From LSD to the IRB

Henry Beecher's Psychedelic Research and the Foundation of Clinical Ethics

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Introduction

Lysergic acid diethylamide (LSD) is one of the most pharmacologically potent psychoactive substances ever identified and became the drug of choice for a 1960s counterculture whose mantra was "turn on, tune in, and drop out." First synthesized in 1938 by Dr Albert Hoffman,[1] a Swiss chemist investigating the properties of the fungus ergot, LSD was explored in the worlds of chemistry, medicine, psychology, and espionage until it was brought to national attention by Dr Timothy Leary. Leary was a well-respected psychologist on the faculty of Harvard University who developed an interest in hallucinogens after a personal experience with psilocybin in 1960 and ultimately developed this interest into both a scientific study and a cultural vision. Throughout the early 1960s, Leary and his colleagues—Dr Ralph Metzner and Dr Richard Alpert—explored the effects of psychedelics at Harvard,[2] resulting in both fame and infamy—especially for their studies on students. While Leary stands out as an early pioneer of psychedelic research at Harvard, it is rarely appreciated that Dr Henry Knowles Beecher had published important work on the psychology of LSD some 10 years earlier. How is it that Beecher found his way to the study of LSD? The answer to this question is a fascinating history that spans from the shores of Italy in the 1940s to the frontiers of bioethics in the 1960s. It appears heretofore unrecognized that Beecher's study of LSD in the 1950s may bear an important relationship to virtually all of his other endeavors.

Beecher's Research on LSD

In 1956, Beecher and coinvestigators published a study on LSD and a related compound lysergic acid monoethylamide.[3] It is important to

note that LSD was legal at this time and remained so until the mid-1960s. The subjects in the study were given predrug and postdrug Rorschach tests and psychologic evaluations and vital signs were observed. It was found that the degree of change in the subject's interpretation of the Rorschach tests was positively correlated with preexisting "personality disturbances or maladjustment." While certainly an interesting scientific investigation, a question naturally arises: why would Henry K. Beecher, whose early work was on the more orthodox topics of pain and pulmonary physiology, be studying Rorschachs and hallucinogens in his "Anesthesia Laboratory"? One answer is that the study reflects Beecher's interest in the preexisting mood and the subjective response of individuals receiving drugs. Indeed, Beecher and his coinvestigators—Dr Louis Lasagna and Dr John von Felsinger—published a broader 2-part investigation on mood and drugs in the 1950s.[4,5] LSD, as was noted in the discussion of one of his papers, was one of the most potent agents in inducing changes on the Rorschach test and could thus be viewed as a window to the phenomenon of subjective response. In this era of hallucinogenic research, LSD was considered more of a "psychotomimetic" rather than a "psychedelic" drug. The former term implies that the drug experience "mimics psychosis," whereas the latter denotes that the drug is "manifest in the mind." Although in the introduction of his paper on LSD it was noted that the substance was associated with schizophrenia-like symptoms, Beecher's conclusion was that it likely expands or reflects the preexisting state of mind. This conclusion would later be echoed by Leary and others, who claimed that experiences under LSD reflect a subject's "set" (ie, mind-set) and "setting" (ie, environment) rather than the mere pharmacology of the drug.[2] To understand Beecher's interest in concepts similar to set and setting, one must consider his experience in World War II. By doing so, intriguing questions arise as to the relationship between his psychedelic research and the US Government.

■ Beecher in World War and Cold War

Henry Beecher enthusiastically entered the conflict of World War II and served as a consultant in the beachhead campaigns of North Africa and Anzio, Italy. While in Anzio, Beecher noted that soldiers who were badly injured seemed to require far less morphine to relieve their pain than would a civilian with a comparable injury. He kept careful notes of his observations and would later hypothesize that pain had 2 aspects: the tissue injury itself and the *meaning* of the pain to the individual.[6] The meaning of the pain clearly related to the environment in which the pain was experienced and the expectations and perceived consequences of that pain. Beecher published these observations after returning to the MGH and initiated a research program investigating the topic of

pain and subjective response.[6] Thus, his work on LSD and the evaluation of its effects was consistent with the broader context of his scientific inquiry of psychologic meaning and drug response that originated in the war.

