The Scientific Status of Concepts of Mental Disorder, Community Concerns, and Precedents from the History of Science.

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Abstract: In this essay I offer a critique of the notion that research in psychiatry is at last truly scientific. In particular the criticism is aimed at those parts of psychiatry which make the strongest claims to be scientific, namely those based on brain biology. Part of my critique, dealt with in the first section is well known to non-specialists in the community, the likely consumers of mental health services and their family members. They know that many of the concepts of mental disorder used in psychiatry do not have the solidity of concepts used elsewhere in science. More broadly I analyse the nature of the natural sciences since their beginning in the late sixteenth and early seventeenth century, in the *natural philosophy* tradition. I focus on the interdependent relationship between empiricism and rationalism (experiment and theory), and the close link between provision of true explanations and secure validation of the basic concepts used in these explanations. Most of the bio-medical sciences arise from a different tradition, of *natural history*, although there are some examples which have followed the natural philosophy approach. In psychiatry however, there are scarcely any cases where explanation, as understood in the natural philosophy tradition has been developed; and this is the chief reason why concepts of mental disorder have such poorly scientific validation. Instead a great deal of research in psychiatry substitutes correlation for explanation, and empiricism is pursued devoid of rationalism. In later parts of the essay I suggest a better way forwards, based on in-depth scholarship on a very large scale of the empirical evidence already available; imaginative reconstruction of what might be the causal links between different pieces of evidence; predictions from preliminary hypotheses; their testing either from existing bodies of published evidence, or sometimes from new experiments; and gradually to the construction of larger scale theories which are truly explanatory. If this enterprise proves successful, it may be expected to give robust validation to the concepts of mental disorder used in the explanations. A number of guiding concepts are also discussed to help this process. In the final section of the essay I invite scholars/theoreticians to join forces with me in what is likely to be a very large task, but one which is vitally necessary, if psychiatry is to acquire a truly scientific status, and concepts of mental disorder and corresponding diagnoses are to be given a more secure foundation than at present.

1. Introduction

Psychiatry at present is attempting to define itself as a scientific discipline, with credentials equivalent to those in other areas of medicine. The thrust of this essay is that this ambition has by no means been fulfilled. In part this shortcoming arises because the task is more fundamental than in other areas of medicine; but it arises also because there is little awareness by current researchers in psychiatry of aspects of the scientific endeavour *per se* which were crucial in the debates from which the natural sciences first emerged in the seventeenth century, and which become highly relevant again, if psychiatry is to gain a truly scientific basis. This essay thus puts considerable emphasis on history of science in areas far removed from the study of mental disorder. However, the essay is also highly relevant to the here-and-now, in that one of the central concerns of lay people, lacking the expertise of modern researchers in psychiatry, points to the need for research at a level more fundamental than that on which research is currently focused. The subject matter then, in which community voices and deepest theoretical researchers have common cause, is the conceptual status of our ideas of mental disorder. The emphasis might be on the question: *Can there be any such thing as mental illness?* However, while some space will be devoted to this, the main aim of the essay is to examine the status of schemes for defining different *classes* of mental disorder, currently in use. This leads to a more basic issue of how scientific concepts in *any* field become validated in a robust way. If we can answer that question generically, it should give us some precedents on how to validate concepts in psychiatry, in such a way that they command respect comparable to that of concepts used in other areas of science.

2. Community Concerns

Disease concepts in psychiatry are generally rather fuzzy, often based just on conventions, sustained by fiat and faith rather than reasoning, and always somewhat negotiable. As long as I have had an interest in academic psychiatry (since about 1973) I have heard debates about classification which seem endless and fruitless. Such debates go back to the nineteenth century, and the circularity of definitions is even referred to in Shakespeare's line from *Hamlet:* "To define true madness, What is't but to be nothing else but mad?".

Lay communities are well aware of shortcomings in this area. Their members are not experts in psychiatry, but they are experts on their own life experiences. What are their concerns? Here are a few examples:

(i) It is the experience of many patients that they receive a variety of different diagnoses from different psychiatrists for one disorder. Ever-more emphatic claims by psychiatrists that "mine is the *correct* diagnosis", cut no ice. This brings psychiatry into disrepute.

(ii) There is widespread concern about the categorical nature of psychiatric diagnoses. People in the community rightly ask: "Isn't it absurd that people be placed into such mutually exclusive, non-overlapping boxes"? Surely human diversity requires something more subtle.

(iii) It is also suggested that the categorical nature of diagnoses is (deliberately or unwittingly) serving commercial interests (e.g. health insurance and pharmaceutical industries), rather than the needs of patients. Many diagnoses seem to be "manufactured" to serve these interests, without a secure rational basis.

(iv) We have seen a major movement across a number of countries, to abolish the word "schizophrenia" as a diagnostic term, coming not least from leading researchers at the Institute of Psychiatry in London. This move is propelled in part by community concern that this diagnosis is stigmatising, that it is "more of a sentence than a diagnosis". It seems likely that this issue will again split North American from British/European psychiatry.

(v) In some parts of the Western world, there is growth of the rhetoric that "schizophrenia is not a disease", and with it resurgence of the anti-psychiatry movement popular in the 1960s and 1970s, and rejection of biological approaches. In some places this move has undermined major aspects of mental health care (including even therapy with antipsychotic medications). It has alarmed psychiatrists, as it alarms me, but the profession seems unable to mount an effective opposition. The "biological revolution" in psychiatry thus seems not to have gained much "grass-roots" support.

(vi) In Britain the term "dangerous severe personality disorder" has been introduced by government edict, purporting to be a diagnosis, but without either a legal or a medical basis, to be used as a basis for pre-emptive detention[1]. In the U.K. it is calculated that it might mean incarceration of six people so labelled for every one who actually commits a violent offence[2]. Such political interference with medical diagnosis is made easier in psychiatry because few of its *other* diagnoses have secure scientific status.

(vii) For another diagnostic entity - attention deficit/hyperactivity disorder (ADHD) - it is asked: Is it really a mental disorder? . . . or is it a

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[1] Corbett, K. and Westwood,T. (2005) 'Dangerous and severe personality disorder": A psychiatric manifestation of the risk society. *Critical Public Health* 15, 121-133.

[2] Buchanan, A and Leese, M (2001) Detention of people with dangerous severe personality disorder: a systematic review. *Lancet* 358, 1955-1959.

relatively normal personality variant, which becomes a disorder only in certain social environments (especially those created in schools). In Australia, children with the ADHD diagnosis cannot attend regular state schools, although in New Zealand, that would be against a recent ruling by the Human Rights Commission, as constituting unlawful discrimination. Another diagnostic category - dyslexia - is certainly disabling, given that our culture relies heavily on the written word; yet it is well understood that people with dyslexia often have unusual talents in other areas, which enable them not only to hold their own, but sometimes to prosper and become truly pre-eminent[3]. In this context, two conferences will be held in 2011 in Australia (in Western Australia and Queensland) on "Positive Schools - mental health and wellbeing". An article in the British *Guardian* newspaper (14.09.10.) ran the headline "Half of special needs children misdiagnosed: Ofsted review says that pupils diagnosed as having special needs require better teaching or pastoral care". To be classified as having "special needs" means, in the end, that a psychiatric diagnosis must be made. There are thus major implications for psychiatry: Perhaps there should be more attention drawn to unhealthy school environments as a public health initiative (and perhaps with advocacy of policies which change them), rather than treating the matter as an issue of personal health care (and, for ADHD, medication with ritalin).

(viii) More generally, there is increasing concern that psychiatry is medicalizing human diversity rather than welcoming (and even celebrating) it. There are real issues here about what constitutes a mental disorder. Psychiatry faced such issues in the past, when it was decided a generation ago that homosexuality was not a psychiatric disorder; but the profession has not yet tackled the issue in a generic way.

(ix) In New Zealand, the government-backed campaign "Like Minds Like Mine", to combat stigma and discrimination related to mental illness is receiving acclaim around the world. Persons with lived experience of mental illness played a major part in shaping this campaign and now in its implementation, yet it avoids diagnostic labels, preferring instead to use direct first-person accounts of those lived experiences. Thus, in some areas, the idea that diagnosis as an essential way to define mental disorders is being overtaken by events, and by public awareness.

All of the above issues point to real problems about the insecure status of many of the concepts of mental disorder used in psychiatry. What has gone wrong? Is there some fundamental misconception? If so, what is it?

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[3] Joanne Black "*In their right mind"* New Zealand Listener, May, 8-14, 2010.

Before we get to the crux of the issue, a few caveats should be addressed:

(i) In focusing on the insecure status of concepts of mental disorder, the assumption is that, ideally, these should have validity as *scientific* concepts, comparable to those used elsewhere in the natural sciences, and probably based at some level on commonality of the language with that used in other areas of science. However medical practice in the clinic is largely an art, not a science (although with a scientific basis). The relationship between patient and physician, one-on-one, is usually uncontrolled in a scientific sense, and is the time when the "art of medicine" (rather than its science) comes to the fore. That art perhaps inherently plays a greater part in practice of psychiatry than in any other medical speciality.

(ii) In addition, the poorly-validated scientific status of disease concepts in psychiatry applies to only part of the "psychiatry as science", since many of the issues with which psychiatry deals cannot be construed as diseases.

(iii) The great strength of the natural sciences is the universality of the basic concepts with which they deal. However, in psychiatry, whether we are thinking of diseases, or with other sorts of personal distress, there are substantial components which are specific to the society and culture in which they occur. Society and culture do not fall within the domain of the natural sciences and its common conceptual language. Therefore, some of the basic concepts for psychiatry do not now (and may never) gain the sort of validation which is the hallmark of concepts used in the natural sciences.

