MeO-DMT provides a neurochemical (material) method which reliably induced the firsthand transcendental experience of nonduality. There are other much more arduous pathways to achieve nondual insights such as mediation and sophisticated yogic exercises. However, they are much more demanding and hence unreliable than the "direct" neurochemical route. Consequently, it would be of great interest to investigate whether these ancient techniques induce neuronal and psychological changes which are similar to those induces by 5-MeO-DMT and its structural relatives. Specifically, future studies should clarify whether the production and release of DMT-related endogenous substances can be intentionally increased by various techniques (e.g., meditation, music, yoga, physical exercise, mood manipulation, stress, pain, anxiety, mortality salience, etc.). It has been reported that average daily output of melatonin from the pineal gland is $\approx 30 \, \mu g$ (Nichols, 2018b). Based on this quantity it has been argued that the endogenous amount of DMT is about $\frac{1}{1000}$ of what would be needed to achieve psychoactivity (the exact threshold is currently undefined). It would therefore be of fundamental interest to investigate if the endogenous synthesis of various tryptamines in the pineal (and elsewhere) can be stimulated, and if so, to determine the maximum output capacity of various glandular systems under varying conditions. 61 Further, it may be assumed that there are interindividual differences in the production and release of various tryptaminergic neuro-hormones (which may be rooted in genetic variability). It is a well-established fact that there are individual differences in pineal gland volume and these have been related to autism (Maruani et al., 2019) which can be regarded as a "disorder" of consciousness. Chronobiology and various "states" of consciousness (e.g., dreaming/waking states) are closely related and tryptamines such as melatonin have been related to various mental disorders such as depression and anxiety.⁶²

5-MeO-DMT exerts extremely profound acute *and* chronic effects on the self-concept (ego). Here, the term ego is not used as defined in the classical Freudian tripartite model (Freud, 1923), but it refers to the concept of an encapsulated ego identity, that

 $^{^{61}}$ It has been argued that the amount of L-tryptophan (a precursor of 5-HT and DMT) is only available in minute amounts in human serum , i.e., the reported concentration is $\approx 12.98 \pm 0.37$ $\mu\text{g/mL}$ (Comai et al., 2010) and that the availability of biochemical basic material constitutes a limiting factor. However, if this data is generalizable across various populations remains an open question which warrants further exploration.

⁶² Interestingly, the adaptogenic properties of melatonin have recently been emphasized (Zakharov, Khivintseva, Pyatin, Sergeeva, & Antipov, 2019) and we submit that 5-MeO-DMT likewise has adaptogenic properties which support organismal homeostasis on various levels (cf. recent research on its anti-inflammatory and neurorestorative effects). The "adaptogen concept" is controversial in mainstream science but there is exists a plethora of evidence in support of its validity – mainly from Chinese research (T.-S. Chen, Liou, & Chang, 2008). Western science is is slowly integrating the concept (Panossian, Wikman, Kaur, & Asea, 2012). 5-MeO-DMT is specifically interesting in this regard as creativity might be seen as a psychological aspect of adaptation and psychological and physiological homeostasis might be intimately interlinked.

is, who we think we are as human beings. Thus, the usage of the term ego is more closely aligned with the ancient Sanskrit term "Ahaṃkāra" as defined in Vedic philosophy (cf. Cartesian positional identity; Comfort, 1979). For example, the great scientist of the mind *Patañjali* writes in Sanskrit:

दुग्दर्शनशक्त्योरेकात्मतैवास्मिता

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"To identify consciousness with that which merely reflects consciousness – this is egoism." (Yoga Sūtras of Patañjali, cap. 2, aphorism 6).

In the Indian contemplative tradition, the overcoming of egocentrism is a precondition for spiritual progress. ⁶³ The founder of quantum physics, Nobel laurate Erwin Schrödinger, was deeply impressed by the depth of Vedāntic philosophy in relation to consciousness and he expressed this eloquently in his seminal book "What is Life":

"The only possible alternative is simply to keep the immediate that consciousness is a singular of which the plural is unknown; that there is only one thing and that, which seems to be a plurality, is merely a series of different aspects of this one thing, produced by a deception (the Indian Maya); the same illusion is produced in a gallery of mirrors, and in the same way Gaurisankar and Mt. Everest turned out to be the same peak seen from different valleys." (Schrödinger, 1944, p. 89).

We suggest that the ancient Indian concept of $M\bar{a}y\bar{a}$ is essential in order to appreciate the unveiling effects of psychedelics. Māyā connotes "that which exists, but is constantly changing and thus is spiritually unreal" (Hiriyanna, 1995). It has been roughly translated as illusion even though this translation has its shortcomings (translations from Sanskrit into English face many hermeneutical difficulties, a

 $^{^{63}}$ Interestingly, a related idea can be found in Islam. The concept of *Jihad al-Nafs* can be translated as "an inner striving or struggle to overcome the ego/nafs" – i.e., the great inner struggle to heal the heart's diseases (see Al-Khomeini, 1940; *Al-Arba'ūn Ḥadīthān*, transl.: "Forty Hadith").

better twofold Vedantic translation is "projection" and "veil"). ⁶⁴ Apropos the propounded differentiation between mind and consciousness Māyā refers to the fluctuating contents of the mind.

In this theoretical/phenomenological framework, the ego can be conceptualized as a filter or a lens which converts experiences and creates the appearance of change and diversity while the underlying reality is timeless unity. Pure consciousness lies beyond the mind and the ego construct and is "that which perceives" (cf. Josipovic, 2010, 2014). While the ego identifies with the dualistic and ephemeral contents of sensory experience, consciousness itself does not (Sivananda, 1972). Consciousness itself has no associated identity. It is a detached unchanging witness of experience. ⁶⁵

Sir Arthur Eddington articulated similar thoughts:

⁶⁴ A connatural concept can also be found in Plato's "Allegory of the cave" (*Res Publica*, book 7, 514a–520a). Plato was very much concerned with eternal forms and most mathematicians can be regarded as Platonists (Burnyeat, 2000; Mueller, 2005) even though they might not be explicitly aware of this philosophical heritage (cf. the importance of Δianoia in Plato's "Theory of Forms" (Cooper, 1966; Tanner, 1970)). Interestingly, Plato's allegory has recently been revived in the context of quantum dynamics and quantum computation, particularly with regard to the quantum Zeno effect (Misra & Sudarshan, 1977; Peres, 1980; Stapp, 2001) and "projected" reality perceived through noncommutative "sequences of measurements" (but see Burgarth et al., 2014).

⁶⁵ Note that this statement is not objectively verifiable in a detached manner. It can only be derived from the first-hand phenomenological experience (i.e., ego-dissolution caused by meditation, introspection, psychedelics, spontaneous epiphany, etc.). Ego-less pure awareness plays a central rôle in many ancient philosophical schools of thought (Advaita Vedānta, Mahāyāna and Zen Buddhism, Taoism, Sufism, i.a.). It also relates to the Western literature on the Cartesian and Heisenbergian cut, where the former refers to the dichotomy between the material world (*res extensa*) and its non-material counterpart (*res cogitans*), while the latter refers to the cut between an object and its environment which is crucial in the context of modern quantum physics (see Atmanspacher, 1997).

"The mind-stuff of the world is, of course, something more general than our individual conscious minds. [...] The mind-stuff is not spread in space and time; these are part of the cyclic scheme ultimately derived out of it. [...] It is necessary to keep reminding ourselves that all knowledge of our environment from which the world of physics is constructed, has entered in the form of messages transmitted along the nerves to the seat of consciousness. [...] Consciousness is not sharply defined, but fades into subconsciousness; and beyond that we must postulate something indefinite but yet continuous with our mental nature. [...] It is difficult for the matter-of-fact physicist to accept the view that the substratum of everything is of mental character. But no one can deny that mind is the first and most direct thing in our experience, and all else is remote inference." (Eddington, 1929, pp. 276–281)

More recently it has been argued along the same vein that physics faces its final frontier – i.e., consciousness (Stapp, 2007). For instance, the "von Neumann-Wigner interpretation", also referred to as "consciousness caused collapse of Ψ ", postulates that consciousness is an essential factor in quantum measurements. Von Neumann used the term "subjective perception" (Von Neumann, 1955) which is closely related to the complementarity principle in psychophysics, viz., the complementarity of sensation & perception (J. C. Baird, 1997). Accordingly, Henry Stapp argued in his seminal paper "Quantum Theory and the Role of Mind in Nature":

"From the point of view of the mathematics of quantum theory it makes no sense to treat a measuring device as intrinsically different from the collection of atomic constituents that make it up. A device is just another part of the physical universe. [...] Moreover, the conscious thoughts of a human observer ought to be causally connected most directly and immediately to what is happening in his brain, not to what is happening out at some measuring device. [...] Our bodies and brains thus become [...] parts of the quantum mechanically described physical universe. Treating the entire physical universe in this unified way provides a conceptually simple and logically coherent theoretical foundation." (Stapp, 2001)

We argue that these epistemological and ontological considerations have deep implications for the philosophy (and hence practice) of science (n.b., there is no science devoid of philosophy — only science which incorporates philosophical axioms as *a priori* given without explicit reflection on their validity/veridicality). The nondual perceptive challenges the predominant reductive materialism stance and it might ultimately facilitate a Kuhnian paradigm shift with far-reaching ramification across disciplines (i.e., a transdisciplinary paradigm-shift). A nondual conception of reality might enable new ways of psychophysical scientific experimentation which are unthinkable in the current materialistic paradigm (which entails a significant amount of unjustified Cartesian/Newtonian assumptions which might implicitly "block" alternative ideas). With respect to scientific experimentation (and data collection) Eddington provided the following brilliant analogy in his book "The Philosophy of Physical Science" (1938) which illustrates how the "conceptual/perceptual cognitive net" determines the character of scientific inquiry:

"Let us suppose that an ichthyologist is exploring the life of the ocean. He casts a net into the water and brings up a fishy assortment. Surveying his catch, he proceeds in the usual manner of a scientist to systematise what it reveals. He arrives at two generalisations:

- $1) \hspace{0.5cm} \textit{No} \hspace{0.5cm} \textit{sea-creature} \hspace{0.5cm} \textit{is} \hspace{0.5cm} \textit{less} \hspace{0.5cm} \textit{than} \hspace{0.5cm} \textit{two} \hspace{0.5cm} \textit{inches} \hspace{0.5cm} \textit{long}.$
- 2) All sea-creatures have gills.

These are both true of his catch, and he assumes tentatively that they will remain true however often he repeats it. In applying this analogy, the catch stands for the body of knowledge which constitutes physical science, and the net for the sensory and intellectual equipment which we use in obtaining it. The casting of the net corresponds to observation; for knowledge which has not been or could not be obtained by observation is not admitted into physical science. An onlooker may object that the first generalisation is wrong. 'There are plenty of sea-creatures under two inches long, only your net is not adapted to catch them.' The icthyologist dismisses this objection contemptuously. 'Anything uncatchable by my net is ipso facto outside the scope of icthyological knowledge. In short, what my net can't catch isn't fish.' Or — to translate the analogy — 'If you are not simply guessing, you are claiming a knowledge of the physical universe discovered in some other way than by the methods of physical science, and admittedly unverifiable by such methods. You are a metaphysician. Bah!"

We submit that 5-MeO-DMT is by far the most effective pharmacological agent for the controlled induction of nondual states of consciousness and consequently the restructuring of the "cognitive net". Given the postulated complementarity between psyche & physis, nondual states of consciousness are accompanied by physiological changes in the neuronal architecture of the brain, i.e., the conceptual net (mind) and the neuronal net (matter) are complementary aspect of the same underlying "substance", a tertium quid, 66 viz., universal consciousness. In simplistic terms, by changing the brain the mind changes and, vice versa, by changing the mind the brain changes. Consciousness itself remains unaffected. Therefore, it does not make much sense to speak about "states of consciousness". Consciousness is an immutable singular — it is the experiencer (that which experiences change — viz., "it" is the nontransient observer of the fluctuating contents of the mind).

5-MeO-DMT has been described as a prototypical entheogen (Metzner, 2015) and it is psychologically and pharmacologically much more potent than its structural relatives (e.g., N,N-Dimethyltryptamine), i.e., qualitatively and quantitatively. An entheogen (Ruck, Bigwood, Staples, Ott, & Wasson, 1979) is a chemical substance (used in a religious, shamanic, or spiritual contexts) that has the potential to produce profound psycho-spiritual insights and changes. From a philological point of view, the

⁶⁶ Irenæus (c. AD 196) wrote the following in "Against Heresies" (§2.1.3): "Since they say that something exists outside the Pleroma, into which they think that Power wandering from above came down, they must choose one of two views. Either this "outside" will contain the Pleroma and the Pleroma will be contained—otherwise there will not be something "outside," for if anything is outside the Pleroma the Pleroma will necessarily be within what they call outside the Pleroma, and the Pleroma, with the first God, will be contained by what is outside; or else the Pleroma and what is outside it will be immensely distant and separated from each other. But if they say this, there will be a 'tertium quid' with this immense separation between the Pleroma and what is outside it, and this 'tertium quid' will limit and contain the other two, and will be greater than both the Pleroma and what is outside it, since it contains both in its bosom." (Grant, 1996, p. 108, cap. "Divine transcendence"). Here the term pleroma could be translated as "fullness" and it thus emphasizes holism and totality in contrast to reductionism and the separation of constituent parts, e.g., pleroma tes theotetos (transl.: "the whole completeness of the divine nature" (Colossians 2:9). The antonym of pleroma is hystêrema (incompletion). Interestingly, a diagrammatic representation of pleroma (after the gnosticValentinus) which consists of nested triangles and pentagrams is very similar to the Sri Yantra in Hinduism which symbolises nonduality. Valentinus held there exists a tripartite typology of human beings, 1) the material, 2) the psychical, 3) the spiritual, while only the latter would be able to receive gnosis (knowledge) of the ultimate.

etymology of the neologism "entheogen" is a compound lexeme derived from the ancient Greek ἐνθεος (entheos) and γενέσθαι (genesthai) and translates into "generating the divine from within" (cf. "enthusiasm"). 5-MeO-DMT is a ceremonial sacrament (eucharist) of the "Church of the Tree of Life". Hence, interdisciplinary research on 5-MeO-DMT might provide further impetus for the emerging new neuroscientific paradigm which goes by the name "neurotheology" (Winkelman, 2004). Following this line of thought it has been stated by the eminent neurobiologist Efrain C. Azmitia that "the ability of these drugs to induce a feeling of closeness to God is a special property of the indoles and this property is attributed to activation of the cortical 2A serotonin receptor" (Azmitia, 2012).