Although it is certainly clear why Beecher might have been interested in LSD, it is a more fascinating question as to why the US Army was interested. Beecher's work, as noted in the paper, was "supported in full by a grant from the Medical Research and Development Board of the United States Army."[3] It is likely that the Army was less concerned with the mysteries of the mind than the mysteries of mind control. Indeed, it has been reported that[7]:

> *The intelligence agencies working through the US government financed drug research. An example is that Dr Beecher of Harvard University was given via the US Army Surgeon General's Office $150,000 to investigate "the development and application of drugs which will aid in the establishment of psychological control."*

It was common for investigators who were funded by such sources to publish some results in the medical literature and transmit other results directly to the government. It is thus unclear how extensive Beecher's research on hallucinogens actually was. Beecher's work on this topic may also have been funded or in some other way supported by the Central Intelligence Agency (CIA). In a book on the history of LSD, Beecher is referred to as "an esteemed member of the Harvard Medical School faculty who conducted drug experiments for the CIA".[8] The CIA had a secret project exploring drugs for mind control (a project called MKULTRA) and they were at the very least aware of Beecher's research for the army. Beecher's name appears in several files of the CIA and MKULTRA program that were obtained after declassification of the documents (present author's emphasis in bold)[9]:

> *CIA-020795-A 1 folder; 0.1 cu.ft. Source:* ***Central Intelligence Agency Collection****: Army Contents Description:* ***File on Henry Beecher describing LSD research*** *and experiments for the Army, along with Louis Lasagna. Descriptors: Biological Effects; Human Subjects; Medical Diagnosis; Medical Records; Research—Nontherapeutic; Scientific Data; Robert Stone; Harvard Medical School; War Department (War).*

> *Subproject 107:* ***MKULTRA****: American Psychological Association: Army Testing: Assassination: Raymond A. Bauer: Berlin Poison Case: Biometric Lab: Biophysical Measurements:* ***Beecher (Henry K.)****: Brainwashing.*

Beecher's involvement in these programs was revealed decades after his death by his research associate Louis Lasagna during interviews with the Advisory Committee on Human Radiation Experiments in the 1990s.[10] As an investigator who was one of the early pioneers of ethics in human experimentation, it comes as little surprise that Beecher was reticent to discuss such work. It may appear paradoxical that Beecher both advocated the ethical treatment of human subjects and had also engaged in potentially unethical work on hallucinogens for the

government. A more compelling hypothesis, however, is that Beecher advocated ethical treatment of human subjects largely because of such work.

■ Beecher's Psychedelic Research and Other Contributions: Pain, Placebo, and Protocol

The impressive list of Beecher's accomplishments includes his work on pain, his study of the placebo effect, and his advocacy for ethical considerations in human experimentation. Although a relatively small part of his work, Beecher's study with LSD nonetheless has a clear relationship to his other important contributions. It was described above that Beecher's interest in the relationship of set and setting to drug response was likely stimulated by his observations of analgesia during World War II. This interest has relevance to his study of the placebo effect: Beecher had an interest in the psychologic aspect of subjective response to a drug. Although this was certainly clinically relevant, it also carried an important scientific significance. Beecher astutely realized that to study analgesics, his experimental conditions required comparison with proper "inert" controls.[6,11] Note that in his work on LSD, he compared the drug's effect with that of the closely related (but less psychoactive) compound lysergic acid *monoethylamide*.[3] This reflected his interest in distinguishing the effect of the drug from the effect of the subject's expectations regarding the drug. It was, in part, through the use of inert substances as experimental controls that Beecher came to elucidate the role of the placebo effect.