(iv) Causal principles for disorders of biological systems *might* be accessible to analysis in the natural science tradition, and this *might* lead to concepts grounded in the common language of science. However, for this, the analysis should be confined to these principles (especially those based on brain biology), leaving the individual experiences of each person, and the meaning each individual ascribes to them to a different area of study (the humanities rather than the natural sciences). Thus, although research in psychiatry uses paradigms from both the humanities and the natural sciences, the focus for scientific analysis is likely to be biological psychiatry.

(v) These questions are confounded by the institutional history of psychiatry. In past decades, psychiatry was mainly about large institutions, committal procedures, locked wards, and coercive treatment. The discipline was then separated from the rest of medicine. A major challenge for modern psychiatry is to re-invent itself as truly one of the "caring professions". However, this is an issue separate from that upon which the above examples focus. To get to the bottom of *that* issue we need to go further back in history, and to origins of the natural sciences generally.

3. Two Basic Dichotomies

I start from two basic dichotomies. The first goes back to medieval times, the split between two approaches to study of the natural world (precursors of science). The other is the distinction between experiment and theory as methods of exploring the natural world.

(i) Natural Philosophy versus Natural History. Before the birth of the natural sciences, their precursors were two areas of scholarship, *natural philosophy* and *natural history*. The role of *natural philosophy* was to *explain* natural phenomena with reasoning based on various assumptions (natural or supernatural). This developed into what we now call physics, and the approach spread to various other areas (chemistry, biophysics, etc). The role of *natural history* was to *describe* nature as it appears, in all its complexity. In origin it was qualitative, but later came to be expressed quantitatively. Correlations and associations are part of this tradition, being aspects of description, not to be confused with explanations. The critical difference between natural philosophy and natural history is that natural philosophy - that is physics - deliberately simplifies the systems it studies, so that very few variables are relevant. One then really does have a chance to explain things. Natural history deals with the natural world, life, and history in its full complexity, leaving room for a wealth of descriptive detail, which is then far too complex to work out fundamental principles for explanation or cause.

(B) Experiment versus Theory. The second dichotomy applies historically mainly within the natural philosophy tradition, although there are now many cases where it applies in biomedicine, but not yet within psychiatry. This is the distinction between *experiment* and *theory* (or, if you like, between ideas, defined and inter-related via reasoning, and observations, where experiment is all-important, and where statistics rather than causal reasoning may be critical). Before the seventeenth century, when science as we now know it became recognisable, for two thousand years, the two approaches, empiricist and rationalist, had a long history of rivalry. Mainly the rationalist approach was dominant, because of the power of the Catholic church. In the seventeenth century, for the first time, the two started to be combined. Empirical observations were sometimes descriptive (as in astronomy), but later came increasingly from systematic experiments, where all extraneous factors except those under study were excluded or controlled. The reasoning, from the time of Galileo, tended to be quantitative and mathematical terms, although that is not a necessary part of the tradition.

The first era when this came about involved interaction between three prominent figures from the sixteenth and early seventeenth century. Profiles

of these three give insight into the relation between theory and experiment more generally.

Nicholas Copernicus (1473-1543) was a polymath from Northern Europe (present day Poland), whose talents and interests included mathematics, astronomy, translator, Catholic cleric (he never joined the Protestant reformation, proceeding during his lifetime), military leader and economist. He did a little observational astronomy during a period at Padua in Italy, and is famous for the proposal (published on his deathbed) of the heliocentric view of the solar system. This was based on mathematical neatness, not on new empirical observations.

Tycho Brahe (1546-1601) was a man of totally different stamp. A Danish Nobleman, he was a student in Leipzig. While there, in 1563 he saw alignment of Saturn and Jupiter one month away from the date predicted on the old Ptolomaic system. The discrepancy led him to undertake systematic regular long-term study of how planets *actually* moved. In due course he enlisted the help of the King of Denmark, who gave him the use of a small island in the Baltic, which he called Uraniborg, where a palace was set up for his work. He recruited assistants to do the observations, all at night (this being before telescopes were invented), and others for the calculations involved. He produced accurate data on planetary motion night-by-night, on clear nights, over a period of nearly thirty years, the best empirical data ever produced up to that point on any subject.

One of his calculator assistants was the third of my trio *Johannes Kepler*. From a humble background, in what is now south Germany, he studied at the university of Tübingen, initially to become a protestant cleric. He was an imaginative young man, had a flair for mathematics, and secretly studied - and became convinced of - the Copernican system (although the university still taught the Ptolomaic system). When he met Tycho Brahe, Brahe respected Kepler's skills in computation, if not his belief in the Copernican system, and, in 1597, invited Kepler to join him at Uraniborg. They worked together for a few rather fractious years, before Tycho Brahe died, leaving Kepler with a vast quantity of high quality empirical data, upon which he could employ his mathematical skills and theoretician's imagination. On his death-bed, Tycho is said to have pleaded with Kepler not to adopt the Copernican system. Kepler wouldn't have a bar of it. Kepler soon made the momentous discovery, which put another nail in the coffin of the Ptolomaic system, that the planetary orbits were not circular. This defied Pythagorean notions of perfection, and two thousand years of teaching since Aristotle. Further work revealed the mathematical system which *did* describe planetary orbits, first for Mars, then for other planets: They were elliptical, with the

sun at one pole. Further study revealed the extraordinary finding that the area or sector swept out between a planetary orbit and the sun was equal in equal times, despite changes in velocity. He published this in 1609, and full astronomical tables based on this principle followed in 1627.

I offer some comments on these three remarkable people: Copernicus and Kepler were both theoreticians rather than experimentalists, Brahe was an empirical scientist. From what one can gather the first two had totally different temperaments from Brahe - vivid in imagination, but concerned about rigour in mathematical reasoning, whereas Brahe, less imaginative, had a dogged, perhaps obsessive concern for getting the best possible data, regardless of theory or explanation. The two theoreticians needed little finance, and worked as isolated individuals; Brahe needed big money and a big team. Kepler and Brahe, much as they needed each other's skills, did not get on too well. Their different temperaments, and habits of thought were unlikely ever to be combined in one person, and relationships between the two types are likely to be tense. Nevertheless this is probably the first time that the rationalist and the empiricist approaches could work in synergy; and of course the combination provided Isaac Newton with a starting pointed for his own monumental work, seventy years later.

About this time we have the prophetic writings of *Francis Bacon* (1561-1626), the first to write on the basic method of what we now call "science". He is often held up a the first real advocate of empiricism, and compared with the two-thousand year dominance of rationalism since Pythagoras, through the dominance of the Catholic philosophers, up to his own time, that is fair comment. But what he actually advocated was a measured balance between empiricism and rationalism. Here is a wonderful example of his elegant writing:

> "Those who have handled sciences have been either men of experiment or men of dogmas. The men of experiment are like the ant, they only collect and use; the reasoners resemble spiders, who make cobwebs out of their own substance. But the bee takes a middle course: it gathers its material from the flowers of the garden and of the field, but transforms and digests it by a power of its own. Not unlike this is the true business of philosophy: for it neither relies solely or chiefly on the powers of the mind, nor does it take the matter which it gathers from natural history and mechanical experiments and lay it up in the memory whole as it finds it, but lays it up in the understanding altered and digested. Therefore from a closer and purer league between these two faculties, the

> experimental and the rational (such as has never been made), much may be hoped. (from *Novum Organum,* 1620).

Since the time of these pioneers, the interplay between ideas and experiments (between theory and observation) has been the cornerstone of the endeavour of research in the natural philosophy tradition. A form of reasoning emerged - of which there are now many examples - which I would like to call "cross-level explanation", and this came to make up some of the decisive steps in science. In this, arguments are presented by which phenomena well known at a "higher level" are accounted for by simple premises made about lower level processes. Often those premises are entirely hypothetical, because they cannot be evaluated by techniques currently available. We see such explanation in the reasoning leading Dalton to his atomic hypothesis, and later in the formulation of the kinetic theory of gases, by which the gas laws were accounted for in terms of motion and collision of hypothetical molecules. With the Scottish mathematician, James Clerk Maxwell, one encounters for the first times a physicist who was almost *entirely* a theoretician. From that time, in physics, theoreticians and experimentalists have tended to be different people, with different skills and attitudes, both groups dependent on and respectful of the skills and attitudes of the other - a synergy which has made progress in physics so rapid, and secure. One sees this synergy at its best in the twentieth century, for instance in the collaboration between Ernest Rutherford and Neils Bohr.

4. Validation of concepts

Precise reasoning requires precisely-defined concepts. In the physical sciences the key concepts were length, time, mass and force. Length can be defined precisely since it can be easily and reliably measured. Introduction of time as a quantitative variable came more slowly, being absent in ancient Greek science; and it was Galileo who first used "time" as a quantitative variable in explanatory arguments about empirical data. The most important step in conceptual definition must however be attributed to *Isaac Newton* (1642-1727). Before Newton, the words mass and force had no proper definition, just like the concept of schizophrenia today. It was the very solid reasoning of Newton, involving the quantitative relations between length, time, mass and force (the latter two properly defined) which validated the scientific definition of those concepts. We easily forget that *formulation* of fundamental concepts is far more difficult than using them once they have been formulated; by then, they seem so self-evident that we quickly forget the times before they were formulated. But, since the time of Newton, it has

been possible to define many other scientific concepts built up from that solid base. Newton's staggering achievement was to define key terms in particular ways, and to devise a system of precise reasoning (mathematical reasoning, but it need not be mathematical) such that his overall conceptual scheme would *explain* many phenomena in the natural world.