We would like to recapitulate the crux of our argument: Given its phenomenological profundity and its unparalleled efficiency to dissolve ego structures we propose that the psychological effects of 5-MeO-DMT and associated neural correlates should be systematically investigated in order to elucidate the postulated connection between nondual (ego-less) states of consciousness and the stipulated enhancement of creativity. One pillar of this hypothesis is the idea that ego-dissolution is associated with a breakdown of linguistic structures ⁶⁷ (hence the characteristic ineffability of its phenomenology/quale). According to the Sapir-Whorf hypothesis of linguistic relativism (Sapir, 1929), language structures cognition and perception in significant ways. Ergo, we hypothesize that a release from the strong aprioristic schematising influences of linguistic processes facilitates a more unrestrained (pre-linguistic) style of cognition and perception. Further, we argue that the collapse of the psychophysical "subject versus object" dichotomy into nondual experience has enormous potential for complex cognitive restructuring at multiple levels of analysis (cf. Josipovic, 2010). "Ego exitus" (the apex of ego-dissolution, i.e., ego death) is emotionally and cognitively extremely challenging, an observation which resonates with the "hardship model of creativity" (Forgeard, 2013). At the same time the extremely challenging experience

⁶⁷ Indeed, anecdotal reports indicate that it can cause glossolalia and xenolalia which are very interesting linguistic phenomena that have been investigated in the context of religion and altered states of consciousness (cf. Grady & Loewenthal, 1997; Kavan, 2004) and also from a neuroscientific perspective (Philipchalk & Mueller, 2000). We therefore suggest that 5-MeO-DMT is of great interest to researchers in these fields.

of ego-dissolution and ultimately ego-death may have significant positive therapeutic/cathartic effects which are of essential pertinence in in relation to creativity research (e.g., release from severe traumata, access to repressed unconscious materials, surfacing of archetypal symbolisms, etc.). The experiences induced by 5-MeO-DMT are tremendously radical ⁶⁸ and therefore capable to disperse deeply engrained cognitive/perceptual schemata ⁶⁹, thereby enabling a more unrestricted style of cognition. ⁷⁰ Specifically, we argue that due to its unparalleled ego-dissolving properties 5-MeO-DMT facilitates a less self-centred and hence more unbiased style of cognition which is a *condicio sine qua non* for creativity. This hypothesis is empirically falsifiable in the Popperian sense and various established cognitive testing procedures ⁷¹ could be utilized to test this hypothesis experimentally.

⁶⁸ It has been argued elsewhere that "increased creativity may [...] constitute a manifestation of posttraumatic growth, defined as retrospective perceptions of positive psychological changes that take place following experiences of highly challenging life circumstances" (Forgeard, 2013, p. 245).
69 Interestingly, preliminary evidence suggests that psilocybin is effective in the treatment of addiction, depression, and obsessive-compulsive disorders (Bogenschutz et al., 2015; Carhart-Harris et al., 2016). This is congruent with the formulated idea that 5-MeO-DMT has the potential to change persistent habitual modes of thought.

This idea could be empirically tested, for instance, by utilizing a semantic priming paradigm in order to investigate spread of activation (as proxy for verbal creativity). Exemplary studies have been conducted with the dopamine precursor L-Dopa by, for example, Kischka et al. (1996) in order to investigate the rôle of dopaminergic neurotransmission in verbal creativity. Anecdotal evidence suggest that serotonergic psychedelics can enhance verbal creativity significantly (longitudinally). In the acute phase, many psychedelics interfere strongly with the linguistic system (a breakdown of semantic and syntactic facilities is oftentimes reported). Ergo, frontal and temporal lobe language areas such as Broca's and Wernicke's area and the arcuate fasciculus are likely involved. We suggest that temporarily induced receptive and expressive aphasia are of interest in this context. Further, the differential influence on the left and right hemisphere are a topic of great interest. It would be interesting to examine if 5-MeO-DMT releases the right hemisphere from contralateral inhibition, that is, does it influence hemispheric dominance (i.e., local versus global processing in the context of asymmetric hemispheric lateralization of function); cf. "right hemispheric dominance theory of creative thinking" (W. Shen et al., 2013).

⁷¹ It should be noted that psychedelics might cause serious psychological harm to certain populations with psychopathological dispositions (possibly due to specific 5-HT receptor polymorphisms). In rare cases the DSM-5 diagnosis "Hallucinogen Persisting Perception Disorder" (HPPD) is applied (low incidence rate) (for a review consult Halpern, Lerner, & Passie, 2016). Careful psychological screening is crucial for ethically responsible research (for research safety guidelines see Johnson, Richards, & Griffiths, 2008).

(Creativity is generally conceptualised as a multi-dimensional construct and various facets of creativity may be affected differentially.) The logic which undergirds our theorizing can be formalized using propositional logic, i.e., in form of a syllogistic argument (see Syllogism #1 below). Specifically, we postulate that ego-dissolution can culminate in a state of nondual consciousness which is phenomenologically, biochemically, and neuroanatomically similar to those reported in numerous ancient wisdom traditions such as Advaita Vedānta and Mahāyāna Buddhism. Nondual experiences have been reported since time immemorial and, for the first time, science is now in a position to investigate them in a systematic fashion (ideally in a holistic manner across multiple levels of explanation, i.e., by combining the epistemic/qualitative with the ontic/quantitative level of analysis). It is hypothesized that nondual states of consciousness induced by 5-MeO-DMT shift the global connectivity patterns between intrinsic networks and extrinsic networks. These networks are thought to be anticorrelated. In terms of large-scale neuroanatomical organization. According to current knowledge, the intrinsic network includes rather broadly defined areas in the medial prefrontal cortices, the posterior cingulate cortices, the precunei, the inferior parietal lobule, and temporal areas such as parts of the hippocampi (Cavanna, 2007; Josipovic, 2014). Its activity has been associated with a broad array of self-referential cognitions such as self-awareness and self-reflection, executive functions like future planning, and also creativity. For instance, it has been experimentally demonstrated that distraction (i.c., mind-wandering) can enhance creativity (B. Baird et al., 2012). We argue, in abstracto, that "a release from the limiting self" is an important aspect in the context of creativity enhancement (to put it metaphorically, the unleashing of creativity from the grip of the ego). The general idea is that signal transduction in neuroanatomical areas associated with selfreferential cognition is reduced. For instance, it has been demonstrated that meditation is associated with decreased activity in the default mode network, i.c., decreased activity in medial prefrontal and posterior cingulate cortices (Brewer et al., 2011). We expect similar (but more pronounced) effects with 5-MeO-DMT,

specifically given the phenomenological similarities between 5-MeO-DMT and meditative (nondual) states of consciousness. Based on previous conceptually related work which investigated the neural correlates of nondual states in meditators it seems indicated to examine if the neuronal activity changes induced by 5-MeO-DMT are congruent with ROIs related to nondual states of consciousness achieved via mediation, e.g., the involvement of the DMN and specifically the central precuneus (cf. Josipovic, 2014). This line of research is particularly warranted given the plethora of studies which correlate meditation with creativity (Baas, Nevicka, & Ten Velden, 2014; Capurso, Fabbro, & Crescentini, 2014; Colzato, Ozturk, & Hommel, 2012; Dawson, 2004; Ding, Tang, Tang, & Posner, 2014; Domino, 1976; Horan, 2009; B. C. N. Müller, Gerasimova, & Ritter, 2016; Ostafin &

Kassman, 2012; Peet, 1979). Our primary argument can be stated in form of a logically valid Aristotelian categorical syllogism.⁷²

Syllogism #1

Major premise: Ego-dissolution enhances creativity.
 Minor premise: 5-MeO-DMT induces ego-dissolution.
 Deductive conclusion: ∴ Ergo, 5-MeO-DMT enhances creativity.

Syllogism #2

Major premise: Increases in FCD are predictive of creativity.

Minor premise: 5-MeO-DMT increases global functional connectivity density.

Deductive conclusion: : Ergo, 5-MeO-DMT enhances creativity.

 72 A categorical syllogism (Greek: συλλογισμός, syllogismos, conclusion or inference) consists of three parts: the major premise, the minor premise and the conclusion, for example:

Major premise: All men are mortal. Minor premise: Socrates in a man. Conclusion: Ergo, Socrates is mortal.

Or in Aristotle's terms: "Whenever three terms are so related to one another that the last is contained in the middle as in a whole, and the middle is either contained in, or excluded from, the first as in or from a whole, the extremes must be related by a perfect syllogism. I call that term middle which is itself contained in another and contains another in itself: in position also this comes in the middle. By extremes I mean both that term which is itself contained in another and that in which another is contained. If A is predicated of all B, and B of all C, A must be predicated of all C: we have already explained what we mean by 'predicated of all'. Similarly also, if A is predicated of no B, and B of all C, it is necessary that no C will be A." (Aristotle, Organon Analytica Prioria, Book 1, §4). Based on an extensive psychological analysis of the foundational question "Where does mathematics come from" (Lakoff & Núñez, 2000) it has been argued that syllogistic reasoning is based on the logic of containment, i.e., it makes use of mental manipulations of container schemata which form the basis of inferential logic. From an embodied cognition/conceptual metaphor perspective, humans mentally represent (Boolean/set-theoretical) inferential laws in a quasi-Venn diagrammatic manner (Venn, 1880) by utilizing specific spatio-relational image schemata (cognitive container schemata). Container schemata serve as mental representations of classical logical laws (e.g., principium tertii exclusi, modus ponens, modus tollens, etc.). Recent neuroimaging data support this "line of thought". For instance, an event-related fMRI study (Goel & Dolan, 2001) reported the involvement of the parietal visuo-spatial system in abstract three-term syllogistic reasoning (occipital-parietal-frontal network). Investigations of the neuroanatomical correlates of syllogistic reasoning thus corroborate the notion that syllogistic reasoning recruits neuronal circuitry associated with the computation of spatial relations (see also Goel, Gold, Kapur, & Houle, 1998) as already implicitly psycholinguistically implied by Aristotle's formulation.

Syllogism #3

Major premise: Downregulation of the DMN enhances creativity.

Minor premise: 5-MeO-DMT downregulates the DMN.
Deductive conclusion: ∴ Ergo, 5-MeO-DMT enhances creativity.

According to syllogistic logic each of the three distinct terms represents a category, i.c.:

[Ego-dissolution] — [5-MeO-DMT] — [Creativity]. For example, in Syllogism #1 the category [Creativity] is the major term and [5-MeO-DMT] constitutes the minor term. Crucially, the premises have a single term in common (the middle term) ⁷³ which appears as the subject or predicate of the categorical proposition, *in casu*, [Ego-dissolution]. According to the principles of propositional logic, the conclusion follows deductively ⁷⁴ *iff* the major and minor premise are accepted as veridical. Based on these syllogistic arguments we formulate the ensuing falsifiable *a priori* hypotheses:

H₁: Downregulation of the default-mode network (DMN) predicts subsequent increases in creativity (see below for details on the incubation/integration-phase and the "DMN rebound effect"). In addition, we conjecture that 5-MeO-DMT decreases depression similar to results obtained with psilocybin and we predict a correlation between reduction in depressive symptoms and isochronous increases in creativity.

H₂: The self-reported intensity of 5-MeO-DMT phenomenology (*post eventum* introspective assessment) predicts subsequent increases in global functional connectivity density which are in turn predictive of creativity (the differential effects on various facets of creativity should be investigated — we suggest that "mathematical creativity" is a specifically interesting aspect given the highly

⁷³ The absence of the middle term in both premises leads to a syllogistic fallacy, i.e., the fallacy of the undistributed middle (viz., *non distributio medii*).

⁷⁴ From a philological vantage point the term "deduction" is etymologically derived from the Latin *deducere* "to lead, to derive". Thus, the premises lead (automatically) to the conclusion, i.e., the conclusion is logically derived. This formalization constitutes the basis of the deductive-nomological model (Popper–Hempel model) of scientific explanation.

geometrical characteristics of DMT phenomenology). Further, we predict that 5-MeO-DMT induces neuro/synaptoplastic changes which are crucial in the context of creativity and cognitive/neuronal restructuring (cf. Dakic, 2017). In addition, we predict based on prior research that 5-MEO-DMT induces neurogenesis via various neurotrophic growth factors, e.g., hippocampal neurogenesis (Catlow et al., 2013). Dendritic complexification and synaptic sprouting may have a psychological analogon. H₃: Self-reported ego-dissolution phenomenology predicts subsequent enhancements in creativity, as quantified by various creativity test batteries (e.g., J. C. Kaufman, 2012) in a dose-dependent manner. This effect is mediated by the profundity of the experience, e.g., how challenging the experience was, intensity of the "peak experience", personal meaningfulness of the experience, etc. (cf. Barrett, Bradstreet, Leoutsakos, Johnson, & Griffiths, 2016; Forgeard, 2013; Griffiths et al., 2006; Majić, Schmidt, & Gallinat, 2015).

 H_4 : The intensity of 5-MeO-DMT induced ego-dissolution predicts longitudinal increases in aesthetic perception, biophilia, and feelings of fundamental existential interconnectedness 75 (viz., OTE – similar to studies which focused on the structural analogue psilocybin (MacLean et al., 2011), but more pronounced; a direct comparison between compounds would be of interest to infer structure-activity relationships based on neuroimaging-data and qualitative phenomenological differences). H_5 : The intensity of ego-dissolution predicts the longitudinally measured significance of the life-event in a non-linear dose-dependent manner, similar to the patterns observed in studies with the psilocybin (Griffiths, Richards, Johnson, McCann, & Jesse, 2008).

