Ethical considerations in clinical training, care and research in psychopharmacology

Rael D. Strous

1 Beer Yaakov Mental Health Center, Israel
2 Sackler Faculty of Medicine, Tel Aviv University, Israel

Abstract

Psychopharmacology is a powerful tool in psychiatry; however, it is one that demands responsibility in order to deal with the ethical complexities that accompany advances in the field. It is important that questions are asked and that ethical mindfulness and sensitivity are developed along with clinical skills. In order to cultivate and deepen ethical awareness and subsequently solve issues in optimal fashion, investment should be made in the development of an ethical decision-making process as well as in education in the ethics of psychopharmacology to trainees in the field at all stages of their educational development. A clear approach to identifying ethical problems, engaging various ethical concepts in considering solutions and then applying these principles in problem resolution is demanded. An openness in identifying and exploring issues has become crucial to the future development and maturation of psychopharmacologists, both research and clinical. Consideration must be given to the social implications of psychopharmacological practice, with the best interests of patients always paramount. While ethical issues related to psychopharmacological practice are varied and plentiful, this review focuses on advances in technology and biological sciences, personal integrity, special populations, and education and training.

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Introduction

The practice of psychiatry is a noble endeavour. It has been made all the more effective with breakthroughs in evidence-based psychopharmacology management options over the past 50 years. In fact, never in the history of psychiatry has so much hope been offered to long-suffering patients with mental illness, and never in the history of mental illness have so many been offered such relief by means of rational pharmacological interventions. This flash of optimism, however, is tempered by a minefield of potential dangers in the arena of ethical practice. It is clear that knowledge and scientific advances may be transformed into powerful tools that demand responsibility. It is here that ethics contributes to dealing with the inevitable challenges, providing a framework for coping with the issues that arise naturally out of research and clinical care of individuals with mental illness. Often there are no clear solutions. While legislation can be helpful in guiding practitioners in some cases, it is only one of the many sources of moral knowledge about how to engage ethically in the psychopharmacological field. In many instances, ethical decisions lie in the hands of individual doctors. What is of utmost importance is that questions are asked and that ethical awareness becomes as important in clinical skill development as other more explicit physician skills such as heart auscultations and mental status examinations. While the challenges are formidable, there is hope, and the literature on the subject is gradually accumulating as sensitivity regarding the importance of the issues increases.

Undoubtedly, the powers that exist in the hands of a psychopharmacologist today are considerable. With the administration of a few pills, over time, personality and behaviour can be affected markedly.
Accompanying this power, however, is an unwritten social contract between the psychopharmacologist and the community. The administration of medications has to be carried out with the utmost ethical and professional behavior, with dedication, commitment and accountability. Rank implies obligation. Psychiatrists and psychopharmacologists who engage in medication administration need to be aware of the ethical issues that are inextricably linked with its practice. It is no more important to be aware of how a dopamine blocker affects neurotransmitter balance than it is crucial to obtain optimal informed consent for any medication administration, and it is no more important to be aware of doses of SSRI medication management for the treatment of OCD and depression than it is to be aware of potential conflicting interests in relationships with the pharmaceutical industry and drug representative-sponsored ward lunches.

Awareness of the issues and their repercussions is integral to the critical development of ‘ethical mindfulness’ (Guillemin et al. 2009). While ethical concerns are varied and plentiful, a consistent approach in identifying the ethical problem, engaging various ethical concepts in considering solutions and then applying these principles in problem resolution is demanded. Certain ethical issues may be solved in different ways depending on factors such as time, ethnicity and cultural considerations (Lombera & Illes, 2009). However, other central concepts of medical ethics involved in ethical psychopharmacological practice are not bound in these ways.

Given the length of such a discussion, it would be impossible to explore in any depth the wealth of ethical issues appertaining to the ethics of psychopharmacological practice in this framework. The intention here is to touch on a few of the more relevant and current concerns relating to ethical practice, and to increase awareness of the pertinent issues, rather than to solve each individual challenge. The analysis will focus on advances in technology and biological sciences, integrity, special populations, and education and training. While the focus of the discussion is aimed towards clinicians engaged in psychopharmacological practice, the issues also have relevance to those engaged in psychopharmacological research who have no direct clinical involvement.