In more detail, "mass" was defined independent of weight, as "resistance to acceleration"; and "force" was defined as that which causes acceleration (or deceleration), but unnecessary for uniform motion. The laws of motion and the law of gravity, used these definitions, and provided explanations of planetary motion and many other things, with a precision and certainty never seen before. As a result the terms mass and force became concepts which *were* validated, in a strong way. Thus the basic language of the natural sciences was established, a language which, since Newton's days, has been greatly extended, modified, and (in relativity theory) deepened, but not fundamentally overturned. That language is valid in all countries and cultures, and crosses generations. That is why "science" has such world-wide appeal. Concepts like mass and force *do* have more precise definitions than ones widespread in political or humanistic debate (such as "democracy" or "freedom").

The messages here are: Explanation and validation of concepts are mutually interdependent. The *only* way in which scientific concepts can be securely validated is when they are defined in such a way as to support strong explanatory arguments. This is *exceedingly* difficult, because the explanation depends on the way concepts are defined, but one doesn't know how to define the terms until the explanation is in mind. There is no short cut, no easy algorithm, no linear chain of reasoning bound to succeed; and there is no alternative, if the aim is strongly validation of concepts. The process is circular: The conclusion depends on the premises and the premises depend on the conclusion. Difficult it may be; but when it works, it works like wildfire, and "feeds on itself".

5. The Natural Philosophy Approach in Bio-medicine.

The origins of biology, are essentially descriptive rather than explanatory. Natural history is not confined to biology, but since biological systems are inherently complex, and not easily simplified (as in physics) to reveal single variables at work, natural history *has* tended to focus on biology. This was the tradition in which Charles Darwin had his formative experiences. The origins of medicine are also within this tradition; and in psychiatry, pioneers such as Pinel and Esquirol saw their task as to describe, not to explain.

Although biology and medicine started from a different tradition from the physical sciences, there have been notable successes where something akin to natural philosophy was possible, including true cross-level explanations. The germ theory of infectious diseases (if not the later discovery of specific infectious agents) is possibly the first such success. Early in the twentieth century, the behaviour of chromosomes at meiosis (at a lower level) provided an explanation of facts of Mendelian genetics (at a higher level) which had been revealed a generation earlier. Other examples include the unravelling of the ionic fluxes underlying the action potential in the 1950s, and, in the same period, the biggest of all such insights, the revelation of how the molecular structure of DNA could explain macroscopic facts of reproduction of cells and organisms, and many facts from genetics. It is notable that two of the key figures in the latter revelation were Maurice Wilkins, who had a physics degree from Cambridge University, and Francis Crick, who studied at the Cavendish physics laboratory in Cambridge, before his contribution to this breakthrough. Another pioneer of molecular biology, Jacques Monod, was quite clear that he was working in the natural philosophy tradition, when he gave his book "Chance and necessity" the subtitle: "an essay on the natural philosophy of modern biology".

Mainly however, in biology, and even more so in medicine, the systems studied are inherently more complex than in physics, so complex that description has been the primary aim. Isolating the impact of single variables is difficult and often assumed to be impossible. If "explanation" is claimed it is of a kind different from, and weaker than that in the natural philosophy tradition. "Biological variation" is accepted without question, and submitted to statistical analysis; it is rarely itself the object of explanation as it might be in physics, where most systems are exactly-reproducible. Thus statistics become more important, and true theoretical reasoning (whether or not quantitative and mathematical) is less so than in physics. More typical in biology and medicine is the style of research formulated in the nineteenth century by the physiologist, Claude Bernard. His objective was to establish the use of the scientific method in medicine. However, his concept of "scientific method" was very different from that in physics. He writes

> "Proof that a given condition always precedes or accompanies a phenomenon does not warrant concluding with certainty that a given condition is the immediate cause of that phenomenon. It must still be established that when this condition is removed, the phenomenon will no longer appear".

(from *An Introduction to the Study of Experimental Medicine,* Claude Bernard, 1865; English translation, published by Dover, 1957, p.55).

This criterion is an empirical one based on results of physiological experiments (perhaps with statistics analysis of results), not one based on exact reasoning, as in physics; and "proof" for Claude Bernard was less certain than in physics. One can make the same point about Robert Koch's criteria for supposing a microbe to be the cause of an infectious disease, or Henry Dale's criteria for establishing that a particular chemical substance was a neurotransmitter. Since biological variation is treated statistically, rather than by looking for its explanation, major flaws in reasoning arise, of considerable significance in medical research. *Statistically* we know that smoking is associated with increased rates of lung cancer and other disorders, and we may know that "genetic factor X increases the risk for disease Y by two or three-fold". However, from a logical point of view it is a complete *non-sequitur* to go from this to assert that "if I (as an individual) stop smoking" I will avoid lung cancer (etc), or "if I take a medication to counteract expression of gene X, I will avoid disease Y". In complex systems, change of one variable may have effects quite unexpected from simple reasoning. This logical fallacy arises because the Claude Bernard-style of research confuses explanation and causal reasoning with observed correlation (or more generally natural philosophy with natural history). I am not denying that many valuable results have come from this approach; but it is *not* the same, nor as powerful as results obtained in the natural philosophy tradition. We should be aware of its limitations; and we can do better.

In examples where the natural philosophy tradition *has* achieved success in biological systems, principles are discovered which greatly simplify some aspects of these systems. The tradition has not yet made major inroads into biological systems in their full complexity, such as those of interest in psychiatry. The question underlying this essay is whether true explanation in the natural philosophy tradition can be achieved in systems of the complexity of the human brain, and which presumably underlie at least some aspects of the disorders dealt with in psychiatry. I believe that we are not sufficiently ambitious in this area: Real explanations *can* be discovered, based on empirical information we already have. To substantiate this claim, and to show how the search for true explanations can be promoted it is necessary to analyse further the differences between physical and biological systems.

For any scientific explanation to be successful, it is necessary that critical empirical facts are already known, and that no major confounding factors are

ignored. This does not mean that *all* relevant facts should be known in advance. Indeed, in physics, when a hypothesis has been formulated on the basis of known facts, predictions which are made about areas of uncertainty allow decisive test of those hypotheses to be conducted, so that what was a *hypothesis* ("less than a thesis") becomes a *theory* with claim to wider acceptance. Of course the process is easier in systems where the number of variables is small and there are fewer confounding variables than in more complex systems. This accounts for the fact that the natural sciences started off by analysing planetary motion, where the only relevant variables were about time and position in space, in relation to assumptions about motion and gravity, rather than with more complex systems. It follows that true explanations of complex biological systems *might* be possible; but, if they are, it is necessary for the would-be theoretician to be familiar with a far larger body of empirical information than in the physical systems where classical explanations proved successful. Far more needs to be assimilated in the theoretician's mind before theory building can be successful; but then, the reasoning needed may be relatively simple (albeit far from obvious).

6. Weaknesses of Current Research in Biological Psychiatry.

(i) *Background.* Biological psychiatry, sometimes claims to be (and is certainly trying to establish itself as) fully scientific. However, the basic concepts (especially concepts of disease) are poorly established, and (as already explained) are a major cause for community concern; theories or cross-level explanations for those diseases are almost non-existent. Tortuous debates still continue about DSMV and the revision of ICD, and there is no end in sight. In the area about which I know most, schizophrenia, many single criteria might be proposed as short cuts, on which to base a system of classification. These include patterns of inheritance, response to treatment, temporal patterning of episodes, factor analysis of symptoms, long-term outcome, and so on. They are all relevant, but none is sufficient. Only the *coordinated reasoning* which brings them all together within an explanatory framework or disease theory is sufficient to validate a disease concept in the strong way found in established areas of science; yet in mainstream psychiatry there is no such body of reasoning, nor evidence of any concerted efforts to bring it into being. As already mentioned, in the natural philosophy tradition, validating concepts and formulation of theories are interdependent. The same should be true in psychiatry; but because of the vastly greater complexity of systems under study, much more empirical information must be assimilated into any potential theory before it has a chance of providing explanations or validating basic concepts. Thus far this task has proved

beyond mainstream psychiatry; and as a result a variety of other approaches have proliferated, but little so far that can really be called an explanation. Here I describe some of those approaches, all referred to metaphorically as varieties of phrenology:

(ii) "Receptor phrenology": Of course psycho-pharmaceuticals are of vital importance in psychiatry. We need to know much more about actions of transmitters and exogenous agents at relevant receptors, and also to discover many more agents selective for receptors now known, and yet to be discovered. Nevertheless the power of the psycho-pharmaceutical industry has surreptitiously persuaded many people to conceive mental disorders just in terms of excess or deficit of this or that transmitter (and more recently to over-emphasise gene variants for transmitters, rather than other determinants of brain function). The "dopamine theory of schizophrenia" or the "serotonin theory of depression" are prime examples. This is naive. Even at the pharmacological level it is naive, since all central transmitters act via several receptor types, and in a wide variety of brain structures. A mixture of transmitters and receptors in a test-tube cannot reproduce a subjective state: Before this is possible, one must also take account of the great structural complexity of the brain's macro-structures, each with its exquisite cellular structure, and each cell with its complex biophysics, upon which those transmitters act. Before we can predictively match the properties of a new chemical entity to its therapeutic potential we need more realistic models of brain mechanisms underlying mental disorders, based on aspects (perhaps many aspects taken in combination) of brain biology additional to neurotransmitters, receptors and their genes.