H₆: 5-MeO-DMT modulates activity in the limbic system (i.e., amygdala, insular cortex) in a longitudinal manner (cf. Kraehenmann et al., 2015). Various biomarkers

⁷⁵ The concept of interconnectedness is of utmost importance from an ecopsychology point of view (cf. Key & Kerr, 2011). The formulated hypothesis thus has significant real-world societal significance. The illusion of disconnection from nature (Fromm, 1962) lies at the root of many destructive human behaviors which have far reaching detrimental consequences (individual and society, micro and macro are not separable – therefore individual changes translate into global changes). Impetus for the hypothesis at hand is partially derived from recent studies which indicate that classical psychedelics increase nature-relatedness (Forstmann & Sagioglou, 2017; Lyons & Carhart-Harris, 2018).

(GSR, plasma glucocorticoid-levels, etc.) could be quantified to test this prediction. This hypothesis is not only interesting in relation to interplay between stress and creativity (Byron, Khazanchi, & Nazarian, 2010) but also for the treatment of anxiety disorders such as PTSD.

 H_7 : Given that 5-MeO-DMT can have strong somatosensory and viscerosensory effects (somasthæsia, changes in proprioception and body-image, and in some cases out-of-body experiences) we hypothesize that various somatosensitive areas are involved, specifically the temporo-parietal junction (potentially also the anterior insular cortex (Yu et al., 2018)). This hypothesis is particularly intriguing from an embodied cognition perspective on creativity and also in relation to Damasio's somatic marker hypothesis.

H₈: The peak-experience of ego-death (sometimes colloquially referred as "break-through" or in the extensive Indian literature *Nirvikalpa Samādhi* ⁷⁶) is marked by a rapid phase-shift in global neuronal activity (e.g., quantifiable via simultaneous EEG/fMRI). We predict a marked increase in creativity in comparison with states of consciousness which still include rudimentary traces of the self-concept. We term this mnemonically the "less ego => more creativity hypothesis". We conjecture that this transformative nondual peak-experience is accompanied by marked epigenetic changes (cf. Dias & Ressler, 2014). Further, we predict that 5-MeO-DMT effects genetic health on multiple levels (e.g., telomeres and telomerase activity) and that overall genetic health is associated with creativity. This hypothesis is based on studies which demonstrated positive correlations between mediation, mental health, and genetics (Alda et al., 2016; Epel, Daubenmier, Moskowitz, Folkman, & Blackburn, 2009).

⁷⁶ The English language lacks terminology to describe many non-ordinary states of consciousness (cf. Sapir-Whorf hypothesis of linguistic relativism). Sanskrit, on the other hand, is linguistically very rich in this respect. The word Nirvikalpa is a composite lexeme composed of the negatory/contraexistential prefix ni (not, without) and the term vikalpa (thought, conception) and it can be translated as "without conception, free from conceptual thought". In the ancient but timeless Yoga $S\bar{u}tras\ of\ Pata\tilde{n}jali$ it refers to the highest form of samadhi, i.e., mediation without thought and object, a nondual state of absorption without self-consciousness in which there is no distinction between knower and known (epistemology and ontology, the seer and the seen; cf. Drg- $Dr\acute{s}ya$ -Viveka).

H₉: We predict that 5-MeO-DMT effects social cognition in numerous ways. The "realization of unity" fosters prosocial attitudes, empathy, altruism/reciprocity. This hypothesis can be tested using standard procedures from social psychology and we predict interactions of 5-MeO-DMT with the oxytocin/vasopressin neuropeptide systems. The link between empathy and creativity has been noted in prior research (Carlozzi, Bull, Eells, & Hurlburt, 1995). Further, we suggest that terrormanagement-theory is an interesting explanatory framework with respect to egodeath and creativity (cf. Arndt & Vess, 2008; Routledge & Arndt, 2009).

H₁₀: Finally, we predict that 5-MeO-DMT synergizes with other therapeutic modalities in a non-linear fashion, i.e., the effectiveness of other therapies can be enhanced by 5-MeO-DMT because it creates a state of psychological receptiveness in which defence mechanisms are curtailed. We specifically predict that 5-MeO-DMT has strong longitudinal synergistic effects when combined with mediation (particularly types of mediation that foster nondual philosophical contemplations). This hypothesis is partly motivated by recent neuroimaging work which reported quantitative synergistic effects between psilocybin and mindfulness training (Smigielski et al., 2019). The combinatorial effects of mediation and 5-MeO-DMT on creativity are predicted to be significantly "larger than the sum of its parts" (i.e., larger than would be predicted based on a linear additive model).

Ex hypothesi, we argue that the conjectured effects are objectively quantifiable and reliably replicable in rigorously controlled experimental settings. The paucity of research on 5-MeO-DMT is surprising, specifically given that it is an endogenous component of neurobiology which implies an evolutionary function (neurochemical vestigiality is an unlikely explanation). Up to date, we are unaware of any systematic scientific research which focuses specifically on the effects of 5-MeO-DMT on ego-dissolution and creativity. Consequently, we suggest that future studies should be designed in order to elucidate this rich and potentially very fruitful research area. The present discussion is just a start in order to motivate future studies along these lines. Among the various psychoactive tryptamines (e.g. psilocybin/psilocin, DMT/NMT/α,N-DMT, N_{ω} -methylserotonin, convolutindole A, 5-Bromo-DMT, etc.) 5-MeO-DMT is specifically suitable for controlled scientific experimentation due to the

short duration of its acute effects. It can be utilised as an inhalant (e.g., vaporization) and its onset it extremely fast (a single inhalation is sufficient for its full effects which manifest instantaneously, often before the exhalation of the vapor). Alternative routes of administration 77 include IV, intracerebroventricular, intramuscular, intranasal, intrarectal, intravaginal, sublingual, or oral administration in combination with a monoamine oxidase inhibitor (MAOI) to prevent enzymatic deamination in the GI tract (Halberstadt, 2016). However, with the latter synergistic method may change pharmacodynamics (and psychoactivity) in hitherto unknows ways and negative side effects such as increased "body-load" have been mentioned in anecdotal reports. Data indicates that 5-MeO-DMT may, under some circumstances, be toxic⁷⁸ if administered orally in combination with a MAOI. Specifically, there may be genetic/phenotypic interindividual differences in polymorphic cytochrome P450 2D6 (see H. W. Shen, Wu, Jiang, & Yu, 2010) which is encoded by the CYP2D6 gene. Future studies should address interindividual differences in CYP2D6 and their systematic relation to pharmacokinetics and phenomenology. Given the existence of considerable interindividual variations in the efficiency and amount of CYP2D6 enzyme produced, it is plausible to hypothesize that there are subgroups who metabolize 5-MeO-DMT rapidly while other are "moderate or slow metabolizers". Furthermore, interethnic differences in genetic polymorphism of CYP2D6 have been indicated (Teh & Bertilsson, 2012) and it would be of interest how these relate to psychological variables. Pharmacogenomic investigations are thus warranted and we specifically suggest that genetic differences should be correlated with neuronal and phenomenological variables. For instance, slow 5-MeO-DMT metabolism should have significant effects on fMRI/EEG signatures and the duration of the experimental This in turn should correlate significantly with qualitative time-course. phenomenology and intensity of the experience, and hence, with the overall psychological impact and consequently changes in creativity (i.e., genetics variability

⁷⁷ We are nescient about intraocular administration of purified 5-MeO-DMT. However, given its relation to the pineal (which contains photoreceptors) this is a topic of empirical interest (the pineal is has been referred to as the parietal "reptilian third eye" (Eakin & Westfall, 1959).

⁷⁸ The toad venom itself contains numerous bufotoxins which interact with the functioning of the cardiovascular system, e.g., the bufadienolide derivative bufagin $-C_{24}H_{34}O_5$ (Jensen, 1932).

=> pharmacokinetics => neural correlates => subjective phenomenology => psychological impact => creativity).

We suggest that the effects of 5-MeO-DMT on creativity (and cognition in general) should be investigated in a longitudinal design. Controlled experimentation should be interdisciplinary and multi-modal (i.e., brain imaging 79, self-reports, introspective measures, etc.) in order to gain a complete picture of the effects of the compound (i.e., methodological triangulation/complementary measurement methods). For instance, brain-wide network dynamics which undergird creativity are currently a cutting-edge neuroscience topic of great interest (Beaty, Benedek, Silvia, & Schacter, 2016; Beaty et al., 2018) and functional connectivity density mapping (FCDM) is widely utilised (Tomasi & Volkow, 2010). The general idea is that creative thought involves dynamic interactions between large-scale brain systems, specifically between cortical hubs within the default mode network, the salience network, and the prefrontal executive systems. Note that this is a somewhat "fuzzy" neuroanatomical analysis as each of the networks includes a vast number of anatomical structures. Our hypothesis contributes a more precise predictions and we argue that specifically the downregulation of the default-mode network (which, according to theory, is accompanied by the phenomenology of ego-dissolution) is an important component for the enhancement of creativity. Further, we predict a priori that the downregulation of DMN activity creates a rebound-effect (based on the Aristotelian principle of homeostatic self-regulation, which is incorporated into numerous contemporary

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 $^{^{79}}$ We hypothesize that 5-MeO-DMT increases functional connectivity (a reorganization of the richclub architecture) and that this modulation of neuronal connectivity is associated with enhancement of creativity. *In brevi*, as neuronal activity patterns change, and neuronal circuitry is reorganized new connections between concepts and ideas evolve. We argue that John Locke's classical quasi-Newtonian theory "On the Association of Ideas" is relevant in this regard. Connectome-based predictive (CPR) modeling could be employed to evaluate this hypothesis quantitively. CPR is a relatively new statistical method which uses (linear) models to predict cognition (or behavior) based on whole-brain dynamics (i.c., functional connectivity patterns are used as predictors for specific outcomes) (X. Shen et al., 2017). Relating to the proposed hypothesis the predictor would be functional connectivity (e.g., rich-club coefficient Φ) and the outcome criterion creativity (e.g., associative thinking). Whole-brain global functional connectivity maps could be utilized for the purpose of visualization and local density variations could be contrasted *post hoc* (e.g., intrinsic connectivity contrasts).

complex systems/cybernetics theories). ⁸⁰ Hence, pertaining to brain dynamics and FCD the time-course should be taken into account in order "serialize" creative idea formation. The "incubation and integration phase" (after the acute/proximal neuropharmacological effects subside) is of particular interest with regard to neuroplasticity and creativity (i.e., statistical time series analysis should be employed to map various parameters diachronically). Given the profundity of the experience occasioned by 5-MeO-DMT the integration-phase can span several weeks and even months (some would even verify that it lasts a human lifetime).

Preliminary (quasi-experimental) research suggests that structurally related tryptamines can foster pro-environmental "nature-relatedness" and (anti-neoliberal) egalitarian attitudes (Forstmann & Sagioglou, 2017; Lyons & Carhart-Harris, 2018; Nour, Evans, & Carhart-Harris, 2017). Controlled experimental research along these lines is of great importance in the current survival-threatening economic/sociopolitical climate (see also Sugarman, 2015). Hypothesis 8 (H₈) entails a prediction pertaining to potential epigenetic changes induced by 5-MeO-DMT. This ideas is derived from recent genetic studies which reintroduced Lamarckian elements into quantitative biology and thereby challenge the "central dogma of molecular biology"81 (Crick, 1970) which was for a long time unquestionably axiomatic to genetic research. For instance, it has been shown that acquired olfactory conditioning can be epigenetically inherited by subsequent generations (at least up to F2) (Dias & Ressler, 2014). The odorant receptor (Olfr151) was used to condition F0 mice and subsequent generations (which were utterly naïve to the olfactory conditioning paradigm) revealed CpG hypomethylation in the Olfr151

⁸⁰ Aristotle stated: "But as all influences require to be counterbalanced, so that they may be reduced to moderation and brought to the mean [...] nature has contrived the brain as a counterpoise to the region of the heart with its contained heat, and has given it to animals to moderate the latter, combining in it the properties of earth and water."

⁽Quotation adapted from "The Complete Works of Aristotle", Revised Oxford Translation, ed., J. Barnes, Princeton: Princeton University Press, 1984)

⁸¹ The obvious question is: Should science ever be dogmatic? According to current research, "intellectual humility" and "dogmatism" are antithetical polar constructs (e.g., Leary et al., 2017), with the former being conjugate with intellectual traits such as openness, curiosity, tolerance, and the ability to handle ambiguity.

gene. We argue that if simple olfactory conditioning can cause quantifiable quasi-Lamarckian epigenetic effects than a profound 5-MeO-DMT experience should be equally quantifiable at the genetic level (cf. Heard & Martienssen, 2014; Trerotola, Relli, Simeone, & Alberti, 2015). We suggest that genes associated with the 5-HT (serotonin) system (e.g., SLC6A4 gene associated with sodium-dependent serotonin transporter) are a likely genetic locus for *a priori* (planned) comparisons (specifically in relation to depression and anxiety; cf. hypothesis H₁ & H₆). For instance, it has been reported that individuals with specific serotonin transporter (5-HTT) promoter polymorphism (associated with reduced 5-HTT expression) exhibit greater amygdala activation (fear and anxiety-related behaviours) as assessed by BOLD functional magnetic resonance imaging (Hariri, 2002; see also Heinz et al., 2005). Interestingly, it has been experimentally demonstrated that psilocybin decreases amygdala reactivity and that this limbic downregulation correlates with enhanced positive mood (Kraehenmann et al., 2015). Ergo, we predict similar effects for 5-MeO-DMT.

