CURRENT THEMES, OPINIONS AND CONTROVERSIES IN PSYCHIATRY

Trajectory of Psychopharmacology: The role of the clinician and Industry

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ABSTRACT

Psychopharmacology emerged with the discovery of chlorpromazine in 1952. This led on to the discovery of other antipsychotics, antidepressants, tranquillisers, psychedelics and other drugs. Traditional histories tell of a liberation of the insane from their asylums. This history neglects the rise and fall of antipsychiatry, and the fact that many more people are both employed in and treated by the mental health industry now than ever before. The small companies who manufactured the first drugs have since become the most profitable corporations on the planet, apparently able to mould academic debate at will and to market psychiatric disorders more effectively than they can make new therapeutic agents.

In our efforts to govern ourselves through psychopharmacology, we have set up a future of cosmetic psychopharmacology. These developments have been largely unscrutinized.

Key words: Psychopharmacology, antipsychiatry, antidepressants, prescriptions, dependence.

BACKGROUND

In 1952, the European world within which chlorpromazine, the first major antipsychotic agent, emerged was an intensely hierarchical one. A world, at least within Europe where ethnic differences counted for a lot and women had little place. A world that, at least as far as psychiatry was concerned, had little contact with the pharmaceutical industry (Healy, 2002).

But there were a number of things happening in the background that had a critical effect on the reception of the psychotropic drugs. In the course of the Second World War, psychiatrists associated with the military discovered that group therapies could have a dramatic impact on the nervous disorders produced in soldiers by the War. These therapies worked best where they were accompanied by a dissolution of the hierarchies of European social and Army life; the more informal the setting, the better (Harrison, 2000).

North American military psychiatrists viewing this group therapy, in particular Karl Menninger, took home a message that psychodynamic therapy worked. This led North American psychiatrists returning from the War and also those manning the asylums during the War to abandon the asylums and to set up in office practice. The asylums were left to the Europeans, while power and influence in American psychiatry uniquely moved into the community. In so doing, American psychiatrists captured the vast range of nervous and psychosomatic complaints that had previously been the province of neurologists and internists with an interest in psychosomatic medicine.

A second factor stems from a War on Drugs that began with the Harrison’s Narcotics Act in 1914, which made the opiates and cocaine available on prescription-only. In 1951, a Humphrey-Durham Amendment to the 1938 Foods Drugs and Cosmetics Act made the new antibiotics, antihypertensives, antipsychotics, antidepressants, anxiolytics and other drugs, available on prescription-only (Healy, 1997).

Not everybody was happy with the new arrangement. Many complained that a system designed for addicts was not appropriate for the citizens of a free country. A combustible set of ingredients had been put in place that in short order led to an explosion. By 1968, departments of psychiatry from Paris to Tokyo were under siege.

PSYCHOPHARMACOLOGY & THE NEW SOCIAL ORDER

How could chlorpromazine, which liberated the insane from their straitjackets, have led to such an outcome? Previously, asylums were places, where lunatics had been guarded by jailers who treated them brutally. Transformed by chlorpromazine it was now possible for therapists to see the humanity of their patients and talk to them. The level of noise in the asylum had fallen (Swazey, 1974). But chlorpromazine also gave rise to an antipsychiatry and the antipsychiatrists responded that real straitjackets had simply been replaced by chemical straitjackets. They labelled the silence within the walls of the asylums, a silence of the cemetery (Postel & Allen, 1994; Dain, 1994).

There was a revolution in progress that stemmed in great part from the new drugs and the interaction between these drugs and the social order in which people lived. The discovery of chlorpromazine by Delay and Deniker was the discovery of a drug that acted on a disease in order to restore a person to their place in the social order. But out of the same test tubes and laboratories, from which chlorpromazine came, came LSD and the psychedelics, Valium and the benzodiazepines and other drugs. These
were not drugs that restored people to their place in the social order. These were drugs that had the potential to transform social order.