(iii) "Imaging phrenology" and fMRI: Here I am not referring to structural MRI, a technique I find useful for theory building, albeit with some cautions. Functional MRI emerged from studies of regional blood flow in the brain, and, with MRI technology, allowed assessment of activity within the brain with much finer spatial resolution than ever before. There is no doubt that many interesting correlations between fMRI findings and psychological processes or psychiatric symptoms have been revealed since these methods become available. However correlation is not the same as causation or explanation. There are very severe problems with the method:

The basic signals by which information is processed in the brain are electrical "impulses", each lasting about 1/1000 second, occurring in each nerve cell at frequencies of 1-500/sec, but usually in the lower part of this range. In each cubic millimetre of brain tissue there are ~50,000-100,000 nerve cells, richly interconnected with each other by nerve fibre connections, with each cell giving and receiving ~5,000 connections. The human cerebral

cortex contains ~800,000 such 1 mm^3 volumes of brain tissue (i.e. total cortical volume of about 800 cc). It is also divided into about fifty regions ("areas"), each having a volume of a few cubic centimetres. In microscopic anatomical analysis there are differences in structure - that is in arrangement of cells - between these areas, but these are quite subtle differences. Broadly one can consider these fifty areas as "variations on a common theme". Corresponding to this, one can envisage that each of the cortical areas perform roughly the same sort of computation on the signals relayed to it by its input connections. The main reason why one can imagine that different areas of cerebral cortex have different functions is not because of intrinsic differences in the computation between regions, but because the input and output connections are different. Electrical signals conveyed to each area, while basically the same (as in "morse code"), code different messages because of what they are connected to. For examples, these signals may have been triggered by visual, auditory, or touch stimuli (and there are many more complex messages to be considered), yet all are coded by the same sort of electrical signals.

When a nerve cell produces such signals, it uses energy, and so consumes oxygen, and glucose, and, associated with this, local blood flow increases. These measures - glucose utilization, oxygen levels, or blood flow - are detected in fMRI. They are only indirectly related to electrical signals produced in each nerve cell, and respond much more slowly than the electrical signals themselves (response time, at the very best, of ~1second). In fMRI these measures are evaluated for every "voxel", a volume of ~1^3mm. Thus, in each spatial unit for the image, the measure of activity is based on metabolic activity averaged over many thousands of nerve cells. I do not doubt that, on the large scale, this method can reveal important information about *some* areas which are *usually* activated in relation to *some* psychological functions. My reasons for scepticism are as follows:

(a) In neurophysiology there is debate on how electrical impulses code information. This may be in terms of the "average frequency" of impulses over periods of ~1 second. If this is all, it is plausible to suggest that the signal detected in fMRI for a particular cortical area, corresponds to average activity in that area at the time of scanning. Alternatively, it is suggested by some that information may be coded by the exact timing of individual impulses, on a much finer time-scale. In this case, information can be coded by different impulse patterns over time, without change in overall frequency at the 1-second scale, and with no change in energy use, or oxygen or glucose

consumption. All researchers think that information can be coded by "rate" of impulses. Some, myself included, think that it can also be coded by the pattern of impulse timing, even to a precision of a few milliseconds, even if there is no change in overall frequency. If both forms of coding apply, it follows that the absence of activation of a neurone (as far as fMRI signals go) does *not* mean that it is inactive as far as information processing goes. Add to this that the smallest signal detecting in fMRI is an average of at least 50,000 neurones, and the possibility of missing important correlations is immense.

(b) The relation of metabolic activity to impulse activity is not clear, although some progress has been made on this recently[4] This is especially true for the basal ganglia where interactions between neighbouring neurones are mainly inhibitory, although it may be less problematic for the cerebral cortex. Without knowing more about this relationship, fMRI signals, though producing interesting correlations with psychological performance, do not provide data adequate for constructing true explanatory arguments, based on neuronal dynamics.

(c) Given that there are negative feedback loops of many sorts, and on various time scales, in the cortex, it is not clear whether functional activation of an area of cortex, shown by fMRI indicates that neurons in the area are performing their normal function, or are compromised for a particular task (and therefore "struggling hard", in response to feedback signals).

(d) Patterns of fMRI activation depend on patterns of connectivity between the different cortical areas. We know almost nothing about the extent of individual variation in connectivity, and have no way to determine this. Even in experimental animals, there is no systematic study of individual variation in connectivity. It is therefore quite possible for one area to give activity in individual cases, in a function normally attributed to another area. Since fMRI, at its best, would average results over many participants, the possible confounds are immense.

(e) In some reviews of studies using fMRI, summarising results from many individual studies related to a particular psychological function, it is noted that different studies produce quite different spatial patterns of activation. In part this may arise because, at the level of large-scale structure, the pattern of folding of the cerebral cortex shows much individual variation. This means that particular

[4] Logothetis,N.K., Pauls,J., Augath,M., Trinath,T. and Oeltermann,A. (2001) Neurophysiological investigation of the basis of the fMRI signal. *Nature*, 412, 150-157.

areas do not have locations which are exactly fixed from one person to another. Methods have been devised to match areas between subjects despite such large-scale variation[5], yet they are extremely difficult, and seldom used.

(f) Interpretation of data is made more complex by the habit of researchers using fMRI to report results as values normalized in various ways (e.g. by comparison of a region with the rest of the hemisphere) and reported as a percentage, or as statistical parameters (e.g. t-values for comparisons with other conditions or other subject groups). For investigation of some hypotheses, normalization may eliminate the very differences one seeks to define. Which statistical approach is to be used depends on its purpose. Statistical manoeuvres chosen and performed without prior matching to the hypotheses under investigation may be counterproductive.

I do not entirely discount results using fMRI, although EEG or MEG are more useful because of their higher temporal resolution despite lower spatial resolution. If fMRI is to contribute at all to forming true explanatory arguments, the above weaknesses have to be considered very carefully in designing any study. In some countries (especially Britain), the popularity of fMRI is a joint consequence of the excessive pressure to publish and the decline of animal experimentation as an alternative, due to activity of anti-vivisectionists. In the U.S.A. the method is even being used for assessing individuals in forensic situations, despite it best use being for aggregate rather than individual analysis.

(iv) "Genetic phrenology" and molecular genetics: The deciphering of the human genome was supposed to open up a completely new form of medicine, but has not yet delivered much of what was promised. Studies of inheritance make it is indisputable that there is a genetic component to many psychiatric disorders. However, the prominence of molecular genetics has been accompanied by neglect of these basic inheritance studies, and has led to exaggeration and over-simplification of the genetic, compared to other causative factors, especially as purveyed in public media statements. When the human genome was published, an editorial in *Lancet*[6] urged caution, since environmental causes of disease predominate over genetic ones, and represent a far larger proportion of global burden of disease. To illustrate the exaggerated role of genetics, in schizophrenia, the population incidence is ~

[5] Seitz,R.J. (2002) Mapping of human brain function by neuroimaging methods. In: *Cortical areas: Unity and Diversity.* A.Schüz and R.Miller (eds), Taylor and Francis Publ.

[6] The human genome, in proportion, *Lancet* 357, 489.

0.5-1.0%, that in first degree relatives of those with the disorder is ~8% and that in MZ co-twins, approaches 50%. Hence if you are a first degree relative of someone with schizophrenia, there is a 90% chance of you *not* having the disorder, which might be an important fact when couples decide whether to have children or not. This is not the perspective conveyed to the public, for whom the genetic risk is over-emphasised. Psychiatric molecular geneticists bear considerable responsibility for this misrepresentation. At a more technical level, the fallacy is to imagine that all disorders with any genetic tendency are inherited in a categorical, quasi-Mendelian fashion. This *is* true for a large number of inherited disorders, but generally any one of them is quite rare. For *common* disorders (such as schizophrenia and some other psychiatric disorders), which represent a far larger fraction of global burden, evidence suggests that multiple genetic factors, in numerous complex combinations, differing from case to case, are the likely genetic contribution. These complications were well known before the human genome was published[7]. Genetics as taught in secondary schools (in New Zealand) deals with Mendelian inheritance, but not the more complex non-Mendelian inheritance. Mendelian concepts give support to eugenic concepts (still alive in many countries, and government policy in a few), yet non-Mendelian inheritance is more relevant, has better scientific credentials for public policy in most areas, and gives no support to eugenic ideas. There are real dangers here. Medical speciality colleges have a responsibility to challenge current fads and fashions, and have an important responsibility in challenging popular misrepresentations of genetics, and to get a more wholesome emphasis in public media.

The search by molecular geneticists for "the gene" for schizophrenia or similar multi-factor disorders, on which vast resources have been spent in the last twenty years, is likely to be fruitless. Admittedly, molecular genetics is unravelling an increasing number of genetically-discrete disorders, and these include some cases of what were previously lumped in with common, presumed multi-factor genetic disorders. It is not clear yet how far those common disorders will be broken down into a large number of rarer, more discrete ones. Nevertheless, genetic reasoning based on the older inheritance studies (for instance, that based on MZ/DZ concordance ratios) still make it highly likely that disorders such as schizophrenia, in most cases, are the result of complex combinations of genetic factors. Those factors may combine in unpredictable, even paradoxical non-linear ways (subsumed under the term "epistatic" interactions); yet the scientific study of even the

[7] .Zimmern,R.L. (1999) The human genome project: a false dawn? *BMJ,* 319, 1282.

simplest such interactions has scarcely begun. The larger the number of factors implicated, the weaker will their individual effects usually be, the more difficult will it be to find them, and even more to find their combined effects, the less will be their practical importance, and the expenses will accumulate in logarithmic fashion. Can such research really be justified?