Ethical issues resulting from advances in technology and biological sciences

During my eighty-seven years I have witnessed a whole succession of technological revolutions. But none of them has done away with the need for character in the individual or the ability to think.

Bernard Mannes Baruch (American statesman, 1870–1965)

Man is an animal with primary instincts of survival. Consequently his ingenuity has developed first and his soul afterwards. The progress of science is far ahead of man’s ethical behavior.

Charlie Chaplin (English actor and director, 1889–1977)

Pharmacogenetics

Research in pharmacogenetics has proliferated in the past 10–20 years. In the future the field promises to be able to (and in many cases already does) predict individual response to various medications including efficacy, time to response and side-effect profile. This body of research is predicated in major part on the fact that metabolism and sensitivity to medication differs between individuals due to one-base polymorphisms of drug-metabolizing enzymes. Genotyping of these enzymes prior to drug administration would enable the psychopharmacologist to predict individual medication response and possible adverse reactions. This in turn would enable tailor-made therapy and usher in the era of ‘individualized’ medicine (Shastry, 2006).

However, along with often prohibitive costs are problems of an ethical nature. While results give great hope to those who are long-suffering in terms of medication choice that assures an earlier and better response, there remains a great deal of uncertainty regarding the extrapolation of results, much of which is in the early stages and seldom replicated. Moreover, how can confidentiality of genetic information be protected? How should informed consent be conducted? Should the level of understanding be kept at a higher standard? What are the potential repercussions of revealing pharmacogenetic information to families or health insurance agents? Since the results and application of this research will inevitably have immense clinical, economic and social implications, it is critical that potential ethical problems are identified early and addressed.

While not all may agree, genetic research needs to be held to a higher standard based on the potential effects on future generations from improper and potential misuse of information in large databases regarding benefits and rights of individuals. The potential for gross boundary violations exists when dealing with genetic information, since much becomes known about family, community and ethnic groups, presenting ethical challenges if improperly disseminated. Furthermore, these risks are amplified by increased complexity of healthcare delivery systems. Permission
to receive various medicines might be limited or revoked based on the genetic potential of toxicity or efficacy. Thus, while it would be extremely improbable that genetic markers would state that a person has no chance of responding or a 100% chance of toxicity, a health insurance fund may restrict a medication despite a small chance of efficacy (Breckenridge et al. 2004). Since most people have difficulty dealing with probabilities, a sensitive and comprehensive approach as to how to present this pharmacogenetic information to patients must be developed. Increasing awareness of the issues is critical: pharmacogenetics is in its infancy, but promises to dictate much in the future.

Brain stimulation

Apart from ECT, which has been a mainstay of psychiatric treatment for the past 70 years, the past decade has seen the relatively rapid innovation of brain stimulation, electrical and magnetic, in the management of various neuropsychiatric illnesses. This has included techniques such as transcranial magnetic stimulation (TMS), transcranial direct current stimulation, vagus nerve stimulation (VNS) and deep-brain stimulation (DBS) (used especially in the management of Parkinson’s disease). In DBS, electrodes are implanted surgically in one or more brain areas of relevance to the illness. These electrodes are then connected to a battery-operated stimulator and placed in the chest near the clavicular area. Activation of the electrodes, which can be accomplished manually, subsequently stimulates the relevant areas of the brain.

