11

Delirious Brain Chemistry and Controlled Culture

Exploring the Contextual Mediation of Drug Effects[1]

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Today, there is a growing consensus that the dichotomy of nature and culture does not hold up. Deconstructing this distinction is not only a standard move in humanities scholarship, the emergence of the field of cultural neuroscience indicates that brain researchers are also beginning to explore the hybrid ontology of nature and culture. In psychiatry, biopsychosocial models of mental illnesses have been *en vogue* at least since the 1980s (even if, in clinical practice, pharmacotherapies outdid both psychotherapy and social therapy). Most recently, the proponents of a critical neuroscience (Choudhury, Nagel, & Slaby, 2009) have called for linking neuroscience and society by integrating insights from the social studies of neuroscience into neuroscientific research itself. Often these ontological professions go along with calls for interdisciplinary collaborations between natural and cultural scientists. In practice, however, the development of such interdisciplinary research paradigms has turned out to be difficult.

This chapter explores the potential of critical neuroscience in the context of an ethnographic case study from contemporary neuropsychopharmacology showing how neurochemistry and culture broadly conceived interact. It is based on anthropological fieldwork in two laboratories in Zurich and San Diego, which study the effects of hallucinogenic drugs on humans and animals respectively. Hallucinogen research is particularly suitable to explore the tense relationship between cerebral nature and scientific culture because substances such as LSD (Lysergic Acid Diethylamide) and psilocybin are pharmacologically powerful agents and yet their effects depend on a multitude of non-

[1] This chapter is a revised translation of Nicolas Langlitz (2010), "Kultivierte Neurochemie und unkontrollierte Kultur. Über den Umgang mit Gefühlen in der psychopharmakologischen Halluzinogenforschung." *Zeitschrift für Kulturwissenschaften*, no. 2, 61–88. The original German article is followed by a debate between the author and three natural and cultural scientists (Malek Bajbouj, Ludwig Jäger, & Boris Quednow).

Critical Neuroscience: A Handbook of the Social and Cultural Contexts of Neuroscience, First Edition.
Edited by Suparna Choudhury and Jan Slaby.

pharmacological, including cultural, factors. This raises the question whether anthropological second-order observations of how drug researchers observe their scientific objects can be fed back into these neuropsychopharmacological practices of first-order observation. The chapter addresses this issue by critically discussing a stillborn proposal from the 1950s concerning a research paradigm at the intersection of psychopharmacology and anthropology to investigate the cultural determinants of drug action.

Ethnographic Vignette I: Bad Trip

Experiences with hallucinogenic drugs can be emotionally difficult. Therefore, there is a far-reaching consensus within the community of hallucinogen researchers that scientists should familiarize themselves with the effects of these drugs before administering them to test persons. Personal experience is meant to help researchers to treat subjects empathically. Such drug experiences can be acquired legally in the context of so-called pilot studies, which also provide an opportunity to test the experimental setup before the actual trial begins.

During my fieldwork in Franz Vollenweider's laboratory Neuropsychopharmacology and Brain Imaging in Zurich, two scientists were preparing a study involving the drug psilocybin, the pharmacologically active ingredient of magic mushrooms. One of them—let's call her Anna—had never taken this substance. Therefore, Anna and her colleague Patrick decided to conduct a pilot study.[2] When Anna was administered the drug, the experiment worked smoothly. But when her older and more experienced colleague Patrick took the drug he received a nasty surprise. Patrick had already served as a test subject in two psilocybin trials without any difficulties. But this time, his experience was different. The experiment involved an EEG (electroencephalograph) measurement during which the test subject was shown a series of images on a computer screen. These images were part of the International Affective Picture System, which provides photographs of standardized emotional stimuli divided into three categories: pleasant (for example, landscapes, lovers), unpleasant (for example, attack scenes, mutilations), and neutral (for example, furniture, household articles). Even though all images selected for the experiment were meant to be affectively neutral, they scared Patrick. Eventually, he asked for the rest of the measurement to take place without the images.