(v) *Conclusions.* A broad fallacy in the above-mentioned fields of research is to mistake description (in the form of correlation) for explanation, or, returning to my starting point, to confuse natural history and natural philosophy. In the above three areas of research, that confusion was characterised with the metaphor of "phrenology". This was a fashion popular in early nineteenth century of interpreting a person's personality by the bumps on their skull. When the first solid evidence of cerebral localization of function started to appear in the 1860s, the same manner of matching psychological to cerebral functions caught on as actual science, and endures to this day. There were however serious debates amongst neurologist between advocates of cerebral localization of function and those advocating a more holistic approach, in Germany, and then amongst neuropsychologists such as Karl Lashley. I became aware of this fundamental debate in Oxford in the early 1970s[8]. The reason why I use the metaphor of phrenology is that all the areas of research I criticise make the same mistake as the phrenologists: A living organism, especially the human being seen as an person, is an integral whole in which (with some limits) all identifiable psychological functions interact with all others. If we obtain evidence that one function (or trait, or symptom, or disorder) correlates with one region of the brain (or receptor, or genetic factor) we should not conclude that that region (or receptor or gene) is in itself sufficient to display that function (or trait etc): They always depend on the rest of the brain (and the body as a whole, to say nothing of the society in which a person is embedded). Thus the answer we get to questions about functional localization (whether to a brain region, a receptor or a gene) depend entirely on the way a question is posed experimentally. To adopt a simplistic localizationist perspective (in whatever guise it appears) is an insulting debasement of the complexity of human psychology.

If a resolution to this conundrum is to be reached, it is necessary to realise first that it is not so much a scientific issue as a philosophical one. In that form, it is one of very great generality, between parts and organised wholes of *any* sort - between the part ideas which make up a bigger concepts, the parts of a pattern which go to make up integrated perception,

[8] see for instance C.G.Phillips (1973) Cortical localization and 'sensorimotor processes' at the middle level in primates. *Proc Roy Soc Med*., 66, 987-1002.

or the components of the brain whose several specializations make up a much more complex functional whole. As a philosophical issue it can be traced back to early years of Christendom at the Council of Calcedon in 521 C.E., but reappears recently in catch-phrases like *E Pluribus Unum* ("From the multitude comes unity", on coins of the U.S.A.), or *The Whole is greater than the sum of the parts* (from Gestalt psychology). Whether we can ever understand integrated wholes in biological systems in a *scientific* sense, and which we can understand, are open questions. However, we should not go for simplistic ways of thinking just to ease our furrowed brow (i.e. our lack of real comprehension); yet that is precisely what is driving the various sorts of phrenology I mentioned above. Of course the efforts made in the research I have just referred to are often extremely expensive, and, while *sometimes* achieving intellectual progress (and practical applications) often they fail on both counts. They are sustained only because of the incorrigible optimism of their advocates, and the view that, "in the long-term" there will be some elucidation. I am tempted to quote Maynard Keyes: "In the long term we are all dead". We need discernible progress, intellectual if not in immediate practical terms, within our own life-times.

7. A Better Way Forward.

If psychiatry is *really* to become a fully scientific discipline, what is needed are robust explanations and disease theories, and robustly-validated concepts. Precedents from physics indicate that precise explanatory arguments depend on having precisely-defined basic concepts. These in turn depend on already having explanatory arguments in mind. There seems to be a total impasse at this point.

I do not regard this conundrum as insoluble; and I *am* drawing deliberate parallels with the way central concepts came to be defined in the natural philosophy tradition in the seventeenth century. There are several aspects to the analogy: It will be necessary: (i) to carefully distinguish the two traditions (natural philosophy and natural history) in what we are doing; (ii) to aim for a proper balance between empirical study and theory development; (iii) to aim for robust cross-level explanations of the relevant evidence known at a higher level in terms of lower level processes. The evidence to be explained may be psychological, behavioural, symptomatic and (with some caveats about interpretation) first person experiential accounts. The lower level premises for the explanation may be hypothetical rather than established facts, but are especially likely to be about brain biology. I believe these objectives are all within our grasp, eminently possible in many areas of psychiatry, on the basis of empirical evidence we

already have. It will however need drastic reorientation of the focus of research.

I think that the analogy with early research in physics (a.k.a natural philosophy) is relevant for another reason. In the seventeenth century, apart from the struggle to define what "natural science" could be, there was a substratum of even more profound debate, on what are essentially metaphysical issues, about such things as the best meaning for words like "nature", and "causation", and the relation between religious notions of the time, and the nascent concept of natural science. Were scholars to continue using Aristotle's ideas about "final cause", or was there a more profitable way to conceptualise cause ("antecedent cause" as we might now call it). In psychiatry today, there are also underlying debates on metaphysical questions, about the relation between mind and brain (or equivalently between the subjective and objective worlds). In this sense, to define disease theories in psychiatry is far more difficult, and far more fundamental than defining disease theories in other areas of medicine. The germ theory of infectious disease, or theories of autoimmune disease, neoplasia etc, do not require any original thinking at the metaphysical level. Thus, in psychiatry, the task is *very* fundamental, by comparison with much of today's "routine" biomedical science.

Although I draw the analogy with natural philosophy at the time of the origin of the natural sciences, the analogy should not be pushed too far. There are important differences. The major difference is that the brain and its psychological products (behaviour, thought etc) are vastly more complex than the physical systems dealt with by Galileo and Newton. No doubt those systems did seem formidably complex to those who were wrestling with these issues, as yet unsolved, at the time. The whole point of a good explanation is that it simplifies one's ways of thinking; and then we easily forget how complex it all seemed before the moment of illumination. Nevertheless, in the case of the brain we certainly need a vastly larger body of empirical data before precise reasoning can start to get traction. We *do* have a vast amount of factual information both about the normal brain, and about complex disorders such as schizophrenia. The problem is that very few individual scientists know about this except in small areas of their own research. In my view, at least in some areas of psychiatry, there *is* now sufficient empirical evidence to start to employ reasoning for theory development, but we need a dedicated body of researchers who try to get to know much more widely what is already known (by somebody).

The other major implication of the much greater complexity of the brain compared with most physical system studied in the natural philosophy

tradition is that the scope for precise mathematical reasoning is likely to be far less than in physics. What is rather needed is a special style of scholarship. I do see *some* role for mathematics and computer modelling. However, in my view this is useful in special carefully-defined areas. Specifically, I think these methods can throw important light on the electrophysiology of single neurones, or the *abstract principles* of neural network interaction. Analysis using computer simulation or mathematical reasoning of the *reality* of complex biological systems, such as the *real* brains or structures within them, I think is not very helpful, and perhaps wasteful. There are far too many "floating" parameters, and the limits to exact reasoning set by chaos theory preclude exact predictions. Even in physics major theoretical advances sometimes have depended as much on sudden subjective insights in the prepared mind of the theoretician on how things "fit together", as on sophisticated formalized mathematics.

So, to, construct those cross-level explanations, the area where I see room for much greater emphasis is in very systematic, and very large scale scholarship, guided by reasoning which is often relatively straightforward. Only with such scholarship can one begin to get a feel for the full complexity of a biological system. Only with such thorough scholarship does the theoretician have a mind adequately prepared for those flashes of insight when new explanatory premises are conceived. Relatively simple reasoning then leads first to small-scale preliminary conjectures or predictions, which can then be checked against the wealth of published empirical information. Occasionally predictions are made on which no data exist, so then the ball is in the experimenter's court; and by repetition and extension, small-scale conjectures build up iteratively into larger theories.

There are already a few areas where such cross-level explanations in the brain and behavioural sciences have emerged. Since this is the area on which my own work has focused in the last 35 years, I will mention some of that work in this section. My aim here is not to boast about these successes. As always, in real science, conclusions are for ever *sub judice,* always subject to challenge. Rather it is to show that a radically new approach, with great potential is not only possible, but promises great practical dividends.

(a) *The rubric of instrumental conditioning, the discovery of the self-stimulation phenomenon, and the impact of this on psychiatry.* In the first half of the twentieth century a great deal of work by psychologists in animals and humans analysed processes of learning using associationist paradigms. The rubric of instrumental conditioning, while far from a complete account of learning in any species, is nevertheless arguably an important component of learning systems, as described in psychological

terms. Referring to the idea of cross-level explanations, this is the "higher level" in this example. What could be the lower level, that is, its neurobiological basis? In the early 1950s, James Olds and Peter Milner addressed this issue. (It is noted here that Peter Milner, the theoretician of the pair, was an engineer by training before becoming a physiological psychologist. He was no doubt used to analysing physical systems with built-in feedback loops.) As a result they reasoned that there must be an internal reinforcement system in the brain; and that by linking an animal's behaviour directly to this system (by-passing the sensory systems which normal activate it), behaviour could be reinforced, regardless of its usual motivational significance. The reasoning was thus a classic piece of cross-level explanation in the natural philosophy tradition. It led to the celebrated "self-stimulation", or "brain stimulus reward" experiment, published in 1954. Behaving animals, with electrodes implanted in the brain, were able to lever-press to deliver electric pulses through the electrode. With some electrode placements, the animals would repetitively stimulate their own brains, regardless of other prevailing motivational drives. From this developed a vast body of experiments, examining the electrophysiological, anatomical and pharmacological aspects of the internal reinforcement system. In due course this had a major influence in psychiatry, as evidence accrued that a major part of this reinforcement system involved dopaminergic pathways linking the midbrain with the forebrain. I became aware of this literature in the early 1970s, and used the idea to explain a singular paradox about the effects of antipsychotic drugs: While they block dopamine receptors within, at most, a few hours, the beneficial clinical effects accumulate over weeks or even months. From that insight the idea grew that psychosis was an exaggeration of the reinforcement functions of dopamine, expressed mainly through distinctively human cognitive processes rather than necessarily through outward behaviour. My first paper on this was published in 1976[9]. In the early 1980s Rick Beninger from Queen's University (Kingston Ontario) independently came up with a very similar concept for psychosis, and, since we met in 1989, we have worked together, and published several jointly-authored papers. Nowadays it is becoming mainstream understanding of psychosis, although the terminology has been changed (to something like "aberrant salience" rather than exaggerated reinforcement). However, many of the subtleties of the reasoning have been lost, and few people know the origin of these ideas. If the full story were better understood, it would be clear that it has

[9] Miller,R. (1976) Schizophrenic psychology, associative learning and the role of forebrain dopamine. *Medical Hypotheses* 2, 203-211.

considerable practical implications for how antipsychotic drugs should best be prescribed, perhaps leading to more rational prescription than at present.