N.B.: We close this section with a cautionary note. Despite the centrality and prominence of neuroscientific research in contemporary popular discourse (cf. representativeness heuristic) our current knowledge about the brain is very limited (neuroscience is still in its infantile developmental phase) and therefore any intervention (be it electrical, chemical, or otherwise) into this highly complex system should be considered very carefully and thoroughly. Deliberate ethical considerations are of utmost importance (intellectual humility is a genuine scientific virtue in this respect (see Gregg, Mahadevan, & Sedikides, 2017)). The rather "dark" history of neuroscience (unfortunately) demonstrates an absolute lack of caution and ethical conscience (e.g., frontal lobotomy/leucotomy, electroconvulsive "shock therapy", destructive psychopharmacological interventions in children, etc. pp.). Some of these ethically highly questionable "treatments" are still utilized today (cf. U. J. Müller et al., 2013; Schläpfer & Kayser, 2014). For an excellent discussion of neuroethics and the amoral history of psychiatry and neurosurgery see (Breggin, 1998, 2008). For a critique of psychopharmacology with reference to human values and various "rational principles of psychopharmacology" see (Breggin, 2003, 2016).

We submit that endogenous compounds such as 5-MeO-DMT (with a long evolutionary history of human usage) are a casus specialis. Note that 5-MeO-DMT has been associated with neurorestorative adaptations (Dakic, 2017) whereas widely prescribed psychopharmaceuticals such as selective serotonin reuptake inhibitors (SSRIs, e.g., fluoxetine/Prozac®) and norepinephrine-dopamine reuptake inhibitors (NDRIs, e.g., methylphenidate/Ritalin®) are known to cause chronic brain impairment (CBI) and various psychological disorders (Breggin, 2008, 2011; Breggin & Breggin, 1996). Consequently, 5-MeO-DMT should not be grouped together with novel/synthetic psychopharmacological substances which are oftentimes completely alien to human neurobiology (an evolutionary/pharmacokinetic argument could be formulated). However, besides "side-effects" such as neurotoxicity there are other significant complications pertaining to powerful psychedelic agents which can produce dramatic changes in consciousness. For instance, how can anyone give "informed consensus" to an experience which is ineffable (cf. the ineffability of *quale*). Moreover, 5-MeO-DMT can induce the phenomenon of timelessness, or to use William Blakes poetic expression: "Eternity in an hour". 82 Superficial descriptions such as "the experiment lasts one hour" thus become meaningless because the compound interact with consciousness per se (cf. Kant on space and time as a priori mental constructs). 83 Thus, it should be explicitly emphasized that the human brain and consciousness are still largely terra incognita (we do not even understand their relation; cf. "the explanatory gap") and consequently a high degree of caution, foresight, and genuine ethical consideration are advisable with respect to any intervention which might interfere with sensitive and fine-tuned biological processes.

 $^{^{82}}$ From the poem "Auguries of Innocence" from William Blake's notebooks named "The Pickering Manuscript" (1803).

^{83 &}quot;Kritik der reinen Vernunft" (transl.: Critique of Pure Reason) published in 1781.

Brains in chains: Neuropolitics, neurodiversity, and cognitive liberty

In January 2016, the "Psychoactive Substances Act" (PSA) reached Royal Assent in the United Kingdom. 84 The PSA generically prohibits all mind-altering substances besides the most harmful and addictive ones which are of commercial significance (e.g., alcohol and tobacco were explicitly exempted; but see Nutt, King, & Phillips, 2010). This novel legal framework classifies relatively harmless substances like psilocybin on par with the most harmful and detrimental substances such as heroin and cocaine. The UK thus became the first country in human history which generically banned all psychoactive substances, viz., a juridical *omnibus* prohibition of all mind-altering chemicals was ratified, irrespective of their well-documented historicity and their comparative safety profile (King, 2013), for example, as objectively quantified by the conventional LD_{50} and TD_{50} toxicity indices. For instance, psilocybin is non-addictive (in fact it has been effectively utilised for addiction treatment (Bogenschutz & Forcehimes, 2017)) and it exhibits remarkably low toxicity. The *in vivo* LD₅₀ in humans remains unknown due to the paucity of any intentional or accidental poisoning death data. 85 The therapeutic window (also known as "pharmaceutical window") for psilocybin is comparatively very safe (Gable, 1993) and the maximum tolerated dose (MTD) is very high (Zhuk et al., 2015). Further, the therapeutic index (TI) is very high (Rucker, 2015). The TI quantifies the toxic dose as a ratio of the effective dose: $TI = \frac{TD_{50}}{ED_{50}}$. From a toxicological point of view a higher TI thus preferable is to lower one.

Rank-ordered therapeutic indices for various psychoactive substances:

- 1. Heroin ≈ 6
- 2. Alcohol ≈ 10

84 https://www.legislation.gov.uk/ukpga/2016/2/contents/enacted

⁸⁵ Alcohol, which is legal and indeed systematically promoted by the alcohol industry (even in academia), has a very unsafe LD_{50} profile and is proven to be neurotoxic (R. Da Lee et al., 2005; Jacobus & Tapert, 2013). Recent longitudinal research has shown that even moderate alcohol consumption has detrimental effects on various neuroanatomical structures (e.g., hippocampal atrophy). Psilocybin, on the other hand, has been shown to induce neurogenesis in the hippocampus in animal studies (Catlow et al., 2013).

- 3. Cocaine ≈ 15
- 4. Psilocybin ≈ 1000

Based on this hierarchical collocation it has been argued that "psychedelic drugs should be legally reclassified so that researchers can investigate their therapeutic potential" (this is indeed the title of the article by Rucker, 2015). A common metric in comparative risk assessment is the margin of exposure 86 (MOE), defined as the ratio between the toxicological threshold (defined as the benchmark dose) and the estimated average human intake. Both, MTD and MOE indicate a very benign safety profile for psilocybin, especially compared to widely used neurotoxic agents like alcohol which, per contra, has a very low MOE (Lachenmeier & Rehm, 2015) and has been associated with numerous detrimental neurocognitive (Weitemier & Ryabinin, 2003), genetic, and epigenetic effects (Y. Chen, Ozturk, & Zhou, 2013). Despite these scientific facts, psilocybin is classified as a "Class A substance" in the UK. The PSA 2016 can be regarded as a lex specialis which introduces serious burdens (viz., judicial onus) on researchers interested in neurobiology and consciousness. Ergo, scientific research on psychedelics is currently legally highly restricted due to the irrational Class A status of psychedelic substances (despite numerous "privileged" exceptions). The classification of psilocybin is *de jure* based on the fallacious presupposition that psilocybin has "no medicinal value" — a conjecture which is de facto clearly not veridical as psilocybin has numerous medical applications (but see Bogenschutz & Johnson, 2016). Therefore, the legal classification is, a fortiori, inadequate. The case of 5-MeO-DMT is specifically paradoxical given that it is a natural endogenous component of the neurochemical composition of the human brain. Furthermore, the PSA has obvious implications for the perception of psychedelics in the public sphere. Contrary to widespread public doxa (Bourdieu, 1977), epidemiological data indicate that psychedelics are not linked to psychopathology or suicidal behaviour (Johansen & Krebs, 2015; Krebs & Johansen, 2013; cf. K. Müller, Püschel, & Iwersen-Bergmann, 2013) as purported by numerous coordinated transnational large-scale mass-media campaigns (starting in the 1960s) which utilized propagandistic/PR methods à la Bernays (Bernays, 1928; L'Etang, 1999) in order justify the governmental "War on

⁸⁶ URL: http://www.efsa.europa.eu/en/topics/topic/margin-exposure

Drugs" (initiated by the Nixon administration) which was clearly politically motivated, for instance, in order to target Vietnam War opponents and racial minorities, and to serve the "prison-industrial complex" (Douglas & Pond, 2012; L. D. Moore & Elkavich, 2008). Given the extensive initial media-coverage of the campaign, the public mind is till this day still under the influence of this intentional misinformation (unconscious/implicit associations play an important rôle in social attitudes). It would require enormous orchestrated long-term efforts to counterbalance these negative stereotypical attitudes (*pro bono publico*).

Well informed legal scholars interpret the PSA as an explicit violation of the fundamental right to mental self-determination (i.e., cognitive liberty; Walsh, 2016) – particularly with respect to Article 9 of the European Convention on Human Rights 1988 (§1-2) which should protect the right to freedom of thought. Fit is obvious that cognitive liberty is a prerequisite for creativity. The PSA reduces neurodiversity and it juridically justifies the homogenisation for cognitive/neuronal processes. It selectively restricts cultural and memetic diversity and, consequently, cultural and cognitive evolution (per analogiam with the crucial importance of genetic diversity for biological evolution). The loss of memetic and cultural diversity (i.e., variability in Weltanschauungen) is a serious problem. From an anthropological vantage point, memetic homogenisation (i.e., the rapidly accelerating trend towards cultural and psychological monomorphisms due to Western hegemony) is a global and rapidly accelerating trend (this "Eurocentric phasing" is also reflected in a global reduction of linguistic diversity, inter alia). Cultural and memetic diversity are as important to the "human superorganism" as genetic diversity is for adaptivity of immune-systems

⁸⁷ Freedom of thought is crucial for democracy as it forms the very basis (s.c., a *condicio sine qua non*) for the right to freedom of speech/expression. As Erich Fromm articulated in his book entitled "The fear of freedom": "The right to express our thought, however, means something only if we are able to have our own thoughts; freedom from external authority is a lasting gain only if the inner psychological conditions are such that we are able to establish our own individuality" (Fromm, 1942, pp.207-208). It can be juridically argued that freedom of thought (mental self-determination) is a cardinal principle in international law (*jus cogens*).

⁸⁸ In an age in which public opinions are systematically manipulated (Bernays, 1928; L'Etang, 1999) and "consent is manufactured" (Chomsky, 1992; P. Fleming & Oswick, 2014) cognitive diversity is regarded as a disruptive factor which might interfere with the smooth workings of the "megamachine" (cf. Fromm, 1962; Mumford, 1967).

(a scale-independent quasi-Darwinian argument which emphasises the general importance of diversity for evolution at the micro and the macro level of various complex systems). In sensu lato, the loss of cultural and memetic diversity reduces the psychological and hence behavioural capacity of the human species to react to novel (unpredictable) challenges. In a similar manner immunodiversity (e.g., antibody diversity) is crucial in order to react to novel immunological challenges, e.g., de novo mutations in the genome of viral and bacterial pathogens, etc. A reduction of diversity ipso facto implies a reduction in degrees of freedom (e.g., possibilities to respond to a given stressor) and hence robustness and mobility, due to a reduction in combinatorial possibilities. "Conformational flexibility" (Rizzo, Tinello, Pearlstein, & Taniuchi, 1999) can thus be conceptually compared to "cognitive flexibility" (Scott, 2006), and perhaps similar dynamical/topological models can be applied. In short, cultural and memetic diversity are as important to human societal systems as genetic diversity is to biological systems.

Summa summarum, the PSA has far-reaching ramifications. It is *de facto* not evidence-based and presents a serious legal impediment to scientific research, creativity, memetic and cultural diversity, cognitive innovation, and cognitive liberty (see also Boire, 2000).

Potential for military abuse: Neuroethics and the "ticking bomb scenario"

Given the fact that 5-MeO-DMT is unparallel in its ability to virtually instantaneously dissolve psychological ego structures (viz., ego dissolution par excellence) it can in principle be utilized as a "neuropsychological weapon", for instance, in the context of military operations. Like every powerful scientific tool, it is a two-sided sword (a neurochemical Janus) that can be used to elevate and unfold human potential, creativity, and consciousness or, vice versa, to manipulate, control, and suppress it. In the past, methods that are capable of dissolving ego structures have been of great interest to the military in relation to "enhanced interrogation" — a euphemism for torture (see also O'Mara, 2009). For example, the collaboration of

Donald Hebb⁸⁹ with the CIA and various military agencies which focused on sensory deprivation/overload and other techniques to "dismantle the self" (Brown, 2007; McCoy, 2006, 2007). Many of the resulting procedures can be found in the only recently declassified U.S. Army and CIA interrogation manuals (known as the KUBARK "torture manuals"). 90 For various reasons the military has vested interests in research on neurochemistry and creativity and the "weaponization of neuroscience" is a general problem with extensive ethical ramifications which should be much more prominently discussed under the generic header of "neuroethics" (e.g., Farah, 2005). In sensu lato, creativity is a prerequisite for scientific innovation. On their official website DARPA explicitly articulates that their "success depends on the vibrant ecosystem of innovation within which the agency operates". 91 It is important to keep in mind that DARPAs enunciated mission is "to create revolutions in military science" and to maintain technological dominance over the rest of the world [...] with an annual budget of roughly \$3 billion" and that "DARPA as an agency does not conduct scientific research. Its [on average 120] program managers and directors hire defense contractors, academics, and other government organizations to do the work" (Jacobsen, 2015; content in bracket added). A related agency which was founded in 2006 is the IARPA (Intelligence Advanced Research Projects Activity) which describes its mission as follows: "To envision and lead high-risk, high-payoff research that delivers innovative technology for future overwhelming intelligence advantage." 92 IARPA provides significant funding for academia and industry research across a broad array of areas including neuroscience, cognitive psychology, chemistry, biology, mathematics, physics, computer science, linguistics, and political science, *inter alia*. IARPAs "moon-shot" programs are intended to enable researchers to engage in "ideas that are potentially disruptive to the status quo". Other research areas are "forecasting tournaments" (Tetlock, Mellers, Rohrbaugh, & Chen, 2014) and "hybrid

⁸⁹ In a symposium in 1958 Hebb stated that: "The work that we have done at McGill University began, actually, with the problem of brainwashing. We were not permitted to say so in the first publishing ..."

⁹⁰ URL: https://nsarchive2.gwu.edu//nsa/archive/news/dodmans.htm

⁹¹ URL: https://www.darpa.mil

⁹² Its neuroscience related agenda can be found under the following URL: https://www.iarpa.gov/index.php/research-programs/neuroscience-programs-at-iarpa

forecasting competitions" which aims to "improve accuracy in predicting worldwide geopolitical issues, including foreign political elections, interstate conflict, disease outbreaks, and economic indicators by leveraging the relative strengths of humans and machines" (see also Weinberger, 2011). Moreover, artificial intelligence is a highly prioritised domain which is actively pursuit by DARPA & IARPA. The book entitled "Mind Wars: Brain Science and the Military in the 21st Century" by Moreno (2012) provides a broader picture on the tight interconnections between science, academia, and the military-industrial complex, specifically with respect to "mind control". Moreno submits the following "hypothetical" scenario which highlights the importance of creativity research from a military perspective.

