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What Shall We Do About Our Concern with the Most Recent in Psychiatric Research?*

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ABSTRACT

Most clinicians and researchers are concerned with recent advances in psychiatry. This involves the danger whether something time-tested may get sidelined for extra-scientific reasons. That the pharmaceutical industry and superspecialist researcher may keep churning out new findings to impress audiences is only a partial truth. Research progresses by refutation and self-correction. Acceptance in science is always provisional; changing paradigms, frameworks of enquiry and raising new questions is integral to breakthrough in scientific knowledge. Hence, there is in science a constant concern with the new. Moreover, the number of treatment non- responders to the time-tested swells with time, and researchers feel challenged to find ways and means of resolving their difficulties. Newer challenges need newer strategies. Obsession with the most recent can lead us astray, but a healthy evidence-based acceptance of the new is essential for advancement in psychiatric research. As indeed of research in all fields of medicine. And of science in general. The role of lithium and newer mood stabilizers in bipolar disorders are taken as examples to highlight this point.

Key Terms : Psychiatric research, Refutation, Paradigm shift, Bipolar Disorders, Lithium, Mood-stabilizers, Treatment non-responders ,Pharmaceutical Industry.

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Introduction

Like in other branches of medicine, in psychiatry too, most clinicians and researchers are concerned, if not really obsessed, with what is the most recent advance in a particular field or area. Enlightened readers scan the references' list and are suitably impressed if there is a generous sprinkling of recent ones. Writers, similarly, want to refer to recent works as far as possible, and sometimes may go out of their way to accommodate them in an effort to appear abreast of contemporary literature. The more recent the work quoted, the greater the impact, and equally greater the research writer's satisfaction. Subtle psychological factors play their role here no doubt, as does the not so subtle need to impress and hold the interest of one's readers, and one's peers.

Ofcourse, in this there is always the danger that something time-tested and well-proven may get sidelined for the new and promising, yet unproven. This can no doubt also disturb, if not damage, so many personal and collective equations. The concern with keeping abreast of recent advances makes us knowledgeable, or at least seem so, and does serve to impress our audiences favourably. But somewhere down the line is also involved the legitimate fear whether we sideline something proven for extra-scientific reasons.

The Example of Lithium

Let us take an example to clarify the issue. When lithium was first introduced as the treatment of choice in bipolar disorders, there was a great welcome for its wonderful effects, both its anti-manic as well as its prophylactic properties. And justifiably so. Over a period of years, however, the enthusiasm seems to have settled to cautious questioning, and has even given way to skepticism in a number of quarters (Silverstone *et al* 1998; Gershon and Soares, 1997; Moncrieff, 1995). Even if the US FDA approved only of lithium as prophylactic for bipolar disorders, a number of studies in the last decade find that 20-40% of classical bipolar patients (i.e. ones with clear cut episodes and remissions) show less than desirable response to lithium, or develop undesirable side effects. And amongst the nonclassical cases (like rapid cyclers, dysphoric or mixed states, and the ones with co- morbid substance abuse), the situation is still less satisfactory. Valproate and Olanzapine have been approved by the US FDA as anti-manic drugs but not as mood stabilizers. Number of clinicians down the years have switched over to Carbamezapine for its anti-manic, antidepressant as well as

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What has changed ? Has lithium suddenly become no good ? Has carbamezapine remained only a hero of yester years ? Are valproate, lamotrigine etc. the new blue -eyed boys, the new stars on the firmament ? Is every medicine to experience its hey days, and sink into oblivion, like film stars and other celebrities ? Do we, as clinicians and researchers, unduly favour the new by neglecting the old but time - tested ?

mood stabilizing properties. But now the emphasis seems to be shifting from carbamezapine to the other anti-convulsants, especially in the treatment – resistant cases. Valproate, Lamotrigine, Gabapentin, Topiramate and Tiagabine are the ones holding promise. As also the atypical antipsychotics like Clozapine, Olanzapine, Quetiapine, Ziprasidone, Risperidone and Aripiprazole. (See Grunze and Moller, 2003, for a review of recent work in the field.)

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More pertinent to the issue here is, are there extra-scientific forces acting to create such a situation ? The pharmaceutical industry, the superspecialist researcher committed to only one circumscribed area of research, who must keep churning out something new to capture audiences, get research grants, generate funds and profits?

Well, to say that this is indeed so, is not entirely false. But it may not also be the complete truth. The reality, as always, lies somewhere in-between.

Refutation and Paradigm Shifts

Research in science has followed the path of refutation (Popper, 1968; 1969). When something is systematically refuted, something new can, and must, be accepted. Sticking to the old and discarding the new in spite of evidence to the contrary can be as reactionary as believing in the new and rejecting the old to appear modern. Or being coerced into

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Historically, theoritical orientations in science typically retain a strong hold over their adherants, even in the face of discomforting evidence and equally plausible alternative explanations of observable phenomena.

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accepting it because of impressive portrayals by 'specialists' presented by pharmaceutical companies at five star seminars. For, just as obsession with the old is stifling, that with the new can be equally anarchical (Singh and Singh, 1988).

The outstanding feature of scientific advance is its capacity for self correction.* Our acceptance of scientific theories is always provisional. This requires an attitude in the scientist of being willing to be proved wrong; though he may believe a theory, he should not be committed to it, or give it his unreserved loyalty (Slater, 1973).