The relationship of Beecher's LSD research to his later contributions in bioethics is perhaps more interesting. Beecher had knowledge of Nazi experiments with mescaline in the concentration camp at Dachau[12] and was well aware of the potential for ethical abuse in the study of hallucinogenic substances. Although one might assume that his knowledge of Nazi experimentation with psychoactive drugs on unwitting subjects would have deterred any involvement in such research, it is important to note that Beecher was a vocal opponent of the application of the Nuremberg Code (crafted in response to such Nazi atrocities) to American medical experimentation. In one of his first important papers on bioethics in 1959, Beecher stressed the difficulty of applying the Nuremberg Code to clinical experimentation and brought into question the very concept of informed consent.[13] In his classic 1966 publication in the *New England Journal of Medicine*,[14] however, Beecher expressed a far more stringent view of ethical violations in medicine, a view that likely led to the implementation of Institutional Review Board protocols and informed consent (It is important to note that Beecher himself believed that ethical responsibility should rest with the investigator rather than the institution or its standardized regulations). It could be speculated

that one component of his more developed bioethical perspective came from his direct knowledge of CIA experimentation with LSD.

In 1953, Dr Frank Olson, a scientist who specialized in biologic warfare, killed himself after being unwittingly dosed with LSD at a CIA-sponsored party (Dr Sidney Gottlieb, the director of the MKULTRA project, had adulterated his drink—along with many others at the party).[15] In the subsequent weeks after the "experiment," Olson became increasingly withdrawn, depressed, and paranoid—and finally jumped, fell, or was pushed headlong through a closed window to his death 10 stories below. Although it is unclear if Beecher knew about this incident (which was extensively concealed by the CIA), he most certainly knew about a similar incident in which a Swiss psychiatrist committed suicide after being administered LSD. The Geneva physician had suffered from a depression that was exacerbated after the LSD experience, resulting in her death. In fact, Beecher prepared a memorandum regarding MKULTRA that was cited in the Senate Subcommittee Hearing on the project in 1977.[16] Beecher's own research suggested that the drug might exaggerate a preexisting psychopathology[3] and recognized that "this case is a warning to us to avoid engaging subjects who are depressed, or who have been subject to depression."[16] It is a matter of speculation whether or how Beecher's knowledge of CIA experimentation influenced his ethical development. Bioethicist Dr Johnathan Moreno[10] has suggested the following:

> *What was the source of Beecher's strong commitment to the ethics of human research? One element was his strong Christian religious commitment. Another was likely his own army-sponsored research in the early 1950s, in which he directed projects that exposed healthy subjects to hallucinogens without their consent.... Thus it was that research sponsored by the national security state inspired one of its own investigators to take on the task of reforming the system of human experimentation.*

In addition to his broader bioethical concerns, it seems that Beecher had also become a conscience for the psychedelic research movement. This claim is based on his report to the CIA described above,[16] his direct criticism of Timothy Leary in the 1960s,[8] and his views on testing the effects of LSD during the experience of death. In 1971, 2 years after his retirement from the MGH and 5 years before his own death, Beecher published a commentary on an article discussing the administration of LSD to dying patients[17]:

> *The results recounted are based entirely on the subjective responses and symptoms, and conclusions are drawn without the use of mandatory controls. In a meaningful evaluation of LSD, it must be known whether it is the LSD or the strong suggestion, which precedes the drug that is operant in this situation; the powerful action of the placebo has been unequivocally demonstrated. Apart from the serious difficulties stemming from the established potential dangers of LSD as a drug, there are those possibly arising from violations of privacy.*

Note the recurrent themes of LSD, subjective response, experimental controls, the placebo effect, and bioethics. This particular subject

even relates to Beecher's interest in end-of-life issues and brain death. Of note, the article was published in the final issue of the *Psychedelic Review*, a journal founded by Timothy Leary. Beecher's perspectives on LSD were thus present in the literature for the entire crucial period of its study.