By 1968, another drug, the oral contraceptive, had begun to produce just such a transformation of the social order by changing relations between the sexes, bringing with it a feminism that challenged the colonisation of women's minds by men.

Nineteen sixty-eight saw the culmination of a project begun by Rousseau and Voltaire, the Enlightenment. This was a project, which overthrew the traditional hierarchical order in society. It led to the dethronement of kings and gods. It claimed that the people should be ruled by the people and of kings and gods. It claimed that the middle aged and middle class men. It had not extended to women, the young, ethnic groups, or others — until 1968.

In 1968, antipsychiatrists and others protested against the colonisation of the minds of ethnic groups by white Europeans, the colonisation of the minds of the poor by the rich, the colonisation of the minds of the young by the old. They castigated the new drugs as a means of controlling the young. Madness was the protest of the colonised (Healy, 2002).

The anti-psychiatrists had a number of powerful weapons in their armoury. One was ECT and the other was Tardive dyskinesia. There is no question that ECT works — the problem with it and for psychiatry was its visibility, which led to its pivotal role in the movie One Flew over the Cuckoo's Nest. Tardive dyskinesia was a syndrome first described in 1960. By 1968, it was clear that it was a common and disabling side effect of antipsychotic drugs (Gelman, 2000). It was neither the most common nor the most disabling side effect, but it was the most visible.

The response from psychiatry to the emerging recognition of tardive dyskinesia was the same response as from psychoanalysis to criticism against psychotherapy. When the treatment produced tardive dyskinesia, psychiatrists claimed it was the disease, in this case schizophrenia, not the treatment that was at fault. Similarly, psychiatry has blamed the disease rather than the drugs in the case of the SSRIs and suicide, and has consistently blamed the disease when it comes to dependence on therapeutic agents, most recently in the case of the benzodiazepines and SSRIs.

The visibility of tardive dyskinesia was an insuperable problem, however, and by 1974, SmithKline & French had settled their first legal case for over $1 million. With this settlement, a generation of antipsychotic discovery came to an end. It was to be 20 years before another generation of antipsychotic drugs emerged. When new drugs came, starting with clozapine, they came not because they were better than the older drugs but rather because clozapine didn't cause tardive dyskinesia.

The combination of tardive dyskinesia and the ferment of the 1960s had enormous effects on psychiatry. In 1957, Leo Hollister had run a double-blind placebo-controlled trial of chlorpromazine in patients with tuberculosis, demonstrating that it produced marked physical dependence (Hollister, 1998). By 1966, a large number of studies had confirmed his observations that there was a significant physical dependence on antipsychotics that was present in large numbers of people taking them, even at low doses taken for a relatively short period of time. This led to the concept of therapeutic drug dependence, a concept that blows a hole in current theories of addiction. These drugs produce no tolerance, no euphoria, but they produce enduring post-discontinuation changes that are as extensive and long lasting as the changes underpinning current disease models of addiction. Tardive dyskinesia was an exemplary instance of the kind of dependence the new drugs caused (Tranter & Healy, 1998, Healy & Tranter, 1999). Given the widespread recognition of this syndrome, and therapeutic drug dependence in particular, it is extraordinary that the concept of therapeutic dependence on antipsychotics vanished in 1970, when a new War on Drugs was declared.

By the end of the 1960s, psychopharmacology was faced with a political problem. The problem was how to distinguish drugs, which restored social order from drugs, which had the potential to subvert that order. The 'decision' was made to categorise as problematic and dependence producing any drugs, which subverted the social order, and conversely to exempt as problem-free any psychotropic drugs which restored that order. This political rather than scientific decision set up a crisis a few years later when physical dependence on the benzodiazepines emerged. This crisis led to the obliteration of the anxioalytics and indeed almost the whole concept of anxiolytics. By 1990, physicians in Britain and elsewhere regarded benzodiazepines as more addictive than heroin or cocaine — without any scientific evidence to underpin this perception.