(b) To link psychological processes to underlying neurobiology, in a truly explanatory sense, we obviously need to know a great deal about the nerve cells of which the brain is composed. A great deal *is* known about nerve cell bodies and their biophysics, but so far, it has not proved very useful for cross-level explanations. However, one part of a neurone has been neglected, especially for central neurones, that is the humble axon. We have known the physical basis of action potentials in axons since the 1950s, and in the peripheral nervous system we have known about conduction properties (e.g., conduction velocity) for longer than that. However, in the central nervous system the evidence, especially on conduction velocity is scanty. As a post-doctoral student in Oxford in the early 1970s I was recording from single cortical neurones in the cerebral cortex of anaesthetised cats, and was able to obtain data on the range of conduction velocities in populations of axons connecting together different parts of the cortex. Some axons had conduction times much longer than anyone would have guessed at the time. The experiment certainly was biased against detecting neurones with such slow-conducting axons. Bearing in mind these likely biases, and scaling things up to brains the size of humans, it is very likely that different axons in a typical pathway have conduction times (from cell body to synapse) ranging from a few milliseconds (in rapidly-conducting axons) up to a few hundred milliseconds (in slowly-conducting ones). Harvey Swadlow, from the University of Connecticut has done much more animal experimental work on axonal conduction in the CNS, and, making similar inferences for humans, reaches much the same conclusion[10]. The slower-conducting axons have conduction times long enough to have major implications for the computation accomplished in the cortex, as might be revealed in psychological experiments in intact humans. Thus we are within reach of true cross-level explanations of psychological findings in terms of brain structure and cellular function. The first time I used this concept (in 1981[11]) to explain a psychological finding was as follows: Each consonant speech sound is, in acoustic terms, a brief succession of acoustic events occurring in sequence over a period of about 100 msec. It is known that human perception of consonant speech sounds is usually performed better with the left than the right hemisphere. The hypothesis I developed was that the left hemisphere has a richer repertoire of "long axonal delay lines" (which can

[10] Swadlow,H.A., Geschwind,N. and Waxman,S.G. (1979) Commissural transmission in humans. *Science* 204, 530-531.

[11] Miller,R. (1981) *Meaning and purpose in the intact brain.* Clarendon press, Oxford.

represent patterns spread over intervals of time of ~100 msec) than the right (where conduction, hypothetically is faster, the hemisphere then being better for analysing *instantaneous* patterns). By the 1990s this simple idea had been worked up to produce a more comprehensive theory of cerebral asymmetry, the central hypothesis being that, in most pathways, the left hemisphere has axon populations whose range of conduction times spans longer time intervals than in the right. From there, I went on to explore an idea which had been around since the late 1960s, that there was some form of *abnormal* laterality in schizophrenia. In the end I was able to account for a very large number of non-psychotic traits associated with schizophrenia, in terms of the hypothesis that (regardless of the hemisphere) there is a relative lack of rapidly conducting axons in schizophrenia, these being replaced by slowly-conducting ones. My magnum opus on this subject was published in 2008. Anyone who wants to get a grasp of the full range of psychological functions for which explanations in terms of population-distributions of axonal conduction times form the basic premises should look at three of my books[12]. The reasoning in these works, as well as the assumptions on which it is based have yet to be given a proper critique. I await that with interest.

There are several important general lessons to be learned from these two examples: (a) True cross-level explanations in the brain and behavioural sciences *are* possible, including ones related to mental disorders (where they may also be related to strategies for treatment), as well as to normal brain function. When such explanations are constructed, they may also serve to provide robust validation of the concepts used in the process; and these may cut across traditional concepts (such as concepts of disease) established in less rational fashion. (b) The two examples given employ two different principles from basic neuroscience. I am sure there are other principles coming from basic neuroscience, which may prove crucial for other explanatory frameworks, beyond these two. (c) Framing cross-level explanations is not possible unless *someone* is familiar with information at both the "upper level" (i.e. psychological findings, behaviour, symptoms or first-person accounts of experience) and the lower level (details of various aspects of brain biology). That means either that basic neuroscientists need to be educated about the fine clinical details of mental disorders, or that psychiatrists, clinical psychologists (etc) need to be educated about the fine details of neuroscience. This may require change in education in both areas.

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[12] Miller,R. (1991) *Cortico-hippocampal interplay and the representation of contexts in the brain.* Springer, "Studies in Brain Function" series.
Miller,R. (1996) *Axonal conduction time and human cerebral laterality.* Gordon and Breach.
Miller,R. (2008) *A neurodynamic theory of schizophrenia and their disorders*, Lulu Enterprises, Morrinsville, North Carolina.

(d) There is no algorithm by which one can determine which upper level evidence is to be related to which lower level principles to form a cross-level explanation. Since the evidence at both levels is far more complex than in physical systems, any would-be theoretician in this area needs to be extremely well-read, before he has much chance of achieving the link. This, I believe, is far more important than expensive computer simulations or mathematical analyses (although occasionally those methods may be useful in theoretical work in this area).

It may well be said that we do not have yet have enough basic evidence to launch a large-scale, library-based theoretical branch in the brain and behavioural sciences, or in psychiatry. I disagree strongly with this view. The problem is *not* that we do not have enough information to commence theory building, but that too few people know enough of it to make any progress, have no confidence that real explanations can be found (because there are no traditions for this), and have no idea how to find them. The information that has been accumulated over the last 100 years at both the higher and the lower levels is immense, overwhelming, staggering, much of it (not all) very solid empirical data, if only we knew how to use it; but who reads it? Who tries to assimilate it even at one level, let alone across levels, or between different fields of experimentation?

What I suspect has happened regularly over the last fifty years is that a new technique is discovered, experimenters rush to exploit it and many very good empirical papers are published, some not so good; but when the whole new area is reviewed it looks too messy and complicated to make *real* sense of it, and no-one knows enough in other fields or at other levels to do this. At this stage another new technique is invented, so researchers, always looking to publish good papers rather than achieve basic understanding switch to the new area; and then they do it again. . . and again . . . and again. Each time there is vast expense, and big profits for those who make the equipment, but little real progress in terms of understanding or at a conceptual level. The metaphor which comes to my mind is of a vast orchard, stretching way beyond the horizon; and wherever one takes a close look, one sees trees hanging low, overburdened with ripe fruit, ready for picking. Tending this orchard obviously took prodigious labours of many skilled and dedicated gardeners in times gone by; yet no-one picks the fruit, and hardly anyone knows of the existence, nor the size of this awesome orchard. No-one realises its wealth and enormous potential; and yet, since the fruit (all those research papers) are securely archived, the fruit will never become over-ripe and fall from the trees.

What this means is that a would-be theoretician should not expect to make a career out of *combining* theoretical work with experimental or clinical work (both of which may in themselves demand complete attention and commitment). S/he needs to be a dedicated theoretician, and we need a new discipline to emerge of theoreticians in brain/behavioural/psychiatric sciences, respected by and fully respectful of the experimental disciplines, both knowing that there is mutual benefit to come from close knowledge of each other's approaches, an alliance based on mutual respect, the one looking for predictions s/he can test, the other hoping to make predictions which the other *can* test. This also means that both sides should understand that (as in physics) good experimental researchers, and good theoreticians are quite different sorts of people, with different habits of thought, never to be evaluated on a single scale for "research assessment". This tradition of interplay between experiment and theory existed in the natural philosophy tradition ever since the time of Copernicus, Tycho Brahe and Kepler. It is now desperately needed if the brain and behavioural sciences are to make further substantial progress. If it could be brought about, in my view, progress would then go further, faster, be more secure, and be *much cheaper.*

8. Some guiding concepts

A few more specific concepts are suggested to guide the construction of true disease theories in psychiatry.

(i) State versus trait. Research on schizophrenia clearly shows that, in addition to active psychotic states, there are many non-psychotic trait markers of the underlying predisposition. The distinction between state and trait aspects of mental disorders may apply to other disorders (bipolar disorder, depressive disorder, anorexia nervosa etc) although not yet defined so well as in schizophrenia. For disorders where traits, and their separation from corresponding states are not well-defined, there is need for more descriptive work. Abnormal *states*, being transient are likely to be based on dynamic aspects of brain function, such as transmitter release, or electrophysiological variables. The more dramatic and obvious symptoms (often aspects of transient states rather than enduring traits) may be the ones most accessible to explanation in the first instance. Their biological mechanism *may* emerge first, as a prelude to more fundamental understanding of enduring traits (as has occurred in schizophrenia research, where understanding of psychosis has been well ahead of understanding of non-psychotic traits). Traits, being long-lasting, are likely to be based ultimately on static aspects of the brain, that is on aspects of cellular

structure or stable aspects of neuronal dynamics, and are therefore more fundamental to understanding those disorders. Therefore a focus on the relation between stable traits (symptoms, or psychological or psychophysiological traits) and evidence or hypotheses at the level of neuronal structure may be more fruitful in the long run than those which focus on transient, dynamic changes in the brain. The relation between the state and trait aspects of these disorders is also not to be neglected, but may be a more complex question, for which fundamental explanations may not easily be found, until explanations of both state and the trait features have been provided.