"Here's a science fiction scenario: an army of robots capable of movement nearly as precise as that of a human soldier, each controlled by an individual hundreds or even thousands of miles away. These automata could undertake actions that would be foolhardy for human beings but worth the tactical risk for machines; because they are controlled by people, they would have the benefit of creativity that might limit even the most advanced android. But the old-fashioned remote control scenario would have the operator pushing buttons or moving levers while seeing on a monitor what the robot is seeing, a method that would be far too clumsy for the instantaneous reactions often required in combat. What is wanted is a technology that would allow the robot to respond as soon as the distant operator does. Such a technology would, in effect, have to be able to read the intentions of the operator, his or her thoughts themselves, not merely respond to the operator's muscle movements through a mechanical apparatus." (Moreno, 2012, p.39).

Human creatures have the unique capacity for creativity which even the most complex automata hitherto lack. Creativity is thus a topic of great interest with regard to brain-computer interfaces (Vaadia, 2009) and a detailed understanding of the cognitive, neurochemical, and neuromechanical basis of creativity is of

⁹³ URL: https://www.dni.gov/index.php/newsroom/press-releases/press-releases-2017

fundamental interest to AI research which is currently utterly unable to emulate genuine creativity *in silico* (cf. Boden, 2014), a problem which, we argue, is intimately related to the "hard problem of consciousness" (Chalmers, 1995), i.e., the unsolved question of how quantitative processes such as electrochemical neuronal signal transduction relate to consciousness (and hence creativity). This "explanatory gap" (Block & Stalnaker, 1999), which is based on a dualistic Cartesian mind-matter conceptualisation, is a serious obstacle for reductive materialism (Levine, 1983) and consequently military research on robotics and AI. This research domain is currently heavily funded by various sectors of industry. Particularly autonomous weapon systems are a very active area of research (but see Bohannon, 2015). "Autonomous creative systems" (Saunders, 2012), "creative cognitive computation" (d'Inverno & Luck, 2012) and "creative evolutionary systems" (Bentley & Corne, 2002) are at the cutting-edge of contemporary transdisciplinary AI research.

Closely related to computational applications, creativity is also a crucial asset with respect to game theory (e.g., enhancing one's own creativity while reducing the opponent's capacity for creativity is an effective stratagem). For example, artificial swarm intelligence systems utilise game-theoretical calculi which require "computational creativity" for the self-organisation of networked multi-agent systems (al-Rifaie, Bishop, & Caines, 2012) and it could be argued that creativity determines the "degrees of freedom" of a given system. In sum, autonomous systems are most effective when they have the capacity to execute creative manoeuvres (predictability and cognitive/computational inflexibility are an operational and strategic disadvantage). With history in sight, the question how these evolving "creative" autonomous systems are utilised in the future is a topic of great humanistic concern, specifically given the concentration of financial and hence political power alluded to in the introduction of this paper (see also Lin, Bekey, & Abney, 2008). It needs to be accentuated that surveillance of the general civil populace is an ongoing issue (Bauman et al., 2014) and that we are currently observing a restriction of freedom of speech (e.g., algorithmic censorship) in many domains (Arquilla, 2011; Mausfeld, 2017, 2019). We argue that the developments of creative military AI have to be evaluated against this broader historical and societal background as these systems, once installed and implemented, could be utilized for plutocratic/totalitarian

cybernetic social control (and not just the ostensible "war" on alleged terrorists which might indeed be a deceptive pretext — a fairly creative and demonstrably effective "foot-in-the-door" technique, as social psychologists call it (Freedman & Fraser, 2017)).

With respect to "deceptive pretexts" another obviously related area of vested military interest is research on lying and the detection of lies. Numerous studies have demonstrated that creativity is related to the ability to deceive and to conceal information (Gino & Ariely, 2012; Gino & Wiltermuth, 2014; H. Kapoor & Khan, 2017) which is pivotal in relation to military operations as the military routinely makes use of deceptive manoeuvres, as for example evidenced by operation NORTHWOODS. 94 That is, the ability to lie is linked to various facets of creativity such as divergent thinking (Walczyk, Runco, Tripp, & Smith, 2008). Likewise the ability to detect deception (e.g., deception detection accuracy) appears to be correlated with creativity measures (cf. Walczyk & Griffith-Ross, 2008). Hence, creativity is pivotal with regard to military interrogation tactics (which frequently include torture).

A historical vantage point is crucial to frame the discussion appropriately. Psychopharmaceutical interventions were a decisive component of the German

⁹⁴ Operation NORTHWOODS is a paradigmatic historical example which illustrates the dark side of creativity (Cropley, Cropley, Kaufman, & Runco, 2010). The pseudonym refers to a plan which was formulated in 1962 (by the US Department of Defense and the CIA) to commit acts of terrorism against American civilians (false-flag attacks) in order to justify a war against Cuba (Bamford, 2001). The proposal included highly creative and deceptive strategies such as hijacking planes and orchestrated violent terrorism in U.S. cities such as Miami and Washington (inter alia). Moreover, the malignant (psychopathic) proposal included the blowing up a U.S. ship, the attacking of a U.S. civil airliner (alleged passengers were a group of college students off on a holiday), the spreading of rumors in Cuba via clandestine radio, and even the manufacturing of evidence to blame the Cuban government for the accidental death of the astronaut John Glenn. The plan was approved by the Pentagon but rejected by president Kennedy. This geostrategic example demonstrates that the importance of creativity in U.S. military expansionism and it shows the importance of gametheoretical creative thinking. The world is seen as a "grand chessboard" (Brzezinski, 1997) and creative moves and deception are essential "to win the war game". The book entitled "PsyWar on Cuba" provides detailed background information on the case and obvious parallels to the 9/11 "terrorist attacks" have been drawn (Elliston, 1999). The original NORTHWOODS document (which was declassified in 2001) is accessible under the following URL:

Blitzkrieg in WWII, for instance, the utilisation of methamphetamine (Heal, Smith, Gosden, & Nutt, 2013) as an analeptic cognitive and physical performance booster. During the 3rd Reich, Nazi "scientists" conducted extremely inhuman medical and psychological experiments in concentration camps (even on children). These experiments also involved psychedelics (and other neuroactive chemicals)⁹⁵ for the purpose of interrogation and psychological control, e.g., mescaline experiment in concentration camps in Dachau and Auschwitz. Mescaline was the first psychedelic known to Western science and it was used in the brutal "aviation tests" at Dachau in which prisoners were crushed and frozen to death (Jay, 2019). The specified objective was "to eliminate the will of the person examined"⁹⁶ with the overarching goal to develop a "truth serum" (see also Keller, 2004).⁹⁷ The mescaline experiments were

⁹⁵ Given that the brain uses "electro-chemical" signal transduction there are two pathways to interfere with its functions: 1) the chemical route 2) the electromagnetic route. Of course, both are of interest to the military and associated intelligence agencies. The former is discussed here to some extend while the latter is omitted. We refer the interested reader to the highly controversial and influential work of José Delgado on the electrical manipulation of the brain (e.g., Delgado, 1964; Delgado & Hamlin, 1956) which has later been used for the purpose of "behavior modification" in humans, e.g., direct electrical stimulation of the amygdala via brain implants – intracerebral radio stimulation (cf. Delgado, J.M.R. (1969). *Physical Control of the Mind: Toward a Psychocivilized Society*. Harper and Row). Related contemporary neurotechnological successor systems are, for example, implantable brain–machine interfaces such as NeuralinkTM, a chronically implanted cortical neuroprosthetic device (cf. Wang et al., 2013) which is currently widely popularized by Elon Musk *et alii* (see Anjana, 2019). In theory, the cortical implant provides (hackable) read & write access (770/777) to the brain. Musk outspokenly expressed the transhumanist long-term goal to achieve "symbiosis with artificial intelligence".

⁹⁶ Further information on the utilisation of mescaline in Dachau can be found in the referenced report:

U.S. Naval Technical Mission in Europe, *Technical report no. 331-45*: "German aviation medical research at the Dachau concentration camp" (1945).

⁹⁷ Such pharmacologically assisted techniques facilitate "coercive interrogation without causing physical assault". In the context of contemporary praxis it has been pointed out that "shockingly, a great majority of countries despite the implementation of laws against the torture and being signatories to various international treaties are using torture (physical and mental) to ferret out truth from an unwilling person" and further that "hypno-sedatives and psychotropic drugs are presently being used to create a 'twilight zone' or 'trance state' to break down the psychological defenses of enemy spies" (P. Kapoor, Chugh, Kapoor, & Sinha, 2008).

conducted by Dr. Kurt Plötner (University of Leipzig). After the war more than 1700 high-ranking German scientists (some of whom committed the most appalling crimes against humanity) emigrated to the USA via the top-secret operation PAPERCLIP (so named because of the tons of "paperclipped" German documents which were brought to the USA). Eventually, these scientists worked jointly in classified programs with code-names such as CHATTER, BLUEBIRD, ARTICHOKE, and MK-ULTRA (but see Jacobsen, 2014). Dr. Plötner was amongst them and joined the BLUEBIRD task force. A review of Jacobson's book (op. cit.) which is published on the official CIA website (see URL in footnote) provides the following synopsis:

⁹⁸ More humanistically oriented researchers worked on the psychotherapeutic effects of mescaline using "deep relaxation and free ideation" via "drug-induced dream-like states" in order to "shorten the course of psychoanalysis" by facilitation of profound insights (Frederking, 1955, p. 262). During the therapy the patient is confronted with his "essential problems" while the substance is psychologically active and further a "close connection between the subject and his dreams" is established.

⁹⁹ To "sing" like a bluebird.

¹⁰⁰ Several CIA subprograms systematically investigated extrasensory perception and telepathy (Jacobsen, 2017). Note in this regard that the harmala alkaloid "harmine" (which is found in the psychedelic phytochemical concoction Ayahuasca) was previously termed "telepathine" (A. L. Chen & Chen, 1939). Harmine is a β-carboline which functions as a MAO-blocker to enable the oral activity of DMT (i.e., it is present in the vine $Banisteriopsis\ caapi$).

¹⁰¹ The recruitment of Plötner by the CIA is reported in the book "Mescaline: A Global History of the First Psychedelic" (Jay, 2019). A very different story is disseminated on Wikipedia (*.de and *.com) according to which Plötner lived in Schleswig-Holstein into the early 1950s under the alias "Kurt Schmidt".

In recognition of his "scientific merits" Plötner became in 1954 a professor at the Albert-Ludwigs-Universität Freiburg. The university stated in 1961 in a letter to the ministry of education (Baden-Württemberg) that Plötner did not violate any ethical norms and that that his behaviour was immaculate — expressis verbis: "daβ Herr Dr. Plötner in keiner Weise gegen menschliche und ärztliche Ethik verstoßen, ja sich menschlich und ärztlich trotz der gegebenen schwierigen Umstände ohne Tadel verhalten hat." It is now evident that Plötner lied during the investigations. For example, he conducted human experiments with aggressively toxic chemical chlorine trifluoride and asserted later that the compound would be completely harmless.

See also: https://link.springer.com/content/pdf/bbm%3A978-0-230-50605-3%2F1.pdf

102 https://www.cia.gov/library/center-for-the-study-of-intelligence/csi-publications/csi-

 $studies/studies/vol-58-no-3/operation-paper clip-the-secret-intelligence-program-to-bring-nazi-scientists-to-america. \\html$

"In 1949, the CIA created the Office of Scientific Intelligence. Its first director, Dr. Willard Machle, traveled to Germany to set up a special program to interrogate Soviet spies. The CIA believed the Russians had developed mind-control programs and wanted to know how US spies would hold up against this capability if caught. He also aimed to explore the feasibility of creating a 'Manchurian candidate' through behavioral modification. Thus, Operation Bluebird was born. Bluebird, later called MKULTRA, was a research activity experimenting in behavioral engineering of humans. The Nuremberg Code prohibits experimentation with humans without their consent. During this program, Dr. Frank Olson, a US Army biological weapons researcher, was given the drug LSD without his knowledge, leading to his death by leaping from a building. DCI Richard Helms ordered much of the documentation destroyed, and the circumstances of his demise remain controversial to this day."

Given that a large proportion of documents was intentionally destroyed the full scope and the scientific results of the MK-ULTRA programmes remain unknown. Furthermore, central figures were granted legal immunity and numerous leading scientists simply continued their prestigious careers in psychology, psychiatry, and neuroscience — oftentimes in highly influential positions within mainstream academia. The public never received an adequate explanation why these illegal programs where conducted (besides the usual exorbitantly exaggerated enemy image

of Russia).¹⁰³ It is likely that the published information only reveals the "tip of the iceberg" and one can only speculate about how far MK-ULTRA really went. It has been stated by Dr. Robert Lashbrook (deputy director of MK-ULTRA) that the available documents were "boiler plate" cover files.¹⁰⁴ However, even the superficial cover stories are clearly extremely alarming from a human rights perspective.