The eclipse of the tranquillisers gave rise to an era of depression. The contrast between Western developments and the case of Japan is striking in this context. In Japan, there never was a crisis with the benzodiazepines, and the concept of anxiolytic remained respectable and the market for anxiolytics much greater than the market for antidepressants. As of 2001, no SSRIs were available on the Japanese market for depression. This indicates as little else can how the era of Depression that we have lived through in the 1990s in the West has arguably been a politically and economically constructed one that bears little relationship to any clinical facts (Healy 1999). Nevertheless, this has been an era that has changed popular culture by replacing a psychobabble about low serotonin levels and the like.

The antipsychiatric argument that madness doesn't exist is now discredited but the unarticulated force behind the antipsychiatrists' arguments was that they perceived that in some sense the ways in which we govern ourselves had changed, that psychiatry was now part of the new order of government, and that people had not been consulted on whether this was a desirable development. This development is caught in the redesignation of mental illness services as mental health services.

Everyone agreed there had been a de-institutionalisation. But was it a de-institutionalisation of patients? Where patients are concerned, in Britain at least they are
being detained at 3 times greater rate than 50 years ago. They are being admitted at a 15 times greater rate than before, and on average, patients are spending a longer time in service beds than ever before in history. New conditions such as personality disorders began to be admitted to mental health services from the 1960s and the management of violence and social problems from the 1960s was becoming an issue for psychiatry (Healy et al, 2001). These figures are more consistent with a de-institutionalisation of psychiatry and psychiatrists than with a return of psychiatric patients to the community. Unselfconsciously, psychiatrists claim we are treating more patients than ever before. We are.

THE EMERGENCE OF CORPORATE PSYCHIATRY

Antipsychiatry gave rise to the occupation of Departments of Psychiatry from Tokyo to Paris. The fact that nothing like that happens now suggests that the establishment fought back and won. There is however no history of the period. No textbooks of psychiatry record the sacking of the office of Jean Delay the discoverer of chlorpromazine. None refer to the fact that the key figures behind the revolutions of late 1960s, were psychiatrists or philosophers appealing to examples from psychiatry — Franz Fanon, Michel Foucault, R.D. Laing, Thomas Szasz, Erving Goffmann, Herbert Marcuse. An amnesia as dense as that happens now suggests that the establishment of Departments of Psychiatry from Tokyo to Paris was underpinned by the need of governments and their diseases. This required knowledge of the people who were governed and their diseases. This requirement led in the 18th century to a mapping of peoples rather than just the traditional mapping of land that governments had undertaken. The new population statistics, allied to probability theory, gave rise to the insurance industry. The new population statistics demonstrated a differential distribution of diseases and risks, and in so doing these figures combined to produce the notion of a rule of the people by the people, and to the creation of social science and epidemiology (Gigerenzer et al, 1989). Within health and psychiatry, there was an emergence of a moral movement.

The same forces led by the end of 19th century to the first attempts to map the human individual, their attitudes and abilities, personality, or intelligence. Scales such as the IQ scale led to new concepts of norms and deviations from those norms and psychologists emerged to take a place in the educational system, the legal system, and in the government of ourselves — it was this that underpinned the dynamic revolution (Rose 1989; 1998).

The truth probably is that, rather than orthodox psychiatry winning, the world changed. Both psychiatry and anti-psychiatry were swept away and replaced by a new corporate psychiatry. Galbraith has argued we no longer have free markets; corporations work out what they have to sell and then prepare the market so that we will want those products (Galbraith, 1971). This formula works for cars, oil, and everything else, why would it not work for psychiatry? Prescription only status for psychotropic drugs makes the psychiatric market easier than almost any other market — a comparatively few hearts and minds need to be won.

Within psychiatry, two further factors have helped. One was the emergence of Big Science. As of the early 1970s, neuroscience came into play. Radiolabeled images of receptors began to drive drug development, and academic debate. The development of these receptor assays and their use to pinpoint the action of antipsychotic drugs on D₂ receptors by Solomon Snyder was one of the triumphs of modern psychopharmacology (Creese et al, 1976; Snyder, 2000). This work remains as valid and accurate today as when it was first published.