By losing this attentional anchor his world was thrown completely out of kilter. First, a sweater appeared like a threatening grimace. Then the small EEG chamber grew bigger and bigger. Eventually Patrick saw himself as a midget in a huge white space. He felt like the only human being in the whole universe. In a self-reflexive moment, he began to worry that this onslaught of negative affects might interfere with the measurements. He felt nauseous and wanted to break off the experiment. But this thought scared him even more: didn't it prove that he was indeed in real trouble? As a psychiatric researcher, he conceived of hallucinogen intoxication as a kind of psychosis. Now he experienced how he himself gradually slipped into a schizophrenia-like state and felt threatened. The situation was further complicated by

the role reversal between Patrick who was responsible for the study and his younger colleague Anna who now had to take care of him without anyone directing her. In retrospect, Patrick said:

> I tried to stay in charge, supervising how Anna was looking after me, checking how I was affected by the stimuli, whether the room would be bearable for the subjects, etc. I tried to evaluate all of this. The problem was that I wanted to keep everything under control, which is simply impossible on psilocybin. That made me fully aware of the fact that I was losing control. So I got all worked up about this. You need to let go.

After this test run the researchers decided to decorate the EEG chamber to make it look friendlier. They also replaced the allegedly neutral images by photographs from the category "pleasant."

Ethnographic Vignette II: "This is it!"

When I entered the EEG laboratory the experiment was already under way. The room was lit only by a computer screen displaying the brain waves of the test person. Through an observation window I could look into a neighboring chamber where the subject was located. At first glance, I could not see anything. But as my eyes got used to the darkness I began to make out the shaved head of a Zen master dimly illuminated by a monitor in front of him. He was sitting upright in a leather armchair. A tangled mass of wires seemed to be growing out of the back of his head only to disappear in the dark. Jan, a Swiss meditation teacher in his 50s, had been administered psilocybin to examine how the drug affected his consciousness. The young brain researcher who had invited me to observe this measurement was very excited. While Jan was meditating his brainwaves were particularly "calm," the scientist explained to me, showing strong activity in the alpha range.

After the measurement, Jan appeared happy and serene. The researcher interviewed him to hear about the experience that had accompanied the peculiar EEG pattern, which had been recorded. Jan reported that, at the beginning, he had seen frightening faces and carnivalesque processions of ghosts. But he remembered the *Tibetan Book of the Dead* and the fact that such visions are a mere projection of the ego. Eventually he turned to a simple mantra and began to focus his awareness on his breath. Thereby, he managed to free himself from this spooky spectacle and moved on to a "higher state of consciousness," as he called it. To his surprise and even disappointment the following experience of cosmic unity was associated with the name of Jesus. This must have been due to his upbringing in a Christian family, the dedicated Buddhist mused. But, finally, he also thought of Buddha and this further deepened his state of ego-dissolution. In comparison with his everyday consciousness, he recounted, he attained a much more profound insight into the fact that all existence was love. "Divine love," he specified, "or even better: being." This realization appeared to him as a perennial truth: "It has always been that way and it will always be that way. [illegible] that state," he told us, "I thought: This is it! This is it!"—the state

The Persistence of the Subjective

These two ethnographic vignettes demonstrate that the same pharmaceutical can elicit very different, almost diametrical experiences. As far back as the 1950s, the British writer Aldous Huxley (1954) described that hallucinogenic drugs could take one to heaven or to hell. Accordingly, they were used for both the experimental investigation of mystical states (Griffiths, Richards, McCann, & Jesse, 2006; Langlitz, in press; Pahnke & Richards, 1966) and as pharmacological models of schizophrenic psychoses (Beringer, 1927; Langlitz, 2006; Vollenweider, 1998). However, representatives of these two approaches were often divided by their antagonistic worldviews. One party was indignant at the pathologization of spiritual experience while the other party ridiculed the mystification of a deranged brain metabolism. This conflict is based on the assumption that both camps are talking about the same brain chemistry, which they only interpret differently. As a pharmacologist from the Vollenweider group put it: "Hallucinogens enable you to have limit-experiences. Whether one regards such liminal states as mystical experiences or as psychotic delusions is mostly a matter of interpretation" (Hasler, 2007, p. 39 [my translation]).