Ethical issues with these procedures are numerous. Based on psychiatry’s experience with psychosurgery, it becomes vital to explore these issues. First, it remains unclear precisely how these techniques work in the altering of mental states of relevance to thought, behaviour and personality. It is also unclear which brain sites are most optimal for effects and at what frequency stimulation should be delivered (Glannon, 2009). The ethical issue becomes whether it is acceptable to induce certain effects without knowing the precise mechanisms of action and long-term effects. While other such examples of treatments in psychiatry exist without clearly defined modes of action (including various psychotropic medications and ECT), they nevertheless remain in use since their efficacy and safety profile is evidence-based. However, the quest to unravel their modes of action should continue. Second, many positive reports of these techniques are based on ‘selective publishing’ with an excessive reliance on single-patient reports, thus introducing bias, since there are no cohort studies upon which to rely (Schlaepfer & Fins, 2010). Third, based on the unique effects, it has been reported that some patients select management with DBS for disabling motor effects from illnesses such as Parkinson’s disease, only to find themselves disabled by severely impaired psychiatric states (Glannon, 2009). Issues of autonomy, competence, the role and opinion of the physician, and informed consent thus become critical, especially if the individual chooses the dysfunctional mental state over that of the dysfunctional motor state (Glannon, 2009).

Since the field of DBS is in its infancy, but potential implications and effects of its management are significant, groups have met to discuss ethical implications before the field expands exponentially. One such group recommended that further studies of the efficacy and safety of DBS compared to other treatments should be done and that for disorders of mood, behaviour and thought, DBS should only be used in the context of carefully designed research trials with the highest level of scientific standards (Rabins et al. 2009). DBS should also be carried out only by multidisciplinary teams and with adults. One also has to ensure that the excitement surrounding DBS does not exclude future consideration of tried and tested techniques such as ECT, which, while it has engendered a negative reputation amongst the public in many countries due to outmoded misconceptions, might be excluded as a treatment option, despite exciting technological developments in its use. Particular attention needs to be given to issues of informed consent, including discussion of what is and is not known about DBS. Furthermore, there should be no financial barriers to the inclusion of those suitable and it should be clear who is responsible for follow-up and removal of the device if necessary (Rabins et al. 2009). Others have added that disclosure of any potential conflicts of interest by investigators or clinicians is important and that the procedure should never be used for political, social or law-enforcement purposes (Merkel et al. 2007; Nuttin et al. 2002). Implementation of various safeguarding guidelines will be challenging; however, if employed sensibly they will only enhance the contribution of this exciting new field.

Cognitive enhancement

Perhaps no field in psychiatry has managed to occupy the attention of the public and media as much as psychopharmacology’s potential to offer cognitive enhancement or ‘cosmetic pharmacological’ benefits (a term coined by Peter Kramer). These medications have been referred to as ‘lifestyle drugs’ and may be
defined as medications used to satisfy a non-medical or non-health-related purpose (Flower, 2004). Individuals who take such medications are not ‘sick’ in the traditional sense and the question becomes when precisely a ‘need’ becomes an ‘illness’ requiring medication. Such designer medications target specific neurobiological processes that control cognition and emotions and may be used for purposes of spiritual experience, shyness, alertness, low self-esteem, confidence, memory and other similar cognitive enhancements (e.g. Stein, 2005). While this is not a new phenomenon, today much of their use is evidence-based. However, many questions of an ethical nature are raised including what level of adverse effects is acceptable. It should be borne in mind that many other day-to-day practices continue to proliferate despite some element of danger, e.g. cars, smoking and alcohol use (Flower, 2004).

Since physicians are ultimately the gatekeepers of the proliferation of these medications, several ethical issues need to be addressed. When should attempts be made to limit their use, if at all? Is it ethically permissible to investigate long-term use of enhancers in healthy individuals? One of the most commonly used substances of relevance includes methylphenidate whose use in various school districts and on college campuses far exceeds the highest estimate of the prevalence of attention deficit hyperactivity disorder (Diller, 1996). Following their widespread use, employers and educators may prefer those who are enhanced over those who are not enhanced, or vice versa. Other ethical issues include the potential prescription of its use as a form of ‘neurocorrection’ by the justice system, whether it is followed voluntarily or not. Can parents decide to ‘neuro-enhance’ their children with or without their consent? What are the social implications, especially if there is unfair access to such ‘enhancers’?