But these binding data introduce something else as well, for which neither Snyder, nor others who developed radiolabeled techniques can be held responsible. They introduced a new language, a language of Big Science, and a meeting place for physicians and companies. Where previously psychiatrists, antipsychiatrists and patients were using what was recognisably the same language, this no longer applied. Both sides had been governed by the visible presentations of the patients in front of them. Now to get into the debate participants had to have a manifold filter and a scintillation counter.

And as a matter of historical fact, where antipsychiatry was fuelled by many legitimate complaints of antipsychotic side-effects, far from this new science working in the interests of patients and leading on to more sensitive treatment regimes, it led on to mega dose regimes. No longer answerable it seems to how the patients in front of the physician actually looked, following the science, prescribers moved to mega dose regimes of antipsychotics that may have caused as many brains to be injured as were ever injured with psychosurgery (Healy, 2002).

Another scientific development, which played a part in the development of corporate psychiatry, stems from the work of Rene Descartes, Blaise Pascal and others, who, in producing statistics and probability theory, had helped lay the basis for the Enlightenment. The emergence of statistics was underpinned by the need of governments to raise monies (Hacking, 1975). This required knowledge of the people who were governed and their diseases. This requirement led in the 18th century to a mapping of peoples rather than just the traditional mapping of land that governments had undertaken. The new population statistics, allied to probability theory, gave rise to the insurance industry. The new population statistics demonstrated a differential distribution of diseases and risks, and in so doing these figures combined to produce the notion of a rule of the people by the people, and to the creation of social science and epidemiology (Gigerenzer et al, 1989). Within health and psychiatry, there was an emergence of a moral movement.

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This was not just the replacement of methodology and philosophy, the qualitative sciences, by a new set of quantitative sciences. The new statistics set up a market in futures, a market in risks. We were on our way to becoming a Risk Society. In the case of the IQ test, deviations from the norm were now something that predicted problems in the future. Parents sought out psychologists in order to improve the futures for their children. In the future we would govern ourselves through the marketplace.

Psychotropic drugs entered this new market in many different ways. The oral contraceptives for instance are clearly not agents for the treatment of disease. They were a means of managing risks. Where once, the risks of eternal damnation had governed selves, the possibility of managing a much more immediate set of risks now regulated behaviour. The best selling drugs in modern medicine do something similar. Agents such as the antihypertensives and lipid-lowering drugs manage risks rather than treat disease. In the case of the antidepressants, these have been sold on the back of efforts to reduce risks of suicide.

The key statistics in the new era are
clinical trial statistics, a development that again can be traced back to the first probabilists. The use of randomised clinical trials to evaluate new treatments has led to a new era popularly portrayed as an “Evidence Based Medicine” era. What can go wrong if we have clinical trial evidence to demonstrate what works and what does not work and we adhere to this evidence? What more can we do than that?

Clinical trials in psychiatry, however, have never showed that anything worked. Penicillin eradicated a major psychiatric disease without any clinical trial to show that it worked. Chlorpromazine and the antidepressants were all discovered without clinical trials. Clinical trials are not needed to show haloperidol and other agents work for delirium. Anaesthetics work without trials to show the point. Analgesics work and clinical trials aren’t needed to show this.

What clinical trials demonstrate are treatment effects. In some cases, these effects are minimal. One may have to strain with the eye of faith to detect the treatment effect. The majority of trials for sertraline and for fluoxetine failed to detect any treatment effect. This is not evidence that sertraline or fluoxetine do not work. In clinical practice, there is little doubt that these drugs do work. The gap between practice and evidence points rather to the inadequacy of our assessment methods. To show that something works, we would need to go beyond treatment effects to show that these effects produce a resolution of the disorder in a sufficient number of people to outweigh the problems such as dependence syndromes that these drugs also cause. If our drugs really worked, we shouldn’t have 3 times the number of patients detained now compared with before, 15 times the number of admissions and lengthier service bed stays for mood and other disorders that we have now. This isn’t what happened in the case of a treatment that works, such as penicillin for General Paresis of Insane (GP).