Initially, psychedelics were intended for a new type of warfare. For instance, Dr. Wilson Greene was a proponent of "psychochemical warfare", i.e., "hallucinogenic or psychotomimetic drugs [...] whose effects mimic insanity or psychosis." Greene argued that if these substances would be used against enemy soldiers that "there can be no doubt that their will to resist would be weakened greatly, if not entirely destroyed, by the mass hysteria and panic which would ensue." (Jacobsen, 2014). Later, the CIA foresaw much more extensive applications than just psychochemical warfare on the battlefield and it extended these initial programs into new domains (e.g., for the purpose of interrogation and to destabilise individuals and certain "uncongenial" groups within society — such as anti-war political activists). For instance, MK-ULTRA subproject #40 focused on "LSD-type compounds both in laboratory and human beings" and the application of aerosols ("nebulizing nonaqueous solvents") to

 $^{^{103}}$ It is noteworthy that the USA is by a large margin the absolute world leader in military spending – there is serious competition (but a lot of propaganda to justify military spendings). The estimate for 2018 was \approx \$649 billion for the USA, \approx \$61.4 for Russia, while the world total was \approx 1822 (Stockholm International Peace Research Institute database, SIPRI). This expenditure is reflective of the explicit goal of "full-spectrum dominance" (Joint Vision 2020, U.S. Department of "Defense"). According to Wikipedia "full spectrum dominance includes the physical battlespace; air, surface and sub-surface as well as the electromagnetic spectrum and information space. Control implies that freedom of opposition force assets to exploit the battlespace is wholly constrained" (see also Armbrust & Chomsky, 2005). The Nobel lecture by Harold Pinter addresses this topic.

 $[\]label{eq:urconstraint} \textbf{URL:} \ \underline{\textbf{https://www.nobelprize.org/prizes/literature/2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter/25621-harold-pinter-nobel-lecture-2005/pinter-nobel-lecture-200$

Based on this ubiquitous doctrine (i.e., a ruthless domination philosophy) it follows that the domination of the "psychedelic space" is likewise of military/hegemonic interest, specifically in reference to psycho-cybernetic control. We submit that this topic is of utmost psychological relevance in the current political climate which places great emphasis on indoctrination and mind control.

 $^{^{104}}$ Source document: $\underline{https://www.cia.gov/library/readingroom/docs/CIA-RDP99-00498R000100120112-7.pdf}$

deliver various psychochemicals of interest to "non-psychotic humans". ¹⁰⁵ One can only speculate about real-world application methods of such creative ideas.

Psychedelics became a crucial component of the CIA MK-ULTRA "mind control" agenda (which consisted of more than 140 known subprojects, involved more than 80 universities and governmental institutions, and remained completely unnoticed by the public — even congress was allegedly entirely unaware of the multimillion-dollar program). The covert program was outright illegal and utilized LSD-25 and other psychoactive compounds in the most unethical ways possibly imaginable (on unwitting "subjects"). The main purpose of the program was to manipulate and control human beings, both on the individual level and the level of mass psychology. MK-ULTRA weaponised science while the general populace was absolutely nescient about the unethical experiments which were conducted which the aid of taxpayers' money. In 1975, the "Church Committee" (formally the "United States Senate Select Committee to Study Governmental Operations with Respect to Intelligence Activities") investigated the voluminous case. The committee's final report was published in 1976 in six books. 106 The report reveals how clandestine and utterly unethical the governmental agencies operated. Remarkably, one of the topics of focal interest was retrograde amnesia, i.e., how to the erase memory of past events and to then reprogram the mind with new thought and behaviours, e.g., via hypnosis (A. Winter, 2011). Psychedelic played a crucial part in this regard. The permanent changing of personality structures was a related agenda. Techniques involved countless drugs, hypnosis, sleep and sensory deprivation, electroshock experiments, induction of traumata and dissociation, et cetera. Experiments on tens of thousands of people were carried out in the most callous and merciless ways (in universities, hospitals, prisons, military facilities, i.a., without any regard for consensus of the naïve subjects). A large spectrum of human psychology and behaviour was systematically investigated in this large-scale program (Price, 2007). It is noteworthy

¹⁰⁵ Source document: https://archive.org/details/DOC 0000190090

¹⁰⁶ Official reports on illegal intelligence gathering activities by U.S. federal agencies can be accessed under the following URL: http://www.intelligence.senate.gov/churchcommittee.html

that one of the main private sector funding bodies was the notorious Rockefeller Foundation.

A disturbing case which has been associated with MK-ULTRA is the legal case referred to as the "Unabomber" (alias Ted Kaczynski). From 1959-62 Harvard psychologist Henry Murray subjected sophomores to psychologically damaging experiments which entailed the administration of LSD-25 and subsequent severe attacks on the personality structures of participants. Evidence indicates that Murrays experimentations were covertly funded via the MK-ULTRA program (Chase, 2000). Interestingly, Murray founded Harvard's Social Relations Department "which was funded by covert intelligence agencies and the Rockefeller agency through which much of his research was conducted" (Sand, 2007, p. 8). One of the projects was the euphemistically termed "Multiform Assessments of Personality Development Among Gifted College Men" 107 which subjected participants to a series of humiliating interrogations. The covert purpose of this research agenda was to develop an "interrogation-stress test". The advertised description of the experiment was vague sounded rather harmless: and "Would you be willing to contribute to the solution of certain psychological problems (parts of an on-going program of research in the development of personality), by serving as a subject in a series of experiments or taking a number of tests (average about 2 hours a week) through the academic year (at the current College rate per hour)?" Participants where not informed about the severity of the ego-shattering psychological manipulations which would be applied to them (no informed consensus) and the experiments involved psychological methods which are ethically indefensible (such as brutal attacks on the ego under the influence of psychedelics). It is of course difficult to say in how far Kaczynski's intense hate of psychology and science was influenced by these profoundly traumatic psychedelic experiences and if there is any causal relation between these events and his later crimes which killed numerous people (correlation \neq causation; i.e., the "cum hoc ergo propter hoc" logical fallacy of

 $^{^{107}}$ Full datasets (largely restricted access) and additional information on the study are available under the following URL:

 $[\]underline{https:/\!/dataverse.harvard.edu/\!dataset.xhtml?persistentId=\!doi:10.7910/DVN/NKTIZD}$

implied causality). However, he writes the following in his manifesto "Industrial Society and its Future" (Kaczynski, 1995):

(§157) "Assuming that industrial society survives, it is likely that technology will eventually acquire something approaching complete control over human behavior. It has been established beyond any rational doubt that human thought and behavior have a largely biological basis. As experimenters have demonstrated, feelings such as hunger, pleasure, anger and fear can be turned on and off by electrical stimulation of appropriate parts of the brain. Memories can be destroyed by damaging parts of the brain or they can be brought to the surface by electrical stimulation. Hallucinations can be induced or moods changed by drugs. There may or may not be an immaterial human soul, but if there is one it clearly is less powerful that the biological mechanisms of human behavior. For if that were not the case then researchers would not be able so easily to manipulate human feelings and behavior with drugs and electrical currents." (§158) "It presumably would be impractical for all people to have electrodes inserted in their heads so that they could be controlled by the authorities. But the fact that human thoughts and feelings are so open to biological intervention shows that the problem of controlling human behavior is mainly a technical problem; a problem of neurons, hormones and complex molecules; the kind of problem that is accessible to scientific attack. Given the outstanding record of our society in solving technical problems, it is overwhelmingly probable that great advances will be made in the control of human behavior. Will public resistance prevent the introduction of technological control of human behavior? It certainly would if an attempt were made to introduce such control all at once. But since technological control will be introduced through a long sequence of small advances, there will be no rational and effective public resistance."

This very brief historical discourse provides an informative background which emphasizes the enormous potential of scientific abuse of psychedelic substances, that is, for military dominance objectives, psychological manipulation, and for the purpose of cybernetic social engineering. Unfortunately, humanity has clearly not learned from history ¹⁰⁸ and immoral torture programs (which make perfidious use of psychology and neuroscience) are still being conducted in the 21st century, e.g., Abu Ghraib ¹⁰⁹ (Otterman, 2017). Only very recently APA psychologists were accused of psychological torture in the context of military operations which led to a public refusal of the APA to participate in future operations. ¹¹⁰ In 2003, the CIA and the APA

¹⁰⁸ The following pertinent statements have been ascribed to John Edgar Hoover who was the first Director of the Federal Bureau of Investigation (but see Gentry, 1991): "When morals decline and good men do nothing, evil flourishes. A society unwilling to learn from past is doomed. We must never forget our history." Furthermore, Hoover made the following epistemic statement which is reminiscent of Festinger's cognitive dissonance theory (Festinger, 1957) and Lerner's associated justworld belief hypothesis (Lerner, 1997): "The individual comes face-to-face with a conspiracy so monstrous he cannot believe it exists. The American mind has not come to a realisation of the evil which has been introduced into our midst. It rejects even the assumption that human creatures could espouse a philosophy which must ultimately destroy all that is good and decent." On a different occasion Hoover reformulated this statement concerning "doxastic logic": "The individual is handicapped by coming face to face with a conspiracy so monstrous he cannot believe it exists."

¹⁰⁹ For a morally engaging example which documents the "enjoyment" of psychopathic torture by CIA personnel see the following pictorial URL:

https://en.wikipedia.org/wiki/Abu Ghraib torture and prisoner abuse#/media/File:Sabrina-Harman.jpg

We provide this "emotionally disturbing" information not as hyperrealist "war porn" (Baudrillard & Lotringer, 2005) but in order to raise awareness to the inhuman activities of the military – an understanding which is crucial in order to appreciate the discussion at hand in a realistic context. This is particularly necessary because the military-industrial-entertainment complex (e.g., countless Hollywood movies, the "gaming" industry, etc.) generally depicts the military as an honorable and virtuous organization which "fights" for justice, freedom, and humanitarian values. The militaryindustrial-entertainment complex thus creates implicit associations (cf. Schreger & Kimble, 2017) in the public mind (via hyperreal media in the sense of Baudrillard) and scientists are not immune to these unconscious associative imprints which often take place at a very early neuroplastic stage in Piagetian/Kohlbergian cognitive/ moral development. It is therefore necessary to actively counteract these repetitive quasi-Hebbian strategies via reality-based emotional priming. However, it can be argued that humanity has already been thoroughly desensitized towards moral transgressions (and the suffering of others) due to constant habituation and associated adaptive homeostatic receptordownregulation processes, i.c., emotion-dependent amygdala habituation (for an fMRI-data based discussion of the phenomenon see Plichta et al., 2014). Such learning processes very likely have (quasi-Lamarckian) epigenetic effects which thus affect the molecular biology (e.g., methylation/gene expression) of subsequent generations of human beings (Dias & Ressler, 2014) viz., besides direct environmental effects via Pavlovian/Skinnerian conditioning and Bandura-type model learning/social learning).

¹¹⁰ See letter by the former APA President Alan E. Kazdin to George Bush: https://www.apa.org/news/press/releases/2008/10/bush-interrogations.aspx

conducted a workshop ("Science of Deception: Integration of Practice and Theory") which discussed the use of sensory overload and pharmacological interventions. According to Harper, workshop attendees were asked questions such as "What are the effects of sensory overload on the maintenance of deceptive behaviors? How might we overload the system or overwhelm the senses and see how it affects deceptive behaviors? What pharmacological agents are known to affect apparent truth-telling behavior?"

In a post festum attempt to justify the leaked information the APA subsequently wrote a statement which later disappeared from their website 112: "The workshop provided an opportunity to bring together individuals with a need to understand and use deception in the service of national defense/security with those who investigate the phenomena and mechanisms of deception." It has been argued that the "attempt to hide its history is not surprising, because the kind of activities discussed in these workshops are exactly like those that involved CIA and military mind control torture programs going back fifty years or more, and evidently still operational today" (Kaye, 2010).

5-Meo-DMT can be extremely destructive to the human psyche when it is utilized with the wrong intentions. It is therefore of utmost importance to develop legal frameworks which prevent its application in military settings and especially in "situations of crisis" and in matters of "national security", so called "ticking time bomb scenarios" (Brecher, 2008) in which the principles laid down by the human rights convention (e.g., Geneva Conventions and the U.N. Convention Against Torture) are deemed to be no longer applicable for utilitarian reasons (as implicitly argued, for instance, by the David Horowitz – founder of the conservative think tank "David Horowitz Freedom Center"). Here is an example of a ticking-bomb Gedankenexperiment ¹¹³ (a hypothetical moral dilemma):

¹¹¹ Source URL: https://harpers.org/blog/2010/05/apas-unpredictable-past/

¹¹² The web never forgets and the statement has been mirrored by the Internet Archive under the following URL:

https://web.archive.org/web/20030802090354/http://www.apa.org/ppo/issues/deceptscenarios.html

¹¹³Adapted from the "Association for the Prevention of Torture" (APT).

URL: https://www.apt.ch/content/files-res/tickingbombscenario.pdf

Suppose that a person with knowledge of an imminent terrorist attack, that will kill many people, is in the hands of the authorities and that he will disclose the information needed to prevent the attack only if he is tortured. Should he be tortured? Should the most powerful psychoactive substances known to science (in casu, 5-MeO-DMT) be utilized to completely break down the persons sense of self for the purpose of "enhanced" interrogation?

In the psychological literature on morality similar provocative decision-making scenarios have been experimentally investigated *in extenso*, e.g., the "trolley problem" and the "foot-bridge dilemma" (more recently in virtual reality environments in order to increase external real-world validity and generalizability of results). There are generally two standpoints on morality: 1) a utilitarian view and 2) a deontological view. We maintain that torture should be denied on principle moral and ethical grounds. That is, we argue from a deontological stance (à la Immanuel Kant) as opposed to a utilitarian stance (à la David Hume). Specifically, we submit that there are certain moral and ethical boundaries which should *never* be transgressed, independent of the contextual circumstances (viz., moral absolutism vs. moral

relativism).¹¹⁴ This is a meta-ethical position based on *a priori* principles of moral rationalism.

There are several rather complex "special case" objections to Kant's categorical imperative but, as a general abstract heuristic, the underlying moral principle is very accurate. It also concords with Mahatma Gandhi's philosophy of nonviolence (Sanskrit: $Ahims\bar{a}$) ¹¹⁵ which is rooted in ancient Indian Vedanta philosophy and asserts that violence against another conscious being is never justifiable, under no circumstances (categorically). We regard nonviolence as a moral axiom (an aprioristic foundational moral primitive which defies further reduction) in line with Kant's unconditional stance.

"Handle nur nach derjenigen Maxime, durch die du zugleich wollen kannst, dass sie ein allgemeines Gesetz werde."

Transl.: "Act only according to that maxim whereby you can at the same time will that it should become a universal law."