(ii) Concepts of pathology. If mental disorders are based fundamentally on divergence from normality in cellular properties, there is a distinction to be made which has an important impact on how we conceptualise those disorders: Divergence from normal, in a statistical sense, is not the same as pathology. Quantitative variation in cellular parameters need not mean that there is *pathology* at the cellular level. For instance, low conduction velocity in axons is due to their having a fine calibre or being myelinated, and often with cells bodies of smaller size; yet there is nothing at all pathological about fine calibre or unmyelinated axons, or about small-sized neuronal cell bodies. The cerebral cortex in all of us contains a wide range of sizes of neuronal cell bodies, and a mix of large- and small-calibre axons, and of myelinated and unmyelinated ones. The shifts are in the quantitative aspects of populations of neurones and axons. At what level then is the pathology to be found? I would suggest that for most mental disorders it is at the level of large nerve networks, even the whole brain, in terms of their information processing, and resulting subjective experience, behaviour and symptoms. In other words, it is unusually *psycho*pathology, not *neuro*pathology or *cyto*pathology.

If this is accepted it will have considerable impact on how mental illness are conceived, and how they are portrayed to the public, and to individual patients. In particular, many divergences from the statistical norm will be seen as being in complete continuity with the range of normal personality variations; and they may then turn out not to be truly pathological, except in certain environmental situations (such as in some social contexts). There are serious questions to be faced here for the broad concept of “mental illness”. Do we have a proper definition for mental illness, which would withstand scientific scrutiny? . . .or as some antipsychiatrists have claimed, are we misusing the concept of “illness” to pathologise something which is really deviance against *social* norms, rather than illness as conceived elsewhere in medicine?

(iii) Across how many levels should we seek explanations? There are many levels at which mental disorders can be studied, all the way from the basic "alphabet" laid out as nucleotide sequences, through "words" and "sentences" (amino acid sequences in proteins, and growth factors), to cellular properties, tissues, organized brain structures, whole brains, and their functional expressions in physiological, psychological, symptomatic or experiential ways. Undoubtedly *correlations* can be discovered which are many levels apart, and linked only distantly in causal terms, but these are not *explanations*. The reasoning needed for cross-level explanations initially has greatest chance of success if it does not cross too many levels. The two examples given above reached downwards from psychological findings of symptoms, to link, in one case with effects of the dynamics of a neurotransmitter (but not its determinants in terms of molecular genetics), and in the other to functional properties of axons, closely linked to their structure (but not to *their* genetic determinants). I suspect that this is a profitable avenue to explore - between the psychological/symptom domain and cellular properties. Sometimes the known beneficial effects of a medicine acting on a transmitter in reality signifies a fundamental abnormality not in the transmitter itself (or in its receptors or gene), but in cellular properties which can be normalised by a shift in activity of a neurotransmitter or neuromodulator. Focus on molecular origins may thus be cutting too many corners, along the road to an explanation. There *may* be cross-level explanations to be found between gene sequences and developmental processes in the brain. Although this is not my field, it seems to me *un*likely that this would throw much light on mental disorders in explanatory terms (although correlations may no doubt emerge). To seek explanations of symptoms or other psychological findings in terms of nucleotide sequences is I suggest, attempting too much. As one psychiatrist has said, genes do not code for "auditory verbal hallucinations in the third person"; nor, if we were trying to understand the meaning of Shakespeare's writing, would we get much success by analysing the frequency of different letters of the alphabet, or single words (or even phrases) in his text. As already mentioned, genes interact in immensely complex ways to produce tissue structures, and we have scarcely begun to unravel the principles of such interaction

(iv) Neurodevelopmental disorders. Many psychiatric disorders emerge during adolescence, and have some degree of genetic determination. This implies that they are something to do with brain developmental processes, as specified genetically, perhaps as trajectories of brain development somewhat different from the normal or optimal. Hence, we can call these disorders

"neuro-developmental". One aspect of normal development which we know about is axonal maturation, especially myelination. While some axonal pathways myelinate relatively early in post-natal life, those connecting together the different structures in the hemispheres myelinate progressively between birth and early adulthood, at different rates in different pathways, and perhaps continuing slowly in some regions or pathways into the twenties, or even later. Therefore, alterations in the developmental program for myelination of forebrain axonal connections is an important area where subtle divergence from the normal developmental trajectory may occur, which could underlie neuro-developmental psychiatric disorders. The potential of this area is indicated by the fact that myelination, via the variable it controls (axonal conduction velocity) affects neurocybernetic function and therefore psychological function; and since myelinated axons have larger calibre axons plus the myelin sheath, abnormality in the degree of myelination (if it affects large populations of axons) will have detectable effects on gross structure, as might be revealed in structural MRI or diffusion tensor imaging.

(v) Similarities and differences between neurological and psychiatric disorders. Historical parallels have already been referred to in the debates in psychiatry and neurology in the context of phrenology, the concept of cerebral localization of function, and the alternative more holistic approach to the brain, as an organized whole. Likewise the inference that schizophrenia, or other mental disorders are a form of disconnection syndrome draws a direct parallel to neurologists' ways of thinking. For mental disorders, however, there is hardly ever a real lesion, and no direct evidence for disconnection, so the statement is an inference from functional evidence, or even just a metaphor. Here we can extend the comparison by pointing out further differences (and similarities) between neurology and psychiatry. Most of neurology is based on identifiable pathology in the form of loss or damage to nerve cells in specific locations in the brain. In psychiatry, this is seldom the case, yet there *are* some similarities in symptoms profiles, especially in comparing milder neurological deficits with trait aspects of psychiatric disorders. One possible basis for these similarities comes from the suggestion that abnormal myelination underlies a number of neurodevelopmental psychiatric conditions.

A little detail is needed here: If a pathway contains axons whose conduction times range over the population of axons between (say) 5 and 20 msec, impulses which start off at the same time, will be dispersed a little in time when they reach their destination, but nevertheless most will arrive within the same "neuronal integration time" (order of 10-15 msec) and so

can effectively summate in the post-synaptic neurones. If a corresponding pathway has conduction times all four times longer (ranging from 20-80 msec), far fewer impulses will arrive at their destination in any single integration time, and summation in post-synaptic neurones will be much less. The result may be deficits similar in some way to an actual disconnection syndrome, due to physical damage to cells or interruption of their axons. There may thus be considerable overlap between traits of mental disorder, and neurological problems due to actual brain damage, although at the cellular level, the causes are quite different. However, slowly-conducting axons *do* still conduct impulses, and for some functions, this may show up as *better than normal* performance (as is the case for some non-psychotic schizophrenia traits).

Another implication is that when neurological and psychiatric syndromes overlap they may be more dramatic subjectively for the neurological than the psychiatric patient, because in the former case, impairment is very often the result of actual head injury, or other forms of brain damage. Thus, if the person so affected is capable of reflective insight into his or her impairment, it may be more informative than in psychiatry, because there is more likely to be a striking "before and after" comparison. In contrast, in psychiatry, the present state of impairment may be the only subjective reality a person knows. There may thus be much to learn from dialogue between neurology and psychiatry, and their respective patients. There may also be much to learn from German physicians and researchers, where the separation between psychiatry and neurology did not occur as it did in the English-speaking world, and many specialists combine training and experience in both specialities.

(vi) "Specific energies", and the overlap between trait aspects of different psychiatric disorders. In 1826, Johannes Peter Müller proposed the law of "Specific Nerve Energies", which states (in modern terms) that the function (and subjective impact of) activity in a nerve pathway depends on what it is connected with rather than what initiated the activity (be it a sensory stimulus, an applied electrical or chemical stimulus, or whatever). An adaptation of this principle is directly relevant to the preceding argument, with major implication for classification principles in psychiatry. If there is abnormality in an axonal pathway in the forebrain (whether that is an interruption of the pathway, or a change in the range of conduction velocities in a population of axons) the functional impact depends not so much on the cause of the change, but on what the pathway is connected to, upstream and downstream. This means that underlying factors at the cellular level causing the change (whether genetic, or environmental) are not directly

related to either the details of symptoms and other functional abnormalities, or the supposed disease entity of which they are a part. A similar cause of change (slowing of the range of conduction velocities, or actual damage to axons) may produce quite different symptoms (and be put into quite different disease entities), according to which region or which pathway is involved.

This fact is more relevant to trait aspects of mental disorders than to the state aspects (whose theory is likely to be more difficult to derive from fundamental causes). However, from my knowledge of schizophrenia traits I can give some rather tentative examples of disorders which might be similar at the cellular level, but quite different at the symptom level. *(a)* The historic separation between schizophrenia and manic-depressive illness coming from Kraepelin was known even by him (in his later years) not to be a sharp separation, and has been questioned by later writers ever since. Nevertheless, there *are* some differences between the two disorders as conventionally defined (as well as many similarities). There may be similar processes at work at the cellular level, but in different parts of the hemispheres. (b) If one looks at traits associated with dyslexia, many of them overlap with those of schizophrenia. There are however two major differences, that schizophrenia is associated with vulnerability to psychotic episodes, which do not occur in dyslexia; and in dyslexia there are usually striking disturbances of visual perception, not seen in schizophrenia. This leads to a hypothesis worth investigating, that the abnormality in both disorders is similar at the cellular level, but affects the anterior parts of the hemisphere more than the posterior parts in schizophrenia, the opposite in dyslexia. (c) Similar questions arise from two more examples of co-occurrence of syndromes: Schizophrenia is sometimes associated with noise sensitivity, sometimes not. Likewise, I recently met a person who had the dual diagnosis of schizophrenia and OCD/Tourette's syndrome. Such instances of overlap between supposedly-separate disorders may be quite common, and more than chance coincidence. They need better documentation: There is need for much more epidemiological work on co-morbidity especially for enduring traits or trait-like symptoms. Such research may point to underlying commonalities at the cellular level, while the details of functional abnormalities or symptoms are determined by which region or pathway is primarily involved.