Farah and colleagues (2004) have defined four broad areas of ethical relevance with the use of neurocognitive enhancement. These include factors of safety (unanticipated complications resulting from the complex process of neurocognitive enhancement), coercion (potential pressure on the individual to enhance cognitive function by employers, educational facilities, family), distributive justice (unfair allocation due to cost or social inequality) and personhood issues (conflict with who we are and what it is to value a meaningful life and its responsibilities and imperfections). A central ethical dilemma is the conflict between improving one’s productivity and function via medication administration vs. the value of human dignity and greater investment and effort in one’s activities and challenges (Farah et al. 2004). Does this demand policy development and legislation or should this be left to the decision of the psychopharmacologist? It would become the physician’s responsibility to carefully evaluate each individual case for medical indication, since he/she would be the gatekeeper for medication administration. This would include full informed consent, including knowledge of the medication’s dependence potential, and acknowledging that not all details about potential risks are known both in the healthy and ill.

**Integrity and the psychopharmacologist**

You would expect different cultures to develop different sorts of ethics and obviously they have; that doesn’t mean that you can’t think of overarching ethical principles you would want people to follow in all kinds of places.

Peter Singer (Australian philosopher, b. 1946)

**Relationship with the pharmaceutical industry**

An issue that has taken centre stage in the past few years is the relationship between psychopharmacologists, both clinical and research, and the pharmaceutical industry. Interestingly it is the media who, following several celebrated episodes of alleged conflicts of interest by psychopharmacology practitioners, have led the way by forcing the issue to the front stage of the ethical debate. The issue is complex since a relationship with the industry is unavoidable, given the nature of required research and information distribution following product approval. At each stage in this interaction, however, various precautions are demanded and become critical for the ethical practice of psychopharmacology. Often these issues are subtle, but the ‘slippery slope’ beckons. From the public’s perspective, there are conflicting reports on whether relationships with industry affect medical care. One prominent study among patients enrolled in cancer research trials indicated that most were not concerned about financial ties between researchers, medical centres and drug companies (Hampson et al. 2006). They indicated that such knowledge would not necessarily have affected study enrolment. A more recent study, however, showed that patients believe that financial ties, including recruitment incentives, do indeed influence professional behaviour and impair study quality and therefore should be disclosed. Such financial ties may even influence interest in study participation (Licurse et al. 2010). The consensus appears to be in step with the later study, bearing in mind that the former study investigated patients with
cancer, an illness with which patients will often pursue all available new treatment opportunities, given that in many cases little long-term hope is offered.

While the problem of conflicts of interest exists in all fields of medicine, many claim that the problem is especially prevalent in psychiatry, given the psychopharmacology focus of many pharmaceutical companies (Insel, 2010). For example, antidepressants and antipsychotics are two of the top five classes of medications sold in the USA, with sales of over $25 billion in 2008 (Insel, 2010). Since differences in efficacy between medications are becoming slight, the role of marketing and influence of decision-makers and perceived field-leaders over other physicians and the public are becoming increasingly important. Public trust in psychiatrists has been affected by serious accusations of conflicts of interest arising from failure to report such conflicts. In a 2005 review of 397 published reports of clinical trials in four psychiatric journals, Perlis et al. (2005) found that 60% of papers had industry funding and 47% had at least one author reporting a financial relationship with the pharmaceutical industry. Furthermore, it was noted that articles with industry support are approximately five times more likely to report positive results. While a relationship with industry in a speaking capacity is not unethical per se, it becomes unethical not to report such an association. For example, as shockingly reported by Tom Insel, of the 20 work group members who authored the American Psychiatric Association guidelines for the treatment of schizophrenia, bipolar disorder, and major depressive disorder, 90% had financial ties to industry, 72% as consultants. None of these relationships were disclosed (Cosgrove et al. 2009).

While dialogue between clinical and research scientists is critical, it is important to ensure that the association remains ethical and free of conflicts of interest. The stakes are too high and the demands for progress too vital to waste the potential symbiotic relationship. Constant awareness of these dangers at all levels is necessary and psychiatrists need to ensure transparency by means of disclosure of these interactions with industry, both with respect to financial compensation received and any other associated conflict of interest (Mitchell, 2009). In addition, psychiatric educators need to develop creative methods for educating medical students and residents about industry’s marketing practices so that they may cope with marketing biases in therapeutic information (Yager & Feinstein, 2010). Other more subtle but nevertheless profound influences include the phenomenon of gifting to psychopharmacologists (Stokamer, 2003).