However, it was Vollenweider's laboratory, which endowed these antipodal experiences with objectivity by identifying their neural correlates. For this purpose, Vollenweider and colleagues (1997) used positron emission tomography (PET) in order to measure the metabolic activity in the brains of test subjects under the influence of psilocybin. Afterwards, they asked them to fill in questionnaires to record their subjective experiences. Subjects had to rate statements such as "I saw strange things which I now know were not real," "I felt an all-embracing love," or "I felt threatened without realizing by what" on a scale of 1–10. More than 90 items of this sort were supposed to capture and quantify three dimensions of altered states of consciousness: "visionary restructuralization" encompassing hallucinatory phenomena, "oceanic boundlessness" dealing with ecstatic experiences, and "dread of ego-dissolution" covering the more horrifying aspects of their experiences. Such self-rating scales translated inner experiences into numbers, which could then be correlated with PET measurements. Vollenweider's investigation demonstrated that dread of ego-dissolution and the blissful transgression of ego-boundaries went along with the activation of different brain areas (Langlitz, 2008; Vollenweider, Vollenweider-Scherpenhuyzen, Bäbler, Vogel, & Hell, 1998). Consequently, mystical experiences and bad trips are not two interpretations of the same neurophysiological event, but neurophysiologically distinct states.

In scientific practice, however, this objectifying approach to the study of psycho-pharmacologically induced mind–brain states soon reaches an ethico-epistemological limit. Test persons are not objects of investigation that can be observed from a distance. For ethical reasons, researchers cannot passively watch a subject sliding deeper and deeper into a state of horror. The scientists familiarize themselves with the effects of the applied substances precisely to become more empathic, and to be better equipped to take countermeasures if subjects are about to get emotionally unstable. But bad trips are also detrimental to the scientific study as such. As participation in

experiments is voluntary, test subjects can break off measurements at any time if they feel too uncomfortable. In that case, the scientists would lose their data. In both their own interest and their subjects' interest, they cannot sit back while their perfectly impartial measuring devices register the neural correlates of exacerbating "dread of ego-dissolution."

Despite all objectivizing procedures (standardized experimental protocols, instrumental recordings, and so forth) the experimental space continues to be pervaded by the subjectivity of both test persons and scientists. The epistemic virtue of objectivity (Daston & Galison, 2007) associates itself with the cultivation of intersubjectivity: the art of taking good care of subjects. In practice, the neuroscientific investigation of (altered states of) consciousness cannot be reduced to the correlation of first-person and third-person perspectives, but crucially involves the second-person perspectives and social interactions of researchers and test persons alike (Roepstorff, 2001). In such experimental settings, neuroscientists cannot adopt the position of detached observers, but must interact with their subjects to obtain data and insights marked by these engagements. Here, brain research—just like anthropology—turns out to be a form of participant observation. Consequently, it is equally entangled in the epistemological problematics of the human sciences (Langlitz, 2010).

Setting Matters: The Limits of Placebo Controls

The ethnographic investigation of the practice of contemporary hallucinogen research shows that scientists are well aware of the impact of environment, interpersonal treatment, and expectations on subjects' experiences and brain states. Nevertheless the predominant study design of pharmacological research continues to be the randomized, double-blind placebo-controlled trial. While all other conditions are supposed to be kept identical, subjects randomly receive a pharmacologically active drug or an inactive placebo. Neither the researcher nor the test person knows whether the former or the latter is administered. The underlying assumption is that all psychosocial and cultural factors are also operative when the placebo is given. Hence, when subtracting the placebo's effects from the effects of the pharmacological agent, the drug's own activity is revealed in its purest form. If the psychotropic effect of the drug should have been affected by the organism's environment or mood, this influence is hereby made to disappear.

But what would happen if the pharmacological activity of a substance also changed the relationship between a living thing and its environment—not in a deterministic and unilinear way, but depending on the quality of the environment? In this case, the particular environment would still be inscribed in the observed pharmacological effect when the placebo effect (measured under identical conditions) has been subtracted. Instead of effectively neutralizing the impact of the environment, placebo controls merely render it invisible.