~ Immanuel Kant (1785), Grounding for the Metaphysics of Morals ¹¹⁶

The application of 5-MeO-DMT in a military context can have disastrous consequences because the compound *completely* breaks down psychological defence mechanisms. A person under the influence of 5-MeO-DMT is utterly defenceless and the "interrogator" has consequently "god-like sovereignty" (cf. Améry, 1966). Stimuli which are normally perceived as relatively harmless can be perceived as extremely threatening and their impact can be synergistically amplified in unpredictable ways – thereby causing irreversible psychological traumata. (We use the word trauma in

¹¹⁴ There are rather complex epistemological reasons for this position which we omit in the interest of parsimony (e.g., based on Sôritês paradoxon, deductive logic, and the quasi-Popperian problem of demarcation, i.e., at what point does a problem become a problem of "national security").

¹¹⁵ In fact, $ahims\bar{a}$ is not merely non-violence but it is a principle of non-harming. It is a principle with far-reaching moral implications (but see Marques, 2012) which also applies to animals and it is consequently of pertinence for experimentation on animals in science (see also Singer, 1990).

¹¹⁶ Immanuel Kant, Gesammelte Schriften. Hrsg.: Bd. 1-22 Preußische Akademie der Wissenschaften, Bd. 23 Deutsche Akademie der Wissenschaften zu Berlin, ab Bd. 24 Akademie der Wissenschaften zu Göttingen, Berlin 1900ff., AA IV, 421 / GMS, BA 52.

the etymological sense — a psychological wound.) Physical torture is always also psychological torture, but it leaves open the theoretical possibility to distance (dissociate)¹¹⁷ psychologically from the torturer which allows in principle for a partial coping with the traumata. On the contrary, psychological torture targets the very core of a human being and therefore destroys the entire person and not "just" his/her physical body. In the hands of malignant individuals 5-MeO-DMT can be an extremely cruel and destructive neuropsychological weapon which can induce a form of permanent damage which is unimaginable to a normal person as it intervenes into the deepest core dynamics of consciousness.

Given the rapid breakdown of 5-MeO-DMT within the human organism (pharmacokinetic elimination) it is in principle difficult to prove its illegal application post festum. It follows on legal grounds that an absolute (universal) prohibition of the use of 5-MeO-DMT for military purposes is of great importance (no "margin of discretion"). Nullum crimen, nulla poena sine lege (Jimenez de Asúa, 1951; Rauter, 2017). This is especially pertinent in the present historical context in which basic human rights have been repeatedly violated behind the façade of dubious political motives (e.g., within the justificatory/exculpatory utilitarian frame of "national"

¹¹⁷ We suggest that "somatic disidentification" (i.e., the insight that "I am not the body") is a crucial therapeutic psychological mechanism with respect to the treatment of various traumata with 5-MeO-DMT (e.g., sexual abuse, physical abuse, but also body dysmorphic disorders such as anorexia nervosa which are based on a strong identification with the physical aspect of human existence). In other term, 5-MeO-DMT helps to transcendent the body/ego-identity and enables a higher "spiritual" identification which allows for emotional detachment from traumata. This line of reasoning is based on the premise that the transcendental experiences occasioned by 5-MeO-DMT facilitate a remodeling/recasting of the self-concept (i.e., how the self is conceived).

 $^{^{118}}$ The "Body of Principles for the Protection of All Persons under Any Form of Detention or Imprisonment" adopted by the UN General Assembly in 1988 prohibits "methods of interrogation which impair the capacity of decision of judgment." (A/RES/43/173).

security"). We cannot allow for double standards and moral elasticity when it comes to human consciousness itself! 119

Conclusion

We would like to close by reconnecting the topic back to the introduction of this essay. In a recent PNAS article entitled "Trajectories of the Earth System in the Anthropocene" it has been stated that: "Collective human action is required to steer the Earth System [...] Such action entails [...] behavioral changes, technological innovations, new governance arrangements, and transformed social values" (Steffen et al., 2018, p. 8252).

We strongly agree with this general conclusion (note that the term "Earth System" is used in the singular not in the plural) and we argue that solidarity, collectivism, holism, morality, and altruism (as opposed to competition, individualism, atomism, corruption, and egocentrism) are pivotal for the evolution of humanity on this planet which Buckminster Fuller metaphorically labelled as "spaceship earth" (Anker, 2007) in an attempt to emphasize the common fate of all "passengers". Fuller wrote the following in his final work entitled "Critical Path" (1981):

"History shows that, only when the leaders of the world's great power structures have become convinced that their power structures are in danger of being destroyed, have the gargantually large, adequate funds been appropriated for accomplishing the necessary epoch-opening new technologies. It took preparation for World War III to make available the funds that have given us computers, transistors, rockets and satellites to realistically explore the Universe."

¹¹⁹ For instance, C.G. Jung wrote extensively about the "collective unconscious" and we should be very cautious with any powerful interventions into this domain of existence, especially when we are dealing with severely (dissociative) traumatic procedures in a military context. Neuroscience has only very recently begun to integrate the far-reaching implications which can be derived from the rich history of analytical psychology (for a historical discussion of various conceptualizations of unconscious processes in connection with contemporary neuropsychological findings see Bob, 2003).

A similar argument could be articulated for the "inner universe". Humankind has travelled through outer space and we now possess detailed charts of the moon and many other extra-terrestrial objects. However, hitherto modern science is utterly unable to provide a comprehensive cartography of the human mind (let alone consciousness). Ergo, the great frontiers of $21^{\rm st}$ century science are internal and psychological, and it should be psychologies primary focus to systematically chart the largely unexplored "antipodes of mind" – the "terra incognita" – as Aldous Huxley eloquently formulated it (Huxley, 1954). In view of this it has been effectively argued that the discovery of psychedelic neuroactive substances is scientifically as important to the study of the mind as the invention of the microscope to progress in chemistry or the telescope to astronomy (Grof, 2000, p. 297). We would like to foreground that psychology is not reducible to neuroscience — it is a different level of analysis (the persistent "post hoc ergo propter hoc" fallacy is widespread; correlation \neq causation).

Given the "extraordinary danger of the current moment" it is undeniable that we as human beings need to radically change our egoistic behaviour as a species, otherwise our existence on this planet will come to a catastrophic end soon. It is of pivotal momentousness to unveil perfidious attempts which try to exploit the present potential for positive change for the justification of the implementation of the neoliberal agenda which thrives for further global centralization and hence concentration of power (Coleman, 2005; Mausfeld, 2017; Smith & Chomsky, 1987). That is, real (or strategically self-created) problems are used to legitimate measures (under a false pretence) which would otherwise not be admissable (cf. the politician's syllogism). History has taught humanity that *prima facie* seemingly well-intended motives have often been abused for the consolidation of power, e.g., the "war on terror" (Melley, 2017). The egocentric, competitive, and intrinsically antidemocratic principles of neoliberal capitalism have invaded all domains of life (Mausfeld, 2019). Domains in which they are utterly inappropriate and obviously destructive, such as

¹²⁰ Expressis verbis from the official statement of the BULLETIN OF ATOMIC SCIENTISTS.

URL: https://thebulletin.org/2018-doomsday-clock-statement

¹²¹ The fallacy of the undistributed middle (*non distributio medii*): Major premise: To improve things, things must change. Minor premise: We are changing things. Conclusion: Therefore, we are improving things. N.B. Often the proposed solution is depicted as "the only alternative".

the educational system, ¹²² the health care system, geriatric care, the family systems, and even the scientific endeavour itself ¹²³ (cf. military Keynesianism within the military-academic complex ¹²⁴). The egocentric neoliberal doctrine has thus deeply influenced all aspects of human cognition and behaviour. As an implicit ideology it has been gradually assimilated and is therefore largely imperceptible (indoctrinated ideologies govern behaviour primarily via unconscious processes). Ludwig Wittgenstein termed this type of imperceptibility "aspect blindness", e.g., a fish cannot see water. Sheldon Wolin (*1922;†2015) proposed the term "inverted totalitarianism" to describe a situation in which suppression and servitude are inversely perceived as the highest form of freedom because the mind is no longer capable to make any meaningful comparisons as it is no longer able to even imagine any alternatives to the dominant *status quo* (imagination and creativity are cognate,

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Source URL: https://krugman.blogs.nytimes.com/2009/06/24/weaponized-keynesianism/

¹²² E.g.: Chomsky, N (2003). The functions of schools: Subtler and cruder methods of control. In D. A. Saltman & D. Gabbard (Eds.), Education as enforcement: The militarization and corporatization of schools. New York: NY: Routledge, pp.25-36.

¹²³ The essential Humboldtian ideals of independent academic institutions (which safeguard academic freedom) have been replaced by the military-industrial-academic complex and a profit-oriented business model (Chomsky, 2015); see also the effects of intrinsic vs. extrinsic motivation on creativity (Prabhu, Sutton, & Sauser, 2008).

 $^{^{124}}$ The triad has been addressed in the book entitled "University in Chains: Confronting the Military-Industrial-Academic Complex" (Giroux, 2015).

Military Keynesianism refers to the stance that governments should increase military expenditures to foster economic growth (see also Gilmore, 1999). This principle has been précised by Barney Frank: "These arguments will come from the very people who denied that the economic recovery plan created any jobs. We have a very odd economic philosophy in Washington: It's called weaponized Keynesianism. It is the view that the government does not create jobs when it funds the building of bridges or important research or retrains workers, but when it builds airplanes that are never going to be used in combat, that is of course economic salvation."

Noam Chomsky wrote extensively on the ubiquitous "militarization problem", for instance in 1993 in an article in Z MAGAZINE (entitled: The Pentagon System): "Social spending may well arouse public interest and participation, thus enhancing the threat of democracy; the public cares about hospitals, roads, neighborhoods, and so on, but has no opinion about the choice of missiles and high-tech fighter planes. The defects of social spending do not taint the military Keynesian alternative, which had the added advantage that it was well-adapted to the needs of advanced industry: computers and electronics generally, aviation, and a wide range of related technologies and enterprises."

ergo, the systemic antagonism of these higher-order mental faculties consolidates the *status quo*).

Aldous Huxley foresaw this development of psychologically manufactured consensus in a lecture entitled "The Final Revolution" delivered at the University of Berkley in 1962:

"There will be, in the next generation or so, a pharmacological method of making people love their servitude, and producing dictatorship without tears, so to speak, producing a kind of painless concentration camp for entire societies, so that people will in fact have their liberties taken away from them, but will rather enjoy it, because they will be distracted from any desire to rebel by propaganda or brainwashing, or brainwashing enhanced by pharmacological methods. And this seems to be the final revolution."

In the present tense, Zeese & Flowers (2014) characterized the situation as follows:

 $^{^{125}}$ The lecture was delivered on the 20^{th} of March 1962 at the Berkeley Language Center. The original recording of the lecture can be found in the UCLA Library Digital Collections as tape 157a under the following URL:

"We are living in a time of Inverted Totalitarianism, in which the tools used to maintain the status quo are much more subtle and technologically advanced. These include propaganda and control of the major media outlets that hide the real news about conditions at home and our activities around the world behind distractions such as high-profile citizen trials and celebrity gossip. The major electronic media, owned by six corporations nationwide, also routinely misinforms the public about domestic and foreign policy. A recent example is the "Fiscal Cliff." Another tool is to create insecurity in the population so that people are unwilling to speak out and take risks for fear of losing their jobs and being unable to afford food, a home and health care. Changes in the work environment, such as the attack on unions and the war on whistleblowers, have led to greater job insecurity. Changes in college education also silence dissent, including the trend toward adjunct rather than tenured professors. Adjunct professors, now comprising 85 percent of faculty, are less willing to teach topics that are viewed as controversial. This, combined with massive student debt, are tools to silence the student population, once the center of transformative action."

These quotations indicate that the problems humanity is facing are not confined to the physical sphere (i.e., militarisation and loss of biodiversity) but that the obliteration and eradication is furthermore psychological. The neoliberal agenda has devastating effects on human morals, values, and behaviours. It will take significant longitudinal *collective* efforts to counteract its cumulative effects on the human psyche, or else future generations will become incapacitated to even conceive alternative ways of thinking because the *status quo* is the only *Weltanschauung* they have ever known.

Behaviour is governed by thought and the basis of thought is consciousness. Ergo, the deduced essential question is: How can human consciousness be transformed for the better to change the trajectories of the Earth System and to enable a sustainable and free future for mankind? Science (and, *ipso facto*, particularly psychology and neuroscience) plays a central rôle in answering this question and a systematic investigation of the neurochemical substratum of consciousness (i.e., the essence of humanness) is consequently a decisive research agenda which should be prioritized.