The practice is endemic to the profession. It is always fascinating to record how many times a name of a commercial medication product or company appears in a doctor’s office. The existence of these subtle, almost subliminal forms of advertising is widespread. ‘Direct to consumer’ advertising may also be ethically problematic, often basing itself on the public’s desire for a quick fix (McHenry, 2006). Along these lines, psychopharmacologists need to beware of the overuse of medications when there are no good indications and when non-pharmacological measures might be just as effective, as in mild depression (Fournier et al. 2010).

Although there are problems with the relationship with the pharmaceutical industry, completely ignoring studies with commercial support would also be ethically questionable since it may benefit patients. Thus, careful discrimination between poor and well-designed studies is demanded, along with attempts by academic publications to include a range of studies, including those with negative results. Clear guidelines and a ‘Proposal of Recommendations’ regarding the ‘Ethical Implications of Relationships between Psychiatrists and the Pharmaceutical Industry’ have been published by the World Federation of Societies of Biological Psychiatry (http://www.wfsbp.org/publications). These guidelines are comprehensive and greatly assist the clinical and research psychopharmacologist in managing interaction with the pharmaceutical industry.

Research ethics

Any research that is not carried out by the most rigid of ethical principles and guidelines is simply not worthy and definitely not suitable for publication. The medical profession has learned its lesson from the Nazi-physician experience. The vast majority of research by national-socialist physicians during the Nazi era was pseudoscience and without any value, with research carried out under the most wicked of conditions and no attention paid to informed consent and patient safety (Lifton, 1986). Many physicians believed, however, that what they were involved in was in the genuine best interests of society and the patient including the most egregious of this activity, namely euthanasia (‘mercy killing’).

The medical profession has learned from this, and there has been a substantive change in what is considered ethically acceptable in research and practice. The first official response came with the Nuremberg Code in 1949, followed in the mid-1960s by the World Health Organization’s more extensive Helsinki
risk in research (Young, 1998) and the ethics of offering financial compensation to mentally ill patients who may be unfairly coerced into study participation based on economic need (Marson et al., 2006). Legal requirements for informed consent may differ between countries. However, requirements that are stricter than the law allows may be considered in various situations where ethical principles may preclude certain practices, e.g. especially in consideration of patient confidentiality (Strous, 2009).

Other more practical ethical concerns with research include those of medication ‘wash-out’ phases (medication-free intervals) and the use of placebos. Those who oppose the use of placebo controls in psychopharmacological studies maintain that such a study design negates the beneficent-based, ‘best proven diagnostic and therapeutic method’ that the original Helsinki Declaration of 1964 demanded of all medical research. Others have argued that those administered a placebo, particularly in cases of psychosis or depression, would be adversely affected by not receiving a known efficacious compound (Baldwin et al., 2003). While this argument is cogent, it has been called into question by many maintaining that these risks are exaggerated, as well as several reports of increased risk for suicidality with some antidepressants, and finally the need to prove that the study compound is better than the placebo. This must be explored, since the specific or ‘true’ extent of the pharmacological response is determined by the difference between the drug and placebo response. Sample numbers needed of patient participants are also smaller. The consequentialist response would be that there are net benefits for patients considering the value and quality of data resulting from using placebo controls (Dunlop & Banja, 2009). The use of placebos in research trials may also vary between disorders and between levels of severity. For example, in randomized controlled trials of antidepressant medications, since there is sufficient evidence of their efficacy in severe depression, the use of placebo controls may only be ethically amiss in mild to moderate depression (Fournier et al., 2010). While placebos are often required by regulatory bodies for optimal research, their use is not always in the best interest for the well-being of the patient and needs to be carefully considered prior to inclusion in research protocols. A further ethical consideration in such clinical trials is the concept of clinical equipoise which is satisfied if there is genuine uncertainty over whether the treatment in a randomized clinical trial involving patients assigned to different treatment arms will be beneficial (Freedman, 1987).
An important theme that runs through all ethical issues related to psychopharmacological research is the preoccupation with the best interest of patients and protection of the rights and well-being of participating subjects. With this as a focus, the public will be more open to supporting research in order that hope may be maintained for this long-suffering group of individuals. Most patients participating in psychobiological research actually find it to be a positive experience (Rosen et al., 2007), notwithstanding the public image of such research. Finally, the principles of Morse (2007) represent a good summary of the guidelines to consider in psychopharmacological research studies, namely that medical care has priority over research, that there is an absolute requirement to intervene when safety is a question and to separate clinical and research functions, placing patient well-being above research goals if ever in conflict, and safeguarding patient confidentiality and researcher well-being.

