The Biology of Human Information Processing

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The use of psychoactive drugs to treat illness and reduce the suffering of individuals is important, but such use serves short-range goals. The most important use of psychoactive drugs in general—and 3,4-methylenedioxymethamphetamine (MDMA) in particular—is to help understand the human mind. There are three points that will be made in this article in that regard: (1) Humanity's most pressing problem is to understand the human mind; (2) To date, progress has been disappointing; and (3) Among the tools for studying the mind, psychoactive drugs hold the most promise. The term "mind" will henceforth refer to the human mind: those human information processing operations that are inferred either from observing behavior or through introspection. Thus, it includes emotion as well as memory and perception.

The importance of understanding the mind is obvious. Humanity has in the past been at the mercy of nature. The physical sciences have attempted to control nature in the external world and that task is far advanced. Biology concerns itself with the nature operating inside the human body and that science is also advancing rapidly. Soon, molecular biology will bring even genetic destiny under the control of the mind. Thus, just as external environments are now largely controlled by the mind, so too the internal environments may be equally controlled. So far, what has been done to the external environment is not very reassuring. Obviously, if the mind serves humankind poorly, all the other powers that have been gained can bring grief almost in exact proportion to their potential for giving joy.

The disappointing status of psychology today may also be equally obvious, but the reasons for that are worth considering. The retarded status of psychology can in large measure be blamed on problems in finding independent points of reference. Everyone has a mind that is ready to be studied, and almost all humans consider themselves to be innate expert psychologists. That is what William James was talking about when he said, "Every one knows what attention is." The hazards of using a device to study itself can easily be overlooked; for in point of fact, no one knows what attention is.

When these self-styled experts want to communicate with one another, their empirical references (i.e., their minds) are not directly accessible to their colleagues and so their observations cannot be directly checked. Thus there is a tendency to use the writings of recognized experts in place of empirical data that can be replicated.

It is interesting to notice how many psychologists call themselves by the names of the pioneers who have made significant observations or who at least have made up wonderful lexicons for common observations. For example, psychologists with clinical leanings may call themselves Freudians, Jungians, Skinnerians or Bernians. Those with a more ethical bent may use other names, such as Christian, Buddhist or Mohammedan. By contrast, can one ever recall meeting a molecular biologist who called him/herself a Crickian or a Watsonian?

In the hard sciences, cognomia are generally reserved for techniques of measurement or for measure-

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ments themselves, because individuals in science tend to be less important than the observations. For example, in molecular biology the Southern blot was named for Dr. Southern, but reversing the technique is referred to as the northern blot. This relative irrelevance of the individual vis-à-vis objective data is a sign of healthy science. It is also perhaps to the advantage of the molecular biologist that not everyone has the kind of daily contact with autoradiographs that they do with psychological processes.

The mind has been referred to as a great frontier, an apt metaphor that may easily be expanded on. When pioneers return from the frontier, they have only personal experiences to deliver. The observations may be valuable, but they are essentially anecdotal and must be accepted on the authority of the explorer. When serious developments begin, teams are required and external, fixed points of reference become essential. As long as the mind is used to study the mind, without biological operations as points of reference, one must rely on one's singular experiences or else one must believe what one is told. The only possible exceptions are those rare individuals who can spend years meditating in ashrams until they are able to duplicate the experiences of the masters (or at least say that they can). By contrast, as soon as there are physical points of reference, everyone with a a reasonable level of competence can begin to test things for themselves.

Leaving aside psychophysics, which maintains its scientific status by staying as far out on the periphery as possible, biologically based studies of the mind have largely depended on disease. Neuropsychologists have used the results of tumors and traumas to learn about sensory input, motor output and the organization of language. For the biological psychiatrist, psychiatric disease has been most informative. It has also supplied a major impetus for the development of psychoactive drugs, which in turn have been the source of much of what is now known about neurotransmitters and neuromodulators.

The advantages that drugs now offer as tools for studying the mind are perhaps not so obvious. When one wants to manipulate the brain so as to alter functioning of the mind, drugs are much more satisfactory than disease. With drugs, one does not have to wait for nature to do the experiments. Even more important, however, is the fact that subjects can be used as their own controls.

