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EDITORIAL
Drugs as Repatterning Organizer

Neither the increasing complications nor the ignorance of a definite causal relation have devaluated the status between the pharmacological and biochemical alterations of drug therapy as the basic tool in psychiatric management. The umbrella of drugs has permitted more integrated intensive psychotherapy, particularly with psychotics. It has also augmented the opportunity to uncover the deeper structure of personality make-up to add more profound orientations to the theory in psychopathology .

Basic orientation:

1-Psychiatrists, have no other alternative but to continue using drugs to help masses of patients suffering from psychiatric illness.

2-They have to go on handling all psychotropic drugs as primarily empirical tools with or without some associated knowledge about their biochemical and pharmacological characteristics.

3-This does not mean that there is any rationale to neglect or overlook parallel interpretative pharmacological research. All part informations coming from the laboratories are to be considered seriously but should never be taken as the only or even the main explanatory fact.

4-Searching for new hypotheses should go at the same pace, along with collecting part chemical knowledge.

5-Clinicians are not the least mechanical executors of what pharmacological laboratories inform them about. They are experimenting all the time and are fed back in a conscious and unconscious daily practice. The clinical field is the first and last milieu where drugs could be assessed. All other structured methodologies, pseudo objective techniques, including double blind experiments are inferior to observing the depth and direction of changes occurring in a therapeutic setting where drugs are one of its main active variables.

6-Thus, assessment of drug action, as any therapeutic procedure, should take in consideration the outstanding symptoms, as much as the holistic human change and not less the potentiality to recur, as well as the *possible **how*** of getting through all such changes, towards which goal..etc.

7-Since chronic disorders need rehabilitation rather than drugs, and since acute or subacute disorders are new incidences to supervene, drug therapy needs to be reconsidered primarily, or rather essentially as some first aid, as well as a chemical temporary control along the march of the therapeutic plan.

General clinical observations:

Over thirty two years of active clinical practice with drugs (and otherwise) certain clinical observations have been accumulated throughout our practice. The following are among the most relevant ones. Most of them are, at least partially, culturally related :

(1) There is definite difference between the classical published literature about any drug and the actual clinical observation in practical setting.

(2) For instance, the claimed latent period said to be essential for most drugs to start their action is shorter or even absent in some our practice.

(3)The duration needed to maintain the drug administration is practically shorter than classically recommended and results are rather the same (occasionally better than the published claims).

(4) Drugs *per se* are less specific than claimed in the literature. A drug becomes specifically acting in a particular direction according to the timing and milieu more than according to the symptoms and diagnosis. The same drug can give different responses in different stages of the illness as much as in different stages of the physician/patient relationship. Also the effect of a drug differs in various therapeutic settings. In other words,the same drug seems to become not the very same if other active clinical variable are changed. Accordingly, some relatively very few number of drugs can do the whole job by all means if properly timed and synchronously adjusted.

(5)Then, timing of giving, and withdrawing, the drug (or altering the dose) should be well synchronized with other therapeutic variables, particularly RRT (Rhythm Restoring Therapy i.e ECT) and intensive group (and milieu) therapy (Rakhawy,1980).

Bearing in mind such basic orientation and general observations we can proceed a step further to introduce the *pre-assumptions* for the foundation of the hypothesis:

I-Brain organization and chemical hierarchy:

1-Brain is a complex chemical structure with *chemical* hierarchical organization.Phylogenetic and ontogenetic *neuronal* hierarchical organization are going along in parallel and integrative discipline.

2-The hierarchical organization of the brain should have its corresponding behavioural organization parallely arranged both ontogenetically and phylogenetically (Rakhawy 1981).

3-Psychiatric illnesses, in general, could also be arranged in some sort of hierarchical descending devolutionary discipline which could be just the opposite of the crescendo evolutionary discipline (Rakhawy 1979)

4-The synaptic organization (including elimination and/or sprouting, is not only anatomical but also biochemical. Some hypotheses were relating schizophrenia to certain failure of synaptic elimination and reorganization at adolescence (Feinberg, 1982/83).

5-The organization (and distribution) of certain neurohormones could never be solely responsible for the corresponding holistic chemical organization of certain evolutionary, developmental or behavioral organization.It is but a part of some more complex biological structure, the chemical aspect of which is only partly known.

6-The decrease, or increase (*in the quantity*) of this or that neurohormone does not necessarily have a ***direct*** influence on behavior. It, most probably, alters the whole chemical organization of the brain structure and consequently behaviour is repatterned.

7-Simple altering of chemical organization could be very rarely **directly** responsible for altering behavioral organization.

II-Selectivity of drug action and the possible effect on one, and then the whole, organization.

1-Since the discovery, and use, of phenothiazines, we came to know something serious and valid, that : certain drugs act selectively on subcortical structures (older, deeper brain levels).

2-Simultaneously, we know enough about the nature of many mental disorders where reactivation of older (archaic, infantile ..etc) behavior is partly responsible for the pathology and disease.(e.g.instincts and primary processes of Freud, the archipsyche of Berne,1967..etc).

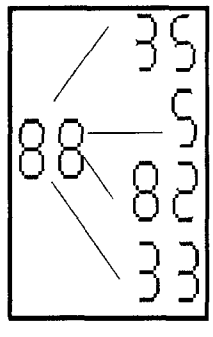
3-The distribution of receptors and synapses differ in different species along the scale of evolution and should differ accordingly in the developing embryo and child. This difference could not be a haphazard one but it should be species (and developmental stage) related organizations.

4-Whatever drug that could effect a specific synapse, receptor and/or neurohormone is effecting the specific distribution to alter the holistic arrangement of the complex chemical pattern of some part, then of the whole organization.