Human beings have a strong tendency to look for explanations and to seek final answers. It is often perplexing to find several competing explanations being advanced to account for the same phenomena. In fact the more complex the phenomena, the greater the number of diverse opinions that emerge. Ofcourse all these viewpoints cannot be valid. Some will stand the test of time and scientific scrutiny, some must indeed be discarded, or become history. But the applicability of a viewpoint is often determined by the extent to which it seems helpful in understanding a given case. Historically, theoretical orientations in science typically retain a strong hold over their adherents, even in the face of discomforting evidence and equally plausible alternative explanations of observable phenomena (Kuhn, 1970). They continue to do so until some new or fundamentally different insight is achieved that appears to resolve the problems left unsolved by the conflicting interpretations of the empirical data. These new insights constitute *paradigm shifts* (Kuhn, 1970), which involve fundamental reorganization of how people think about an entire field of science. They parallel, in certain ways, the momentous cognitive shifts a child undergoes in gaining an adult understanding of the nature of the world, a process well described in the work of Jean Piaget (Carson, Butcher and Coleman, 1988).

Hence, unless we change our paradigms, alter our frameworks of enquiry, raise new sets of questions, there cannot be real breakthrough in scientific knowledge.

**To that extent, science approximates life itself. And self-correction is seen in other fields of human endeavour as well, including spirituality, even though the spiritualists may claim otherwise.*

A problem that is solved no longer bothers us, but that which is not keeps rankling the mind.... Hence the search for newer molecules and newer treatment strategies must legitimately be pursued. The pharmaceutical industry and the super - specialist researcher can no longer remain whipping boys when viewed in this perspective, can they?

Newer Challenges, Newer Strategies

Moreover, we must also understand why there is in science this constant concern with the new. Just to go back to our earlier example. It is not that lithium is not a good medication. In fact we must thank some researchers for pointing it out relatively recently that it has indeed stood the test of time (Baldessarini and Tondo, 2000). When we say that 20-40% of classical bipolar patients do not respond to lithium, we must not forget that it also means 60-80% of classical patients do. *And that is a pretty large number.* But what we cannot also wish away is the fact that 20-40% of classical patients, and the majority of nonclassical ones, do not respond. Moreover, a problem that is solved no longer bothers us, but that which is not keeps rankling the mind. Patients who respond do not trouble us as much as those who do not. Both the clinician and the researcher are concerned, and feel challenged, (and rightly so), to find ways and means of resolving their difficulties. Hence the search for newer molecules, and newer treatment strategies, must legitimately be pursued. The pharmaceutical industry and the superspecialist researcher can no longer remain whipping boys when viewed in this perspective, can they? Also, let us not forget, that the number of non-responders swells over the years, and that further adds to the discomfort, not only of patients and care-givers, but also of clinicians, researchers and their ancillaries. Moreover, subtle nuances of an illness, its processes and outcome, are only laid bare over a length of time. And newer challenges needs newer strategies. The same must happen with bipolar disorders, lithium and the newer medications. Or, for that matter, with *any* disorder and *any* treatment strategy. Not just in psychiatry, but in medicine as a whole. And, come to think about it, in all scientific fields in general.

Concluding Remarks

It is the inherent need of science to give something new. It is the inherent need of man to like something new. And both these needs are liable to be exploited due to unethical practices by market forces, both in the pharmaceutical industry and the research field. While man works mainly at the empirical level, pharmaceuticals work essentially at the business level, and science works

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fundamentally at the process level. How are all these three to be ethically reconciled is the problem before us.

So, then, there we are. While obsession with the most recent can lead us astray and should not become a fad or a game of one-up-manship, a healthy evidence-based acceptance of the new is essential, nay integral, to scientific advance and research in our field.

In this there is an inevitable process of sifting involved, as of personal liking, one's vision for the future, contemporary predilections of peers and superiors, and the pulls and pressures of market forces, both in the research field and the pharmaceutical industry.*

The need for a healthy evidence-based acceptance of the new we must recognize, and encourage. This need the pharmaceutical industry also recognizes, and may sometimes be prone to exploit.

Well, the branch of psychiatry, as indeed every other branch of medicine, has to beware of this.

But, then, we are cautious when we drive. That does not stop us from driving, does it ?

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**We can still call it the research* field*, and the pharmaceutical* industry*. The time may not be far when* field *may turn into* industry*. Some very senior practitioners may hopefully take solace in the fact that it may not happen in their lifetime. Well, they might just be proved right. Indications of being proved otherwise are not weak at all!*

Questions that the Third Monograph raises

Q.1. How can we avoid exploitation of the needs of man and science by unethical practices carried out by market-forces, both in the pharmaceutical industry and the research field?

Q.2 . Is scientific advance always provisional? Does it have no finality?

Q.3. Are we justified in getting excited about recent advances, when what is recent today will become outdated tomorrow?

Q.4. Will scientific progress ever lead to the best, or only, treatment, or explanation, in medicine in general and psychiatry in particular?

Q.5. How do we balance new knowledge with old findings?

Q.6. What is the litmus test on which every scientific breakthrough, old or new, should get tested?

Q.7. Should be give up getting excited with recent advances? Then what should we get excited about, if at all?

Q.8. If refutation is the truth of science, then where is science ultimately going to lead us?

Q.9. Paradigm shifts alter perceptions, reorient thinking. But do they lead to real progress in knowledge, or does it simply mean giving up on one fad to get preoccupied with another?

Q.10. Are there newer problems that need newer strategies in medicine, or most of the so-called new problems are generated by society and nurtured by man, or just recycled, and a whole pharmaceutical industry and the medical profession run their livelihood on it?

Q.11. Are we becoming an overmedicated society in the name of newer and more advanced treatment strategies?

Q.12. Is there any other way of looking at this problem?