One may reasonably wonder why drugs are such marvelous tools if they have delivered so little in the way of helping to understand the mind. One reason is that the effective utilization of a drug to understand the mind by simultaneously manipulating the mind and the brain requires an understanding of what the drug is doing to the brain. It is only very recently that there has begun to be some understanding of the complicated mechanisms by which drugs affect the brain and the mind.

For many years, psychoactive drugs were classified largely on the basis of less than adequate phenomenology. For example, there were sleepy drugs, unsleepy drugs, drugs that reduced delusions and drugs that reduced depression. Remember that most of the currently available psychoactive agents are the result of serendipity rather than of neuropharmacological logic. With *l*-dopa as the exception that proves the rule, current knowledge of neurotransmitters came from drugs rather than the drugs evolving from knowledge of neurotransmitters.

Stimulants (i.e., unsleepy drugs) have been known since time immemorial. Only recently has there been a separation of the monoaminergics (e.g., amphetamine and methylphenidate) from stimulants that have quite different actions on neurotransmitters; and on closer inspection, quite different effects on the mind. Old texts thus included strychnine (glycene antagonist), picrotoxin (GABA antagonist), caffeine (adenosine antagonist) and nicotine (acetylcholine agonist) along with the monoamine agonists.

The reclassification of psychoactive drugs in terms of actions on neurotransmitter systems is very advantageous when it comes to manipulating links between the mind and the brain. It is those drugs that act most evidently on the mind that have been linked to neurotransmitter systems. Those drugs can now be utilized to ask how neurotransmitter systems are related to psychological systems. Now psychological constructs can begin to be redefined on the basis of the biological anchors that the drugs supply.

Although it is not a typical stimulant, MDMA may be considered to be a member of a large class of drugs that can be grossly classified as a monoaminergic. The monoamines are an especially interesting group of neurotransmitters because (a) a few cells of origin innervate wide areas, (b) some monoamine neurotransmitters serve as circulating neurohumors, (c) they are not primary excitatory transmitters, but rather control the way the neuron responds to its excitatory input and (d) they act in the periphery as well as at central synapses.

This brings to mind the mine shaft analogy proposed many years ago by the late Warren McCulloch (1965). Mine shafts have telephones, so one can contact a particular miner. In contrast to such person-to-person calls (represented, for example, by glutamate synapses in the central nervous system), mine operators keep a foul smelling chemical, such as mercaptan, on hand to blow down the ventilating system when emergency evacuation is called for. Such to-whom-it-may-concern messages are presumably carried in humans by circulating neurohumors. More limited messages of this nature may also be

directed to a more limited audience. Pursuing the mine analogy a bit further, one might think of a public address system in a particular tunnel. In the brain, such functions could be carried out by small groups of cells that project to extended, yet somewhat circumscribed, areas.

This to-whom-it-may-concern quality of the monoamines suggests that they may control general parameters of information processing instead of serving to transmit specific data. Psychoactive drugs of course also seem to act on general parameters of information processing. Recent animal studies suggest that norepinephrine and dopamine may have actions that are more readily generalized in terms of information processing. To oversimplify a bit, dopamine seems to facilitate switching, while norepinephrine tunes the signal/noise performance (Oades 1985). Serotonin seems to inhibit mouse killing by rats and to promote relaxation in humans, but this has not been translated into information processing terms.

Psychoactive drugs indeed promise new insights into the mind, and monoaminergic drugs are among the most promising. Examples of monoaminergic drugs in nature include coca, ephedrine and khat, and their use dates back to antiquity. Chemists have been producing synthetic monoaminergic drugs for over half a century, but in spite of this ancient lineage, both the neuropharmacology and psychopharmacology of such compounds are just beginning to be worked out. For example, monoaminergic stimulants can ward off fatigue and make hyperactive children behave better in the classroom. Thus, they have been said to improve attention (attention being circularly defined as the mental facility needed to carry out the tasks that the stimulants facilitate). In fact, using brain electrical potentials to provide operational definitions of attention, the stimulants do not imitate the condition produced by attention induced by a task demand (Callaway, Halliday & Naylor 1983).