It would be ethically important to convert research observations from psychopharmacological research into clinical benefits if the information is considered sound and replicable. This includes the ethical requirement for physicians to maintain ongoing/continuing medical education (CME), updating with journals, conference attendance and regular recertification where mandated. Care and attention should be advised when reading research and reviews from industry-sponsored investigation since they may be less transparent and are often accompanied by limited methodological reservations and considerations. Such reviews consistently demonstrate more favorable results compared to equivalent Cochrane reviews (Jørgensen et al., 2006). It also may be ethically important to notify research subjects of study results and to ensure that all clinical trials are publicized, for example, by means of national and/or international clinical trial databases.

Unfortunately, based on various precautions in clinical research, several subpopulations of individuals are often excluded due to the fear of adverse effects including possible litigation. These include the young, the old, minorities, substance abusers and pregnant women. Other populations often excluded in research protocols include patients receiving chronic maintenance medication including intramuscular depot antipsychotic formulations. While this is understandable, these individuals also suffer from illness and have rights too. Special safeguards may be required, and decisional capacity must be closely evaluated together with legal guardians if applicable, to allow all ill members of society to benefit from participation in research projects.

Collaboration with governmental interests and involvement in social policy

The mandated ‘social contract’ of a psychopharmacologist with the community is to describe, understand, predict, and modify behaviour in cases of mental illness. Most importantly, the mental health-care provider, armed with tools of psychopharmacology, is committed to assisting the identified individual and alleviating emotional pain. The psychopharmacologist as a mental health practitioner has privileged access to the human psyche and behaviour. This privilege demands responsibility and the primary duty to care for patients’ mental health. To act otherwise would constitute abdication of professional responsibility (Strous, 2007). Thus, involvement of a psychopharmacologist in political activity and narrow governmental interests would constitute a gross boundary violation. A psychiatrist with tools of psychopharmacology absolutely has to resist any external pressure, be it governmental or other, to utilize skills and training in areas where they do not belong (Scheurich, 2000). It would be unethical for the psychopharmacologist to allow his skills to be exploited in order to carry out political plans of governing bodies or nations. Utilizing psychopharmacology skills to advance political agendas or other non-medical goals must be considered unethical.

Notoriously, such involvement has included assistance in torture (Gluzman, 1991; Summers, 1992), lie detection in the context of a government-sponsored interrogation or evaluation if some element of coercion or abuse is engaged (Wilks, 2005). This would be true even in the interest of national security. In this manner, behavioural clinicians would be challenging their professionalism and subsequently their ethical standards of conduct. Several medical associations have, for example, prohibited involvement of physicians in judicial executions. In addition, the American Psychiatric Association has deemed treatment of psychosis in order to prepare an individual for the death penalty unacceptable and unethical practice. Since doctors have been allowed the right to develop certain skills and engage in invasive procedures in order to save lives and provide comfort, exploiting this privilege even in the best interests of the state would be considered a serious boundary violation (Gawande, 2006). Court-ordered pharmacological management for criminal behaviour may also be problematic, especially if administered under coercion (Farah, 2002).
Psychopharmacology and special populations

A man is ethical only when life, as such, is sacred to him, that of plants and animals as that of his fellow men, and when he devotes himself helpfully to all life that is in need of help.