The above argument is illustrated mainly with the idea of statistical differences from normal in range of conduction velocity in populations of axons. However, if there were other statistical deviances at the cellular level, the same might apply to them also: The expression of cellular abnormality in

terms of symptoms and signs is conditional on the region and pathway in the brain so affected.

(vii) Symptoms versus Syndromes versus Disorders: Approaches to a new classification, based on robust theory. This line of argument has major implication for how psychiatric disorders are to be classified. Here my comments are about the possibility of defining mental disorders in terms of principles from brain science; but I admit that this can only be part of the story. Some mental disorders are inevitably bound closely to the particular society and culture in which they occur; and since this is not to be encompassed within the universal language of the natural sciences, these aspects of classification cannot be universal. However, for classification related to brain science, current approaches, based on a group of wise persons sitting round a table - or a random sample of 500 wise people surveyed on-line - and then reaching some sort of consensus, are definitely *not* the way to establish an enduring system of classification. We need one based on reasoning from causal principles, and definite disease theories. However, as in neurology, disease classes (and diagnoses) may require to be done at two levels, which are largely independent of each other - one at the level of cellular processes or abnormalities, the other defining the regions or pathways most affected. In any case, trait aspects of mental disorders are likely to be more fundamental for classification than the state aspects, because they are more directly liked to underlying stable cellular abnormalities. Another consequence for classification follows from the fact that abnormalities at the cellular level are more in the nature of statistical deviance than definite pathology: State aspects of mental disorder may be sharply defined categories (e.g. active psychosis, depression, mania, acute aspects of anorexia nervosa). However, the trait aspects are likely to merge with complete continuity into normal variation of psychological profiles and personalities in the general population. They are then better represented in a dimensional than a categorical typology. Furthermore, given that similar abnormalities at the cellular level may give rise to quite different disorders at the whole-person level, dependent on the brain region affected, means that the initial stages for developing explanatory arguments and classifications of mental disorders might better focus on trait-like symptoms and their groupings as syndromes, rather than on disorders, as currently classified.

9. A Personal Invitation to Theoretician/Scholars Interested in Collaboration Leading to more Robust Concepts of Mental Disorder:

(i) My proposal: I am now aged sixty seven. For the last ten years I have been a “freelance researcher”, but have retained my links with Otago

University, in the South Island of New Zealand. My health is good, and my mind is working far better than when I was younger. I have no intention of "retiring"; but I won't be here for ever, and I hear the clock ticking. The bounty of empirical data in the libraries could keep me busy as a theoretician for the next 100 years even if nothing was added to it; but that is not the best way to go.

I probably have the experience to guide other people keen on exploring the unknown, and finding real explanations, developing real disease theories in psychiatry, which in due course could be fed back to the empirical researchers for testing, refinement or refutation. Academia provided me with little opportunity to do this, because it had no interest in research unless big grants were involved (due to the fact that there is usually a big top-slice from the grant, to support the institution). I currently live in Masterton, a small town of 20,000, within easy reach of the capital of New Zealand Wellington. I have electronic access to the excellent library of Otago University, and have all I need to continue this work. I would feel honoured to collaborate with researchers around the world in fundamental research to derive robust theories for mental disorders. These may be psychiatrists or psychiatrists-in-training, neuroscientists, or people in other walks of life, with some experience either in neuroscience, psychology or in some areas of the mental health professions. Collaborators could also include persons with lived experiences of mental illness, or with their family members, friends, carers (etc). Much of this work can be done by e-mail correspondence. However, if keen young researchers in psychiatry, or related fields wanted to join me in Masterton for periods, and later to work together via e-mail correspondence, I would feel privileged. This is a serious offer. If you are interested, please make contact, along the lines of the invitation attached below. I will give an honest response on whether, and in what ways a collaboration could proceed.

(ii) Implications for personnel and other resources, and administrative style. What are the resource implications of this proposal? *First,* and most essential is the researchers themselves. This sort of work probably needs young people, energetic in mind, with active imaginations, yet knowing how to do rigorous reasoning, which can refute as well as support their favoured ideas, capable of large-scale, meticulous and detailed scholarship, and above all, people consumed by fierce curiosity, a desire for real progress in psychiatry to benefit those who suffer from mental disorders, and guided by a secure faith that the world is comprehensible. These, rather than a desire for fame and wealth, are the requirements for this sort of work. I do not see mathematical ability, or facility in computer simulation as so important,

though sometimes it might play a subsidiary role. These people need to be able to work in a climate of intellectual freedom. It would be an advantage for such persons to have access to a reasonably good academic library, which may or may not be electronic. The work I am envisaging would require a great deal of free time. The possibility of travel to meet other researchers, especially those who can do empirical studies relevant to their own work would also be an advantage. I would *not* expect to provide such persons with projects for me to supervise. Instead I look for people who have already formed their own questions, perhaps finding them too daunting, but in any case hoping for guidance from someone who has spent the last thirty-five years reading many thousands of papers. In the first instance, money is less important (except for travel) provided that one can identify the right people. However, further down the track, raising money may become important.

The sort of person I am describing is rare, but I would think that trainee or recently qualified psychiatrists include some such. Others may be working in academic institutions, as neuroscientists, biological psychologists and others. Fostering partnerships with institutions may become important. I admit that (usually) really good theory has to come from a single mind; yet unless those minds have detailed knowledge of critical evidence, their reasoning cannot have a solid base. Therefore the possibility of free exchange of information and ideas between psychiatrists and researchers with other backgrounds would be important. Opportunities for researchers with a non-clinical background to meet patients may also provide the stimuli which can fire the imagination and reasoning in those single minds. Some of the most strongly-motivated persons may be those within service-user communities, who are trying to understand their own experiences. It would be a pleasure to work with them too.

(iii) Difficulties. I anticipate some difficulties: Some people may think the intellectual difficulties would prove insuperable. For me, that is not the major problem, and if, for a would-be theoretician, it seems to be so, s/he is probably not the right person for this task. The real problems are political ones, that "research" is now almost synonymous with money, many universities having forgotten what their real mission with regard to research *is,* the shibboleth of "science" having been thoroughly debased. It is not just university attitudes which hold back this sort of venture, it is attitudes of funding agencies, learned journals, conference organisers, and government officials. I am also aware that the sort of research I advocate does not fit easily into the typical career structures assumed for either academics or health service researchers. It may therefore be that some collaborators in this

venture might have other means of earning their living, and work on *this* in a freelance capacity, as I have done for ten years. I have met a few such persons, and the increasing accessibility of academic library material to the general public may make this a more feasible possibility in the future.

(iv) Avenues of publication: A major problem for the intensive library-based theoretical research advocated in this essay is that it requires a different form of publication from those currently fashionable. In former times research monographs were an acceptable form of scientific communication, and sometimes were the vehicle for definitive statements of major new works. In the last generation, for various reasons, journal articles have become the sole prestige form of academic publication in the natural sciences. In the physical sciences, whether empirical or theoretical, and for empirical work in the biomedical fields they probably serve their function fairly well. However theoretical work in biomedicine requires a bigger canvas, to cope with all the scholarly detail of more complex systems. In this respect the sort of work I advocate is similar to that in the humanities, although it differs from humanities research in that it is assumed that there is a coherent answer to the questions posed, a definite explanation to be found, and predictions are to be made to testing such explanations. Such work may therefore often require publication in the form of monographs, not journal articles. I do have experience in both writing and editing such monographs. If the proposal made in the previous section could somehow be set in motion, there is then a likely corollary: The result should usually be published as monographs, not as papers. If a coalition of researchers working on various topics in theoretical psychiatry could emerge, one possibility for the future is that a publisher be approached with a view to starting a monograph series. On-line publication is another way to go. I might be able to edit it myself, but it would be much better if coordinated and edited by a small team, collectively with wider expertise.

I cannot do what I propose by myself. If I continue to work as a lone wolf, I will probably make some progress, but that work could go further and faster, if there existed a coalition of keen fellow theoreticians especially those from a younger generation. We may then be able to start a fruitful new tradition, which many people now know is needed, but, to my knowledge, has never been developed to the point where it has real momentum in any country.

Robert Miller
13.10.10.

For persons who want to respond to the invitation in the last section of this essay:

Please write to me, telling me a bit about yourself, your experience as a research student, scientist, clinician, family member, or person with lived experience of mental disorder. Give me a brief account of the areas of your interests and expertise. If you have writings you would like to share with me, let me know the reference (if they are in regular academic journals), or e-mail me a copy if they are in books, chapters in books or unpublished manuscripts. (Once e-mail correspondence has started, I can also give you a mailing address.) I am more interested in works of scholarship, even if they have not have reached the stage of a fully formed theory, than in purely empirical papers. I do however hope for reference to sources of relevant empirical studies. I am not able to offer any financial support, but initial stages of this endeavour (which are all that I can envisage at present) are likely to have few costs other than your (and my) time.

My e-mail address is: robert.miller@stonebow.otago.ac.nz