Aside from the inadequacy of our clinical trial methods, professors of psychiatry are now in tail for inventing patients. A significant proportion of the scientific literature is now ghost written. A large number of clinical trials done are not reported if the results don’t suit the sponsoring companies (Healy, 2001). Other trials are multiply reported so that anyone trying to meta-analyse the findings can have a real problem trying to work out how many trials there have been. Within the studies that are reported, data such as quality of life scale results on antidepressants have been almost uniformly suppressed. To call this science is misleading. Arguably, the term “Evidence Based Medicine” would be more appropriate (Healy, 2001).

One of the other aspects of the new medical arena is that the most vigorous and hostile patient groups of the antipsychiatry period have been penetrated by the pharmaceutical industry. Other patient groups have been set up de novo by companies. Part of the market development plans for many drugs these days include the creation of patient groups to lobby on behalf of a new treatment. Meetings are convened for pharmaceutical companies specifically to advise and train on how to set up such groups. This follows a pattern found in other industries over the past two decades, where corporations have engaged their former critics (Stauber and Rampton, 1995).

All of this is perhaps part of the normal rough and tumble between clinical practice, science and business. But there is a further even more important aspect of what is happening, which is contained in the following quote from Max Hamilton: “it may be that we are witnessing a change as revolutionary as was the introduction of standardization and mass production in manufacture. Both have their positive and negative sides” (Hamilton, 1972).

Most clinicians have used the Hamilton Rating Scale for Depression, but they would be mystified at Hamilton’s quote about a revolutionary aspect to using such a simple instrument as this. Rating Scales have been such feature of psychiatric trials and clinical practice for so long now that it is perhaps difficult to see that there are revolutionary aspects to what happened.

Linked into both the clinical trial process and a more general contemporary push for quantification, there is now a profusion of rating scales and checklists used throughout our schools and all walks of life. We quantify aspects of sexual behaviour, aspects of the behaviour of children, all sorts of things we never quantified before. Where once there was life’s rich variety, now the quantified variation in our childrens’ behaviour concerns us in so far as it can be shown to fall inside or outside all sorts of norms.

In the case of children falling outside norms, clinical trial data have given parents the impression that there is something that can be done to bring their children back inside appropriate norms, and thereby minimise the risk for their children’s future. These data, it is widely believed, indicate that by giving their children psychotropic drugs, parents can normalise abnormal behaviour. The clinical trial figures are assumed, just like the figures for IQ, to be capable of generalisation to the population at large. The figures on treatment effects from rating scales used in our clinical trials have set up a new market.

Given that we are now treating children from the ages of 1 to 4 with “Prozac” and “Ritalin”, it is clear that we are not treating traditional diseases (Zito et al 2000). There is an extensive literature on how corporations make psychotropic drug markets (Healy, 1997) but, until very recently at least, pharmaceutical corporations have not sold psychotropic drugs to children. The explosion of drug use in children is arguably a manifestation of the force that makes markets, that underpins the market development of pharmaceutical companies and others. This is the force that creates pharmaceutical companies. The treatment effects from clinical trials have been taken to be findings that generalise across the community - they are taken to indicate that these agents will return children within the set of norms that will minimise future risks. What parent could not want to minimise future risks for their child?

AN ANOREXIC ANALOGY

The eating disorders offer an analogy for what is involved. Clearly people have starved themselves for millennia — for a variety of reasons, good and bad. Anorexia nervosa, however, emerged as something different to previous starving behaviours in the early 1870s. No good epidemiological
figures exist for the rise in frequency of the syndrome, as the epidemiology of eating disorders didn’t exist until recently, but there is a general perception that the syndrome appears to have increased in frequency in the 1920s and 1930s and increased yet again in the 1960s with new variants, such as bulimia nervosa, mushrooming.