The hypothesis:

1-Most of anti-psychotics (neuroleptics) and major antidepressants are to be considered as functioning through primarily inhibiting rather than increasing some specific neurohormone at a specific synapse or receptor.

2-The result of such inhibition, in a particular state of activation at a particular stage of the disease, is to alter the chemical organization of brain structure.The how of this alteration is best understood by remembering the chart for testing *colour blindness* where missing one colour would make the letter 8 read as being 3. This analogue is extremely complex and elaborated in the new light cells of any digital quartz watch or the like. The possible organizations and reorganization as a result of demolishing one single link here or their could be an infinite number of chemical patterns with its corresponding behavioral and existential counterpart.(see figure, where the 88 could be 35, 82, 33 or even the letter S through omitting one or more aspect of the circles of the 88).



This should not leave us in a jungle of probabilities. As previously introduced we can follow certain hierarchical patterns of behavior with the possible corresponding hierarchical patterns of chemical organizations. If we can identify any syndrome in terms of which level of organization is activated and which is dominated and disrupted, we can then determine what we can do through specific drug inhibition along with other therapeutic modalities. In other words, when we say that such drug inhibits such and such transmitter we are but identifying the first step in a series of responsible therapeutic interpretation and management.

Practical Considerations and Possible Applications

The consequences of possible application of this hypothesis is definitely beyond the scope of this paper. However we are no more in the stage of theoretical hypothesizing. It is becoming an every day practice for my self and a good number of my colleagues to diagnose hierarchical levels of activity and to give drugs accordingly.

To sum up certain broadlines I am in a position to put forward some relevant practical points out of clinical experience clearly guided by this hypothesis that have lasted over the last 14 years. The observations provided are mainly related to the psychotic disorders whether spontaneously presenting or arising in mini forms during intensive prolonged therapy.

1-It has become possible to identify in each syndrome not only the presence or ab-

sence of activity (Rakhawy 1983) but also the level of reactivation of this and disruption of that level of organization (Rakhawy 1979).

2-It follows that a structural hierarchical diagnosis is quite possible along with the behavioral descriptive diagnosis.

3- It is possible to correlate between the holistic configuration of the clinical picture of an illness and the possible level of action and effect of some drug having a specific selective inhibitory action on some brain level, more than the other.

4-We are,then, oriented about drug action not only in terms of the chemical substance they can increase or decrease, but also in terms of the holistic consequence on the whole brain as a result of this diminution (or increase) of that specific chemical substance. The language should change from *localization* to *organization.*

5-Drugs are then used as a coherent sentence in a chained text. We do not give this drug to get rid of that excess in this substance but we are demolishing this area of activity responsible for the mal-organized pattern or for the interfering ectopic circuit. A drug, then, can set free the rest of active units to achieve another more adaptive, more efficient , less archaic organization.

6-To achieve such goal, it is not enough to inhibit one area or level, but it is simultaneously important to activate and cultivate the other spared areas (units,levels) of organization to facilitate some higher level of dominance and reorganization. This includes proper inter-personal approach, special meaningful language at most possible levels as well as helpful well-structured surroundings in a major plan of readjustment and rehabilitation.

7-Proper timing for temporary or lasting withdrawal of drugs is dependant on the extent and quality of selective reactivation and cultivation of the proper level.

8-After adequate selective inhibition of the particularly over-active level, the use of rhythm restoring therapy (= ECT) becomes more effective and results are more guaranteed. i.e.the drugs act selectively to partially inhibit the ectopic pace setter giving a better chance for restoring a better pace setter ready to act due to adequate preparation .

9- Timing of the RRT (Ex-ECT, Rakhawy 1983) therapy becomes most important and extremely delicate in relation to dose and duration of drug intake.

10-Psychotherapy does not mean any more *treatment by "talk"* .The words become some biologically relevant tools in the process of selective reactivation as much as the drug is an appropriate tool in the process of selective inhibition.

11- Behavior therapy and milieu therapy become specially designed techniques arranging surroundings to attract and train the desired level to dominate (then to alternate appropriately).The different response to the same dose of the same drug after changing the milieu could be explained through this simultaneous selective activation/ inactivation approach (Rakhawy 1986).

12-The trial to interpret drug action in relation to their effect on REM sleep is a reasonable step in the proper direction (Hefzy,1981). However this tendency has been also aborted and mutilated as a result of the tendency to quantify matters in *how much* of REM is added and how much is deprived (and the possible rebound).There is a definite need to re-interpret data in terms of the function of REM in repatterning and the role of drugs in this direction.(details not possible here).

13-Drug action could then be interpreted in terms of the how of restoration of rhythm, i.e.in physiological terms parallel to RRT. This is opposite to the present

trial to interpret the action of RRT in terms of quantitative change of plus or minus this or that neurohormone.

14-The use of anti-arrythmia (and anti- dysrhythmia) drugs like anti-epileptics (Post et al, 1989) and lithium salts is to be considered as adjuvant to such selective inhibition. Perhaps that is why such drugs can also act, in special recurrent cases, as lasting rhythm-restoring agents.

15-Some of the serious side effects of neuroleptics like tardive dyskinesia or tardive dysharmonia mentalis are to be interpreted in terms of persistent inhibition of a limited *certain* area or level resulting in actual disruption without adequate reorganization in a whole homogeneous pattern.

Conclusion

As much as drugs in psychiatry are indispensable, a need for reorganization of our knowledge is essential. The available data about drug action are valid part knowledge, but the way they are interpreted is extremely dangerous and liable to ultimately devaluate this excellent weapon out of mal-use and prolonged undue application. A need to introduce whatever part chemical information in a more coherent psychophysiological language is increasing. The suggested hypothesis is a trial in this direction.

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