■ Conclusions

Dr Henry Knowles Beecher holds an esteemed place in the history of anesthesiology for his work on pain, the placebo effect, and bioethics, and also the work at Harvard that led to an independent anesthesia department and laboratory. His foray into the world of psychedelic research, although relatively unknown, seems to be intimately intertwined with many of his great accomplishments. It is fascinating to consider that Beecher's study of LSD—and its subsequent abuse by the government—may have led him to the groundbreaking work that established the foundation of clinical ethics.

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■ References

1. Lee MA, Shlain B. *The Complete Social History of LSD: The CIA, the Sixties, and Beyond*. New York, New York: Grove Weidenfeld; 1985:xvii.
2. Leary T, Metzner R, Alpert R. *The Psychedelic Experience: A Manual Based on the Tibetan Book of the Dead*. New York, New York: Citadel Press; 1964.
3. von Felsinger JM, Lasagna L, Beecher HK. The response of normal men to lysergic acid derivatives (di- and mono-ethyl amides). *J Clin Exp Psychopathol*. 1956;17: 414–428.
4. Lasagna L, von Felsinger JM, Beecher HK. Drug-induced mood changes in man. 1. Observations on healthy subjects, chronically ill patients, and "postaddicts." *J Am Med Assoc*. 1955;157:1006–1020.
5. von Felsinger JM, Lasagna L, Beecher HK. Drug-induced mood changes in man. 2. Personality and reactions to drugs. *J Am Med Assoc*. 1955;157:1113–1119.
6. McPeek B. Pain. In: Richard K, ed. *This is No Humbug! Reminiscences of the Department of Anesthesia at the Massachusetts General Hospital*. Boston: Massachusetts General Hospital; 2003:225–237.
7. Government-sponsored programs for mind control have been widely reported. This particular quotation comes from F. Springmeier, C. Wheeler: The Illuminati Formula Used to Create an Undetectable Total Mind Controlled Slave. Chapter 3, The Use of Drugs.
8. Lee MA, Shlain B. *The Complete Social History of LSD: The CIA, the Sixties, and Beyond*. New York, New York: Grove Weidenfeld; 1985:86.

9. These citations can be found on-line at: http://www.nemasys.com/rahome/library/programming/mkultra.shtml; http://www.gwu.edu/~nsarchiv/radiation/dir/mstreet/research/docs/precis.txt.
10. Moreno JD. Bioethics and the National Security State. *J Law Med Ethics*. 2004;32:198–208.
11. Lasagna L, Mosteller F, von Felsinger JM, et al. A study of the placebo response. *Am J Med*. 1954;16:770–779.
12. John Marks states in the first chapter of The Manchurian Candidate (a book on psychedelic mind control experiments, not to be confused with the 1950s novel of the same name): *Information on the German mescaline and hypnosis experiments at Dachau came from "Technical Report no. 331-45, German Aviation Research at the Dachau Concentration Camp," October, 1945, US Naval Technical Mission in Europe, found in the papers of Dr. Henry Beecher*. The book can be found in the Shaffer Library on-line at: http://www.druglibrary.org/schaffer/lsd/marks1.htm.
13. Beecher HK. Experimentation in man. *J Am Med Assoc*. 1959;169:461–478.
14. Beecher HK. Ethics and clinical research. *N Engl J Med*. 1966;274:1354–1360.
15. Lee MA, Shlain B. *The Complete Social History of LSD: The CIA, the Sixties, and Beyond*. New York, New York: Grove Weidenfeld; 1985:31.
16. Transcripts of the Senate hearing on MKULTRA can be found on-line at: http://www.parascope.com/ds/documentslibrary/documents/mkultrahearing/mkultraHearingAppendixA.htm
17. Beecher HK. A physician's response to the psychedelic experience in the death encounter/Response to Pahnke lecture by a physician. *Psychedelic Rev*. 1971;11:15–17.