During my fieldwork in Mark Geyer's animal laboratory in San Diego I discovered a peculiar practice based on such an ecological understanding of psychopharmacology. On the eve of a set of hallucinogen experiments, the rats were brought from their home cages in the basement to the lab facilities to familiarize them with this unknown

environment and their handling by the experimenters. This procedure, prescribed by a special protocol, was based on an experiment which had shown that LSD made rats more afraid of new things and open spaces. In an unfamiliar box, in which infrared rays registered the animals' exploratory behavior, the rats moved around less under the influence of LSD. They preferred to stay close to the walls instead of venturing into the center of the box and generally showed less curiosity. Next, the researchers connected the rats' home cages to these unknown motion-tracker boxes, allowing them to go back and forth between the two spaces. In spite of the LSD effects, they moved around normally in the familiar space of the home cage whereas they displayed increased fearfulness in the unfamiliar space (Geyer & Krebs, 1994). Hence, this dread of the new (neophobia) could neither be entirely attributed to the drug nor to the environment, but resulted from a drug-induced change of the animals' attitudes toward these different environments. The custom of familiarizing the rats with the laboratory on the day before the experiment, which had been derived from this finding, was supposed to minimize the impact of the novelty of the lab space on the rodents' behavior. It did not, however, eliminate the ecological conditioning of the animals' minds.

This experiment and the ethnographic observations presented above point to the fact that the realm of the mental cannot be reduced to the brain, but encompasses the organism's surroundings (Clark & Chalmers, 1998; Noë, 2005). To study the psychopharmacological activity of a drug, it is not sufficient to look only at its effects on the mind/brain while turning a blind eye to the environment, as happens in randomized placebo-controlled trials. The physical, atmospheric, social, and—at least in the case of humans—cultural qualities of the setting, in which a drug is taken, also determine how an organism responds to it. In allusion to Margaret Lock's (1995) discovery of "local biologies" (in the sense of biological differences molding and containing subjective experience and cultural interpretations), the decisive role of the circumstances of drug ingestion can be taken as a powerful indicator of the existence of "local pharmacologies."

Controlling for Culture

The fact that the psychopharmacological effects of hallucinogens depend on the complex contexts of drug ingestion was first described in 1959 by anthropologist Anthony Wallace. Wallace was primarily working on Native Americans. At the time, however, he served as research director at an institute of psychiatry where hallucinogen experiments were conducted. Wallace noted that the experience reports of white test persons who had been given mescaline differed significantly from the reports of Native American participants in peyote ceremonies ingesting a cactus also containing mescaline. After administration of the drug, Caucasian experimental subjects experienced extreme mood shifts—from depressive and anxious to euphoric. When eating peyote buttons, indigenous people, on the other hand, displayed an "initial relative stability of mood, followed by religious anxiety and enthusiasm, with tendency to religious reverence and

contact with a new, more meaningful, higher order of reality". Wallace attributed these and other differences to two factors: the impact of the setting in which the drug was taken and the different meanings ascribed to the physiological "primary drug effects" (Wallace, 1959 pp. 58–69).

From this observation, Wallace concluded that placebo-controlled studies (which, at the time, were only beginning to get established) had to be supplemented by "cultural controls." He proposed not only to vary the pharmacological activity of the administered substance, but also to test the same drug under different cultural and situational circumstances in order to systematically investigate (and subsequently control) the impact of these conditions on psychotropic effects. In this context, Wallace's notion of culture was quite broad. The suggested culture controls comprised the socio-cultural background of test subjects, their personality and expectations vis-à-vis the experiment, their social treatment by laboratory staff, and the experimental setting as a whole. He speculated that these factors would not only affect the effects of hallucinogens, but of all psychopharmaceuticals.

While placebo-controlled studies soon became the gold standard of pharmacological research, Wallace's culture-controlled trials never really caught on. For scientific, disciplinary, economic, and political reasons, biological psychiatry and psychopharmacology had an interest in attributing the effects of drugs to the drugs alone. This ideology of "pharmacologicalism" helped psychiatry to be acknowledged as part of scientific medicine, enabled pharmaceutical companies to fulfill the Food and Drug Administration's regulatory requirement to demonstrate specificity of drug action, and legitimized the War on Drugs (DeGrandpre, 2006).