It had been assumed that a stimulant would stimulate a normal child, so the calming effects of stimulants on hyperactive children was labeled *paradoxical* and attributed to some peculiarity associated with the unknown etiology behind the clinical diagnosis. When this plausible assumption was finally tested, it was found that normal children were affected in exactly the same way as the hyperactive ones (Rapoport et al. 1978). However, one should not rush out and put a 10-year-old child on methylphenidate, for the improvement in classroom performance is not necessarily associated with improved Wide Range Achievement Test scores after several years of treatment.

The commonsense pharmacological assumptions about stimulants thus do not hold up well when critically examined. Commonsense neuropharmacological assumptions have not fared much better. Clinically, the two most commonly used monoaminergic stimulants are *d*-amphetamine and methylphenidate. They have been considered quite similar in action because both seem equally effective in treating hyperactive children and in keeping students awake. Both drugs release and block reuptake of dopamine and norepinephrine, although by somewhat different mechanisms. They also release and block reuptake of other monoamines. Recent work, however, has shown that they produce grossly different changes in urinary excretion of monoamines and their metabolites. Differences in the way they affect the mind are also becoming apparent. In the laboratory, both drugs have been noted to speed up the performance of young adults on a certain task. However, methylphenidate does so without speeding up a component of the brain electrical event-related potential that seems to mark time taken in stimulus evaluation. On the other hand, *d*-amphetamine speeds up that event-related potential. Thus it seems that the two drugs are speeding up the task, but by different means (Naylor, Halliday & Callaway 1985).

These and other findings have led to constructs that are much more precise and useful than previous constructs, such as attention and arousal. Now there is a model that has helped in the design of tasks that show the differences between the drugs more clearly, and to begin other studies intended to test predictions made about other drugs that act on the norepinephrine and dopamine systems. However, as much as one might like to talk about present research, the object here is to point out how mistaken the assumptions about such old friends as amphetamine and methylphenidate have been. Some colleagues in the field seem to paraphrase Reagan's remark about redwoods in saying, "Once you have studied one monoaminergic drug, you have studied them all." One would hope that it is clear that there is much to be learned from the differences between monoaminergic drugs.

MDMA seems to be largely serotonergic, but it lacks the sedating characteristics of *l*-tryptophan. MDMA has yet to be fully characterized neuropharmacologically and its pharmacological actions are still being described with such terms as "empathy" and "love." Studies with amphetamine, methylphenidate and phentermine are already helping to redefine what attention is; or perhaps more precisely, what attentions are. It is not unreasonable to hope that certain aspects of love will be redefined through the use of biological points of reference.

So far, the imprecise language seems to result in confusion when one tries to talk of love. Never mind the very personal experiences individuals may have had in talking about love, but simply consider the mishmash produced when the Greek word for pure love was trans-

lated as *charity* in Corinthians: "And now abideth faith, hope, charity, these three; but the greatest of these is charity." Perhaps psychopharmacologists may learn to be more precise about love and empathy, while also learning to be more precise about serotonin and its actions.

Unfortunately, this author cannot comment on laboratory studies of the sort of love that seems to be facilitated by MDMA. At present there are better ways to study things that contrast with love than for studying love itself. It is known that love and aggression are not orthogonal, but they represent one sort of contrast. It is interesting to note that increasing the dose of amphetamine in humans from 10 mg to 20 mg reduces aggressive behavior, while still increasing activity (Cherek et al. 1986). Autism provides another sort of contrast for love and may be associated with defective serotonin metabolism (Todd & Ciaranello 1985).

Hopefully, it has been shown how psychoactive drugs can provide biological anchors to prevent drifting into mistaken psychological assumptions. Because an understanding of *attentions* is just beginning, it should not be discouraging that the study of *loves* has not yet been undertaken. The task seems intriguing enough, however, and in that effort MDMA could well be one of the more useful tools.

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