Technological progress and economic growth clearly cannot solve the present problems – they are a part of it (mechanistic/materialistic solutions cannot substitute for the lack of love which lies at the very heart of the problem at hand). So far, contemporary science has largely neglected the extraordinary experiences catalysed by various naturally-occurring psychedelic materials, some of which have been used as "neurocognitive tools" since time immemorial across numerous cultures for the purpose of healing and divination, in order to create states of communion, empathy, and transcendence, and to facilitate deep inter- and intrapersonal insights 126 (Jones, 2007; Tupper, 2002). Further, the potential of the extremely powerful endogenous neurochemical 5-MeO-DMT has not yet been explored at all (it is wide-open uncharted scientific territory). Specifically, research in the domain of creativity appears to be vital for species survival because humanity needs to find alternative ways of existence. If there is a chance that endogenous neurochemicals such as 5-MeO-DMT can catalyse a radical novel (less egocentric and more loving) creative way of thinking which fosters biophilia, egalitarian attitudes, solidarity, empathy, altruism, emotional intelligence, and noetic epistemological insights into the interconnectedness of nature, and indeed all of existence, then it is sciences moral obligation to take this potential very seriously as creative change is de facto an evolutionary matter of paramountcy. The transformational ego-dissolving experience of nonduality might prove to be the quintessential antidote to the rigid, habitual, materialistic, dualistic, and egoic mindset which lies at the very core of the existential

The Ancient Greek aphorism "know thyself" (one of the 147 Delphic maxims) is pertinent and some theorist hold that psychedelics were a quintessential spiritual catalyst in the "Eleusinian mysteries" (Bizzotto, 2018; Wasson, Hofmann, & Ruck, 1979), a secret rite of passage which constituted a pivotal event in the lives of numerous Greek thinkers who deeply influenced the very basis of Western thought (amongst the initiates were with all likelihood eminent "lovers of wisdom" such as Socrates, Plato, Aristotle, Plotinus, and Cicero, i.a.). According to Plato, the ultimate purpose of the initiation was the "assimilation of divinity" and "to lead us back to the principles from which we descended" (Taylor, Raine, & Harper, 1969, p. 368) or what Plotinus described as the "the flight of the alone to the alone", an expression which echoes the Kaivalya Upanishad (kaivalya means liberation (but see Deussen, 1906)). It is interesting to consider Plato's allegory of the cave this relation, e.g., the therein described immense difficulty to face the sun after lifelong imprisonment in a confined cell of false perception.

crisis. ¹²⁷ That is, an egoic and competitive mindset is incompatible with the imperative need for collective action and the interpersonal effects of transpersonal experiences might provide significant impetus to realize this communal goal. The transformation of deep-seated *plutonic* self-identity schemata (i.e., how human creatures conceive of themselves) is perhaps the most pivotal aspect. The culturally conditioned dualistic psychological schism which separates man from nature (Fromm, 1962) stands in sharp contrast with an integral, interconnected, unitive, and holistic worldview.

Recently a bipartite model of 5-HT signalling has been proposed which is pertinent in this regard (Carhart-Harris & Nutt, 2017). It has been suggested that *passive coping* ¹²⁸ (stress moderation via passive toleration of the stressor) is the brains default modus (status quo) which is mediated via 5-HT_{1A} receptor signalling. Active coping (engaging and changing the cause of stress), on the other hand, is conjectured to be mediated via 5-HT_{2A} signalling. Specifically, the authors proposed that 5-HT_{2A}-mediated plasticity may be crucial "as the level of adversity reaches a critical point". The concept "plasticity" was generically defined as the "capacity for change" (but see Carhart-Harris & Nutt, 2017).

With respect to paradigm-change (i.e., a shift from a dualistic egocentric tier to an interconnected unitive tier) it is important to note that in the past "revolutions of thought" have been systematically subverted by the neoliberal "financial power élite" (Harvey, 2007; Hill & Kumar, 2009; Mausfeld, 2019) which invests heavily into studies of social psychology, group dynamics, and analyses of social movements (Mausfeld, 2017; Sugarman, 2015). Paradigm-shifting social energy is intentionally diffused and systematically redirected towards substitutional "strawman objectives". Movements are infiltrated, "Red Herring strategies" are employed, and effective activists are coopted or otherwise socially discredited via various *ad hominem* arguments as a *persona non grata*. By this psychological stratagem real change,

¹²⁷ The Chinese logogram for the term "crisis" 危機 (pinyin: wēijī) is composed of "danger" 危 and "opportunity" 機 (also "danger at a point of juncture" but the exact meaning is polysemous and a matter of debate amongst sinologists).

 $^{^{128}}$ The concept of learned helplessness appears to be of relevance with respect to passivity and 5- HT_{1A} agonism/antagonism (cf. Wu, 1999).

which targets the roots of the problem, is prevented. *In brevi*, change is intentionally inhibited by those who benefit from the corrupt *status quo* and powerful slogans such as "save the planet" and "change for a better future" are taken advantage of to expedite the ongoing process of centralisation of power. Tactics to stymie effective change include cognitive infiltration (Sunstein & Vermeule, 2008, 2009), internal/external coöptation, exploitation of the principles of group-dynamics such as group-pressure and conformity, cybernetic methods such as algorithmic censorship of digital information, various forms of psychological manipulation such as induction of fear and distrust, etc. pp. (but see Chomsky, 2016). The antagonism between creativity and control is a long-standing issue which was central in the historical context of the 18th century enlightenment revolution which shares many characteristics with the current situation (Fromm, 1962). Humanistic motives and neoliberal capitalism are incompatible. The former seeks freedom and equality while the latter is based on control and exploitation. 129 Creativity is fundamentally based on freedom and liberty. Per contrast, neoliberal control is based on power and suppression. Both are diametrically opposed cannot coexist in harmony (Gormley, 2018; Harvey, 2007).

Besides challenging the destructive egocentric *status quo*, epistemological insights into the nondual ontology of existence (e.g., dual-aspect monism/neutral monism) ¹³⁰ challenge some of the most central assumptions of contemporary mainstream science, e.g., the notion of detached scientific objectivity which is a cognitive/epistemic illusion (Hoffman, 2016; cf. Wiseman, 2015). A nondual conceptualization of reality might force us to rethink our axiomatic (non-evidence based and naïve) *doxa* (Bourdieu, 1977) about the way we conceive reality and practice science, e.g., the stipulated

¹²⁹ For example, Immanuel Kant's leitmotif *Sapere aude* (dare to think for yourself) which he used in his essay "Beantwortung der Frage: Was ist Aufklärung?" (Answering the Question: What Is Enlightenment?) from 1784.

¹³⁰As Bertrand Russel put it: "The whole duality of mind and matter [...] is a mistake; there is only one kind of stuff out of which the world is made, and this stuff is called mental in one arrangement, physical in the other." (Russell, 1913, p.15). Russel's monism stands in sharp contrast with the (mainly unquestioned) "reductive materialism" working-hypothesis which forms the predominant basis of contemporary science.

dichotomy between observer and observed 131 and the widespread *belief* that the brain produces consciousness. 132 A nondual reconceptualization is therefore implicitly perceived as a threat to the widely adopted "quasi-Newtonian" status quo which has in reality already been fundamentally revised by modern quantum physics, viz., the widely held and mainly unquestioned metaphysical assumption of local realism is no longer empirically tenable (Handsteiner et al., 2017; Schlosshauer, Kofler, & Zeilinger, 2013). A large proportion of mainstream science still operates under an outdated deterministic Newtonian paradigm (from a Bayesian epistemology perspective an update of priors in the light of new empirical evidence is required). "Belief bias" plays a central part in this irrational situation (Evans et al., 1993). In his seminal book "The structure of scientific revolutions" Thomas Kuhn pointed out that it is a general phenomenon that paradigm challenging anomalies "that subvert the existing tradition of scientific practice" (T. Kuhn, 1970, p. 6) are neglected as long as possible. Along the same line Abraham Maslow discussed the "Psychology of Science" in great detail in his eponymous book (Maslow, 1962). Maslow formulated a quasi-Gödelian critique of orthodox science and its "unproved articles of faith, and taken-for-granted definitions, axioms, and concepts". Fundamental research on extremely powerful consciousness-expanding substances like 5-MeO-DMT might thus force us the rethink largely unquestioned axiomatic epistemological and ontological assumptions. Prima vista, this critical line of thought might sound farfetched and even absurd 133 but such an argumentum ad lapidem constitutes no valid reason for the *prima facie* rejection of the idea.

From an anthropological perspective, it might be helpful to look at the way indigenous cultures utilised 5-MeO-DMT traditionally and how they related to the Earth System, to each other, and to the Self (i.e., *psyche* and *physis*). From an evolutionary vantage point it might be argued that ego-dissolving psychoactive plants

¹³¹ Cf. Cartesian dualism and the Heisenberg cut (Atmanspacher, 1997).

¹³² This view is gradually changing, for instance, Christof Koch stated in a 2014 SCIENTIFIC AMERICA article that "the mental is too radically different for it to arise gradually from the physical" (p. 2), thereby highlighting the explanatory gap in contemporary neuroscientific theorizing. ¹³³ "If at first the idea is not absurd, then there is no hope for it." ~ Albert Einstein (as cited in Hermanns & Einstein, 1983)

and fungi played an important rôle in the comparably harmonious (symbiotic) relationship which governed man and nature before the industrial revolution (McKenna, 1992). Again, such a proposal predictably appears absurd to the modern (hyper-technological) mind. However, the present situation is more than merely absurd — it is clearly pathological (e.g., nuclear weapons positioned all over the globe — ready to launch at any time). Any real solution to the "anthropogenic global crisis" will be at odds with the predominant *status quo* and will thus cause intensely virulent cognitive dissonance in the minds of most passively-obedient dogmatic *status quo* followers (cf. Sir Francis Bacon's analogy on "ants, spiders, and bees" expounded in his *Novum Organum*, 1620).

From a general philosophy of science and set-theoretical perspective it can be cogently argued that if science wants to live up to its ideal to capture reality in its entirety, without leaving any residue, it needs to integrate neurochemicals like 5-MeO-DMT into its modelling efforts – especially given the fact that this alkaloid is an endogenous components of the human brain and, ergo, in all likelihood of evolutionary relevance (the rôle of 5-MeO-DMT in neurobiology is currently utterly elusive and we argue that neurochemical vestigiality is an unlikely explanation). In conclusio, any model which incorporates only a specific (a priori selected) subset of the available quantitative and qualitative data is ipso facto at best incomplete (and in the worst-case scenario prejudiced, dogmatic, and systematically biased). We are confident that a mature science will sooner or later investigate 5-MeO-DMT in the context of human psychology and neurobiology. It is just a matter of time — and of neuropolitics (cf. Rose & Abi-Rached, 2014). Nil desperandum. Tempora mutantur, nos et mutamur in illis¹³⁴ – or to use the better-known Greek semantic equivalent: Panta rhei. The fact that we are living in a world which can change let Leibniz to the conclusion that we are living in *le meilleur des mondes possible*. ¹³⁵

¹³⁴ Transl.: "Times are changed; we, too, are changed within them." In the context at hand this implies that no ideology ever survived the test of time. Change is the only historical constant (a tautological statement evocative of the self-referential "*Liar paradoxon*" and Gödel's incompleteness theorem).

¹³⁵ Transl.: "The best of all possible worlds" in *Essais de Théodicée sur la bonté de Dieu, la liberté de l'homme et l'origine du mal (Essays of Theodicy on the Goodness of God, the Freedom of Man and the Origin of Evil*) published in 1710.

We will end with three thematically interrelated quotations from the distinguished polymath William James who was intrinsically interested in mystical and transcendental experiences (as evidenced, *inter alia*, by his excellent book "The varieties of religious experience"). In the introduction of his essay "The hidden Self" James articulated the following (a quotation which might surprise those who stereotype James as a prototypical exemplar of American pragmatism, while, in actuality, his versatility and open-mindedness defies social categorization):

"The scientific-academic mind and the feminine-mystical mind shy from each other's facts, just as they shy from each other's temper and spirit. Facts are there only for those who have a mental affinity with them. When once they are indisputably ascertained and admitted, the academic and critical minds are by far the best fitted ones to interpret and discuss them - for surely to pass from mystical to scientific speculations is like passing from lunacy to sanity; but on the other hand if there is anything which human history demonstrates, it is the extreme slowness with which the ordinary academic and critical mind acknowledges facts to exist which present themselves as wild facts with no stall or pigeon-hole, or as facts which threaten to break up the accepted system. In psychology, physiology, and medicine, wherever a debate between the Mystics and the Scientifics has been once for all decided, it is the Mystics who have usually proved to be right about the facts, while the Scientifics had the better of it in respect to the theories." (James, 1890, pp. 361–362)

James conducted self-experiments with the gaseous chemical compound nitrous oxide and the mescaline ¹³⁶ containing psychedelic cactus "peyote" (*Lophophora williamsii*). He was enthusiastic about the effects of nitrous oxide (which is not a genuine psychedelic) and it has been argued that his first-hand experiences with this dissociative anaesthetic played a central rôle for the development of some of his most

¹³⁶ Mescaline (3,4,5-trimethoxyphenethylamine) is a naturally-occurring psychedelic alkaloid in the phenethylamine class which was first isolated by the German pharmacologist and chemist in Arthur Heffter in 1897 who conducted self-experiments to compare mescaline with peyote (cf. Kauder, 1899; Lewin, 1894).

central ideas on mysticism and revelation (Moon, Kuza, & Desai, 2018). However, his experimentation with the truly visionary peyote¹³⁷ was unfortunately unsuccessful. One can only speculate: Which turn would Western psychology have taken if James' mind would have entered the psychedelic realm? James concluded his paper on nitrous oxide inhalation as follows:

"It seems, indeed, a causa sui, or 'spirit become its own object'. My conclusion is that the togetherness of things in a common world, the law of sharing, of which I have said so much, may, when perceived, engender a very powerful emotion; that Hegel was so unusually succeptible [sic] to this emotion; throughout his life that its gratification became his supreme end, and made him tolerably unscrupulous as to the means he employed; that indifferentism is the true outcome of every view of the world which makes infinity and continuity to be its essence, and that pessimistic or optimistic attitudes pertain to the more accidental subjectivity of the moment; finally, that the identification of contradictories, so far from being the self-developing process which Hegel supposes, is really a self-consuming process, passed from the less to the more abstract, and terminating either in a laugh at the ultimate nothingness, or in a mood of vertiginous amazement at a meaningless infinity." (James, 1882)

Years later, James eloquently articulated the importance of unbiased and eclectic inquiry in light of his "radical empiricism" stance. The entire disquisition is presented in his essay "A World of Pure Experience":

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 $^{^{137}}$ Radiocarbon dating of archaeological specimens of peyote indicate that it has in all likelihood been used since prehistoric times as long as $\approx\!5700$ years ago (El-Seedi, De Smet, Beck, Possnert, & Bruhn, 2005).

"To be radical, an empiricism must neither admit into its constructions any element that is not directly experienced, nor exclude from them any element that is directly experienced. For such a philosophy, the relations that connect experiences must themselves be experienced relations, and any kind of relation experienced must be accounted as 'real' as anything else in the system. Elements may indeed be redistributed, the original placing of things getting corrected, but a real place must be found for every kind of thing experienced, whether term or relation, in the final philosophic arrangement." (James, 1904, p. 534)

Conflict of interest statement

The author declares no conflict of interest.

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