At the same time, culturalist approaches gained the upper hand in the field of cultural anthropology, which became increasingly alienated from the biological part of the discipline. In the last quarter of the twentieth century, the disciplinary unity of anthropology broke apart as anthropologists came to reject the association of non-European peoples with early hominids and non-human primates that had been constitutive of US anthropology's holistic agenda, but was enmeshed in the distinction between the West and the rest. The culturalist response to this complicity of anthropological holism and colonialist racism was not to apply a biocultural perspective to humankind overall instead of non-European others alone, but to exclude biological approaches and to focus on the study of cultures—both Western and non-Western (Clifford, 2005; Segal & Yanagisako, 2005). Rather than identifying the "cultural determinants" of psychopharmacological effects as Wallace (1959) had sought to do, culturally oriented studies of drugs focused on the drug as symbol (for example, Myerhoff, 1974) or on historically and culturally different interpretations of identical neurochemical effects (Becker, 1963; Zinberg, 1984). These approaches were based on the implicit ontological assumption that there is one nature and many cultures.

Having fallen between the two stools of cultural anthropology and psychopharmacology, Wallace's "method of cultural and situational controls" led a shadowy existence. However, such marginalized practices can enable a critique that does not come from outside, but from the fringes of psychopharmacology itself (Dreyfus & Rabinow,

hybrid of natural and cultural science and whether anthropologists are willing to return to an anthropology that is not split into biological and cultural.

Conclusion

Against the background of ubiquitous calls for interdisciplinary perspectives and for overcoming the nature/culture dichotomy, this question might appear rhetorical. But Wallace's proposal to control for culture presupposes a reification and essentialization of culture, which few cultural anthropologists still subscribe to today. In order to understand the cultural dimension of human life, "thick descriptions" (Geertz, 1973) seem to be more promising than the experimental variation of isolated factors in the laboratory because the effect of each individual factor depends on its role in a whole network of factors (Latour, 1999, pp. 174–215). Such networks might well be too complex to be controlled successfully. This makes it difficult for laboratory scientists to extract statistically significant signals from the cultural noise—even if the entirety of non-pharmacological factors has a powerful impact. Therefore, Wallace's culture-controlled trials do not appear to provide a satisfying answer to the question of how to factor in complex environments. If experience is over-determined by intricate contexts, then field studies appear to be a more suitable approach than controlled experiments, but play only a very marginal role in psychopharmacology. What are still missing in the life sciences are methods which are not—not even for heuristic purposes—based on reduction, but measure up to the complexity of life itself (Mitchell, 2009).

Even though cultural anthropologists often denounce scientific reductionism they will not have much to contribute to overcoming it as long as they reject the dichotomy of nature and culture ontologically while continuing to be committed to culturalist methodologies. All too often they look at the natural sciences exclusively as culture—in other words from the perspective of second-order observation. Second-order observation means to observe how others observe the world while ignoring what they look at. Taking up such a perspective can be important because it reveals the blind spots and contingencies of first-order observations of the world (Luhmann, 1998). For example, it allows us to see, as this chapter has shown, that from the point of view of placebo-controlled trials the contextual mediation of drug effects cannot be recognized. But to the extent that cultural anthropology takes part in the scientific cultures that it observes, it should also contribute to their improvement.

For this purpose, it is not enough to restrict oneself to second-order observations and to uncover contingency after contingency. At some point, second-order observation should inspire the invention of new practices of first-order observation (Langlitz, 2007). Therefore, Wallace's proposal of culturally and situationally controlled trials—however dissatisfying it might be—is well worth a second look. A productive debate between natural and cultural sciences is only possible if observations of the world and observations of such observations are discussed together. This is the project of critical neuroscience. But it is still a long way off for this

Acknowledgements

Without the hospitality of Franz Vollenweider, Mark Geyer, and their research groups I would not have been able acquire the insights into neuropsychopharmacological practice informing this chapter. The Volkswagen Foundation's European Platform for the Life Sciences, Mind Sciences and Humanities provided an inspiring and well-funded forum to experience and think through the intricacies of interdisciplinary collaborations. Finally, I would like to thank Donya Ravasani, Suparna Choudhury, Allan Young, Maria-Christina Lutter, and Daniela Hammer-Tugendhat for their helpful responses to earlier drafts of this chapter.

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Part IV
Situating the Brain
From Lifeworld Back to Laboratory?

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A Handbook of the Social and Cultural Contexts of Neuroscience

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