Competing theories have focused on the possible psychodynamics of the eating disorders, the biology of anorexia or bulimia, or socio-political aspects of body image distortions. These competing theories have rarely spoken to each other however. Few, if any, accounts of these events note that in the 1870s weighing scales emerged and with them norms for weight and deviations from the norm and an awareness that deviations in the direction of what had formerly been thought to be healthy and beautiful carried risks. The insurance industry published these figures. In the 1920s, weighing scales increased in frequency and the scales, with their norms printed on the front of them, appeared in pharmacies, drug stores and other retail outlets. In the 1960s, the scales were miniaturised so that we all ended up with a set of scales in our homes (Schwartz, 1986).

Clearly weighing scales don’t create eating disorders in that even blind individuals can become eating disordered. But it’s impossible to imagine eating disorders on the epidemic scale that now exist without the presence of both weighing scales and modern normative ideas about weight that stem from the use of these scales. And it is easy to imagine the removal of the feedback from weighing scales as being in many cases therapeutic in its own right.

These new figures and norms have been a means for women (mostly) to govern their bodies. But the selectivity of the figures also grounds a peculiarly modern neurosis. Just as figures for GDP give us feedback from some areas of endeavour but not others and in so doing encourage the promotion of automobiles and the chopping down of trees, so also figures from this one area of life, which are easy to produce, have the power to control behaviour. Markets can be set up in other areas, such as air-quality and wilderness. Until such time as they are, it requires great wisdom and considerable internal resources to factor into our lives these other values. Similarly individuals with feedback from weighing scales can become unbalanced and end up in physical jeopardy as a result.

This process affects an increasingly large number of areas of our lives. Some of the more dramatic examples come from higher education and health, which have been skewed in recent years toward the reproducible and the quantifiable. It is a problem that to date appears to have no solution, in great part because the quantifiable is so marketable and the alternatives are not.

**PSYCHOPHARMACOLOGY & THE FUTURE GOVERNMENT OF THE SELF**

Under this heading three issues push for consideration, the future of prescription only arrangements, the threat to self-government posed by dependence on psychotropic agents and the possibilities for a cosmetic psychopharmacology.

**A. Prescription Only Arrangements**

One aspect of the future of psychopharmacology is locked into the survival or otherwise of the system of prescription only medicines. This arrangement that was introduced for the bad drugs to restrict their availability, now applies exclusively to the good drugs. It involves a relationship of trust not only between physicians and their patients but also between physicians and pharmaceutical companies. One of the reasons to put the arrangement in place was that physicians would quarrant information out of pharmaceutical companies on behalf of their patients and would provide a counter-balancing wisdom to market forces. Such a system is clearly out of tune with the Spirit of these Times.

Since this arrangement was first put in place, modern pharmaceutical companies have grown to be among the most profitable organisations on the planet. There has been a change from companies run by physicians and chemists to corporations run by business managers who rotate in from Big Oil or Big Tobacco. The pharmaceutical companies are also advised by the same lawyers who advise Big Oil and Big Tobacco and other corporations.

In the case of tobacco industry, it now seems clear that the legal advice in the face of the problems of smoking was not to research the hazards of smoking, as to do so would increase the legal liabilities of the corporations involved. Similar advice given to the managers of our pharmaceutical corporations would be completely incompatible with prescription-only arrangements. In fact, the lawyers who advise the pharmaceutical corporations are the lawyers for the tobacco corporations. If the advice is comparable it would convert prescription-only arrangements into a vehicle to deliver adverse medical consequences with legal impunity.

Against this background, consider the issue of SSRIs and suicide. The following table is taken from a series of articles (Khan et al 2000; Khan et al 2001; von Keitz et al 1986), adjusted in the case of sertraline and paroxetine in the light of reviews by Lee (1991) and Brecher (1991) respectively:

These figures indicate an excess of suicides that is statistically significant for certain individual agents compared to placebo, as well as significant for SSRIs as a group compared to placebo and also for these new antidepressants as a group compared to placebo (Healy 2003). These suicide rates for SSRIs are comparable those found in post-marketing surveillance of the drugs (MacKay et al 1998), while the figures for placebo are comparable to findings for untreated depression from primary care (Simon and Von Korff, 1998; Boardman and Healy, 2001).