Albert Schweitzer
(German theologian, philosopher and physician, 1875–1965).

Ethical considerations in the face of ethnic diversity

While cultural and ethnic factors affect many stages in research and clinical management of various ethnocultural groups, very limited attention has been placed on ethical factors influencing these conditions. In a rare review of the subject, Miskimen et al. (2003) explore how ethnic factors may affect psychopharmacology including recruitment, retention and follow-up of adult minority patients participating in research. For example, while minorities make up more than one-third of the USA, they are grossly underrepresented in research trials, ethically problematic since this limits generalizability of research observations to their communities. While this may be due to researchers wanting to protect ‘vulnerable populations’, under-representation of minority groups in psychopharmacological research is a problem for application of research results for their healthcare. This phenomenon may also partially be due to distrust by minorities of the health establishment; e.g. by African Americans as a result of the Tuskegee experiments and decades of discrimination in the USA. Medication administration in minority populations without adequate research opens up the possibility of idiosyncratic side-effects or inappropriate dosing (Turner & Cooley-Quille, 1996).

Since treatment outcome information is crucial for policy decision-making and resource planning it would be unethical not to consider the interests of minorities (Miskimen et al. 2003).

In addition, informed consent among minorities becomes a special problem due to language inequities (subjects not understanding the process), financial compensation (economically disadvantaged participating for money, thus undermining true voluntarism) and respect (minimal questioning of authority figures). Furthermore, all clinical research centres need to make sure that culturally competent personnel with a common language wherever possible engage subjects/patients when explanation of research or treatment protocols in psychopharmacology is required (Miskimen et al. 2003). Efforts need to be invested in ensuring that ‘inappropriate paternalism’ is eliminated when dealing with patient groups different from that of the study investigators, including when research is done in different countries.

Psychopharmacology in children

Many would argue there is no more vulnerable population, based on size and needs, than the paediatric patient population. As Tan & Koelch (2008) indicate, a paradoxical situation develops when, due to excessive protective mechanisms and fear or resistance to include children in research protocols, minimal data exists regarding safety and efficacy of psychopharmacological treatments. Furthermore, pharmaceutical companies are reluctant to fund studies on children due to the perception that there is less financial gain.

Thus ‘off label’ use becomes the standard for management, which is ethically and scientifically less ideal due to a lower standard of safety. The younger the patient, the truer this is, with a correlation between age and study recruitment potential. While many exclude completely the right and necessity for child study assent and rely merely on parental or legal guardian consent, a concerted effort must be invested in obtaining child assent, especially with older children who are more mature emotionally and intellectually. Evidence for competence of children to understand and make many management decisions exists by age 9, and by age 14 many children can understand treatment information at adult levels (Billick et al. 1998). This holds true despite difficulties with autonomous decision-making, susceptibility to various external pressures and impact of the mental illness (Ondrusek et al. 1998; Tan & Koelch, 2008).

‘At risk’ syndromes

It has been proposed that a new diagnostic category of ‘psychosis risk syndrome’ be included in the forthcoming fifth edition of the Diagnostic and Statistical Manual of Mental Disorders. This may be a welcome addition, due to its potential to generate funds for research of this subcategory of being at risk for developing psychotic illness. While this may contribute to the early intervention, management and modification of the illness (thus potentially preventing or delaying full blown psychosis), several important ethical issues arise. First, there is a significant potential for high rates of false-positives since there is considerable difficulty in differentiating mild symptoms from normal variants. Such false-positive identification could lead to unnecessary stigma, discrimination and even potential exposure to antipsychotic medication at an early age without definitive illness evidence (Corcoran et al. 2010). Since over 50% of identified subjects do not progress to psychosis (Yang et al. 2010), physicians identifying individuals with...
psychosis-risk syndrome are contributing to unfairly labelling them with a potentially severe illness and all its untoward consequences. For an adolescent at a critical stage in development, the repercussions could be marked. For those in whom psychosis is correctly predicted, however, intervention could change the course of the illness. To what extent should physicians attempt to predict future illness at the potential expense of some who may be wrongfully labelled and treated? If the phenomenon of individuals with ‘at risk psychosis’ is real and potentially identifiable, what percentage of false-positive identification would be considered acceptable? How should an unfavourable risk–benefit ratio be defined? While it is clear that better identification of these individuals, for example, by means of biomarkers, is optimal, the issue will continue to interest psychopharmacological clinicians and researchers in the coming years (Corcoran et al. 2010).