There are a number of problems with this data. First, it was generated for the most part in the mid to late 1980s. Despite the controversy that emerged about whether there may be a problem with SSRIs or not, in the domain of suicide induction, and corroborating evidence from these studies, there has not been a single piece of research carried out to answer the questions of whether SSRIs cause suicide or not. Designed yes, carried out no.
A second point is that many of the suicide attempts occurring during the washout period of trials have been classified as placebo suicides. The washout period is a week long after someone has been removed from previous medication before they are randomised to investigative agent or placebo. These figures for the washout period have been used apparently to conceal a problem with new investigative agents. This suggests that data being collected from volunteers in trials is being inappropriately used and this inappropriate use puts all the rest of us in a state of legal jeopardy.

The situation outlined here faces all of us with a dilemma. If these agents were made available over the counter, it might liberate medical physicians to research their hazards in a way that appears not to happen at present. There are many indicators that over the counter arrangements would suit both governments, who wish to keep their pharmaceutical companies happy and at the same time contain costs, and industry. Prescription only arrangements are in fact at present under considerable strain with the emergence of direct to consumer advertising for prescription only products.

A change in the status of psychotropic agents from prescription only to over the counter would have dramatic effects on how we understand and govern ourselves. In their efforts to sell their products, industry have endorsed a set of categorical notions of mental distress, such as depression, social phobia, panic disorder and others. These would be replaced in an over the counter world by notions of stress, burnout and nerves, which would be treated by a range of tonics, stimulants and soothing agents. The moral implications of treatment would be quite different.

B. Dependence on Psychotropic Agents

The figures in Table 1 above suggest a further problem. The suicidal acts during the washout week indicate that discontinuing previous treatment may not be risk-free. Perhaps related to this risk, there are accumulating indications that antidepressants, and SSRI antidepressants in particular, may produce physical dependence.

Dependence is the single biggest spectre psychotropic agents pose. This was the factor that led to the obliteration of the benzodiazepines, and the eclipse of the concept of a tranquilliser, with the replacement of the benzodiazepine tranquillisers by the SSRI antidepressants. It was this factor that produced the Age of Depression that we have lived through in the West during the 1990s. The peculiar problem about dependence on drugs stems from the threat it poses to the government of the self in our current economies.

Drug dependence is the threat that therapeutic establishments, government and industry find most difficult to manage. It was the failure in the late 1960s to manage the issues of dependence thrown up by the psychedelic drugs on the one side and tardive dyskinesia on the other that led to the bewilderment of the benzodiazepine crisis of the 1980s. There has never been a debate in public about dependence that has not toppled into incoherence and hysteria. Without a debate that conceding the possibility of dependence to therapeutic agents, however, it will impossible to distinguish between the risks of dependence among drugs of a therapeutic group and to advance from there to identifying what factors produce physical dependence. This dynamic means that we are probably at risk of an infinite regress of "dependence crises". The next such crisis looms following the filing of a first class action suit for physical dependence on SSRIs in August 2001.

**TABLE 1: Incidence of Suicidal Acts in Antidepressant Clinical Trials**

| Investigational Drug (SSRIs designated by *) | Patient No | Suicides | Suicide Attempts |
|-----------------------------------------------|------------|----------|-----------------|
| Sertraline*                                    | 2053       | 2        | 7               |
| Active comparator                             | 595        | 0        | 1               |
| Placebo                                       | 786        | 0        | 2               |
| Placebo Washout                               |            | 0        | 3               |
| Paroxetine*                                   | 2963       | 5        | 40              |
| Active comparator                             | 1151       | 3        | 12              |
| Placebo                                       | 554        | 0        | 3               |
| Placebo Washout                               |            | 2        | 0               |
| Nefazodone                                     | 3496       | 9        | 12              |
| Active comparator                             | 958        | 0        | 6               |
| Placebo                                       | 875        | 0        | 1               |
| Mirtazapine                                    | 2425       | 8        | 29              |
| Active comparator                             | 977        | 2        | 5               |
| Placebo                                       | 494        | 0        | 3               |
| Bupropion                                      | 1942       | 3        | --              |
| Placebo                                       | 370        | 0        | --              |
| Fluoxetine*                                    | 1427       | 1        | 12              |
| Placebo                                       | 370        | 0        | 0               |
| Washout                                       |            | 1        | 0               |
| Citalopram*                                   | 4168       | 8        | 91              |
| Placebo                                       | 691        | 1        | 10              |

**COSMETIC PSYCHOPHARMACOLOGY**

With the mapping of the human genome, we have the possibilities of creating
new markets. We need this knowledge from the human genome to set up the markets that we need to govern ourselves. It will tell us about some of the underpinnings to our beliefs - why we believe some of the things we do in the religious and political domains. But the products of this research will belong almost exclusively to pharmaceutical corporations. If they are advised in the way that they appeared to be advised at present, this knowledge, which is so democratically important, will operate against the interests of democracy.

In the course of the last 50 years, plastic surgery evolved into cosmetic surgery. Plastic surgery began as a set of reconstruction procedures aimed at restoring a person to their place in the social order — it was a treatment from the same medical universe as chlorpromazine. It evolved into cosmetic surgery when the reliability with which certain procedures could be carried out passed a certain quality threshold. Cosmetic surgery in contrast to plastic surgery offers of means of subverting the natural order (Hallan, 1998).

In recent years, the word “quality” has been to the fore in modern healthcare, but quality in this context does not refer to good interactions between two human beings. Quality refers rather to the reproducibility of certain outcomes. Big Mac hamburgers are quality hamburgers in this sense — they are the same every time! This is an industrial use of the word. In the case of the psychotropic drugs, the quality of the outcomes they produce is currently very low.

The level of quality will however soon be transformed by the development of pharmacogenetics, which by predicting adverse outcomes may minimise them, and by neuromaging which will show whether treatments are working or not in a very immediate way. These new techniques offer the possibility of producing a much better quality of responses without the need for any increase in the intrinsic efficacy of available drugs.

Viagra gives a good indication of what will happen when we get to this stage. Viagra is a drug that produces quality outcomes, in the sense of reproducible outcomes. When this happens, it becomes possible to abandon the disease concept. With the introduction of Viagra, pharmaceutical company executives and others began to talk openly about lifestyle agents rather than therapeutic agents. This is the world that lies in store for us. It is not the world of traditional medicine, where drugs treat diseases to restore the social order. It is a world in which psychopharmacological interventions will potentially change that order. The disease concepts, which has covered for a lack of reliability in outcomes hitherto, will be redundant in the new marketplaces that will result, marketplaces that offer greater returns than disease-based healthcare does.

CONCLUSION

When Delay and his colleagues introduced chlorpromazine in 1952 in Paris, it was into a different world. This was a universe in which Pierre Pichot and Pierre Deniker, the next most senior people in Delay’s department, might be left standing behind Delay for an hour while he received a visitor. Standing at the head of department’s right hand was not experienced by Deniker or Pichot, however, as some exquisite form of torture or as a humiliation. It was a different time. A time when honour and loyalty were more important than they are now. These virtues counted for more than the search for individual authenticity that is so prized now. The hierarchy was something that these men believed in. In the same way, a fear of God was once seen as a good thing that held the social order in place. With Freud, this fear became anxiety, something to be treated, and later with the psychotropic agents, anxiety became a set of anxiety disorders, a competitive disadvantage to be overcome.

What this hints at is that there are forces at play, that can change not only the kinds of drugs we give, not only the conditions we think we are treating, but our very selves who are doing the giving. Forces that can change us as profoundly as we can be changed by a handful of LSD containing dust.

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