Animal research in psychopharmacology

The ethical concerns surrounding animal research with psychopharmacological relevance is poorly addressed in the psychiatric literature. Due to recent increased violent attacks on researchers by anti-animal research activists, aptly termed terrorists by some (Krystal et al. 2008), there is more awareness. It is critical to clarify the necessity for animal research and its beneficial extrapolation to humans (Francione, 2007). Although not all would agree, ethically one could justify such research since benefits to humans are clear, ranging from phenomenal breakthroughs in genetic research with gene–knockout animal models to the very obvious and direct benefits of new medication development with Phase 1 and Phase 2 application. Predictability and transferability, however, need to be more fully confirmed (Perry, 2007).

Various bodies have analysed the problem, with guidelines laid out for ethical research. One such report by an independent UK body, the Nuffield Council on Bioethics, detailed ethical issues with recommendations including the need to assess pain, distress, and suffering in animals during the research process both for scientific and ethical purposes. In addition to exploring absolute limits of research, they emphasize the following issues: What are the goals of the research? What is the probability of success? Which animals are to be used? What effect will there be on animals used in the experiment?, and, Are there any alternatives? It is absolutely imperative that any such analysis of these issues be conducted in a fair and informed manner (Perry, 2007). If not, the phenomenon of terrorism targeting medical scientists (Krystal et al. 2008) will become more prevalent – a tragedy and a disservice to both sides of the debate.

Ethical education and training in psychopharmacology

Education is the art of making man ethical.

Georg Wilhelm Friedrich Hegel
(German philosopher, 1770–1831)

Education in ethics of psychopharmacology

As early as 1931, the German code of medical ethics was already known to be one of the strictest and most advanced in the world. German doctors in the 1930s were well aware of this code. They were trained intensively in its intricacies, as evidenced for example by manuscripts in the literature at the time, and devotion to concepts of physician responsibility and medical ethics in medical education and textbooks (Proctor, 2000). It did not, however, affect their practice. The attitude of psychiatrists to their patients during this period indicates, in a most unjust fashion, how science may be affected by external considerations. Thus without including a focus on the history of where our profession has transgressed, ethics training becomes an empty intellectual exercise (Strous, 2010). While the Nazi-psychiatry experience is one such example of psychobiological theory gone wrong (euthanasia, eugenics), others exist in the history of psychiatry. These include Dr Henry A. Cotton’s preoccupation in Trenton Hospital with infection and ‘focal sepsis’ as the biological source of psychiatric illness. Without true informed consent he removed teeth, tonsils, gall bladders, stomachs, spleens, cervixes, testicles, ovaries and even colons as potential sources of infection. It is estimated that at least 30% of his patients with colectomy died (Scull, 2006).

In order to avert such ethical misjudgement in psychiatric research and clinical practice, education in research ethics is crucial for psychopharmacology trainees. This includes discussing ethical concerns and norms governing research, sensitivity to ethical implications of actions, and proficiency in ethics problem solving. Research ethics can be learned and it is imperative to actively devote time to the teaching of this fundamental issue (Chen, 2003). Chen (2003) has suggested that small-group case-based learning is best for teaching ethics problem-solving skills. It is worth mentioning that the National Institutes of Health (NIH) in the USA has a requirement that any trainee-ship programme sponsored by them must have a
specific element of training in research ethics. Whatever the context, ethics awareness and sensitivity in education needs to be ongoing and maintained as an active aspect of psychopharmacological clinical and research practice.

**Resolution of ethical concerns**

Since ethical issues are abundant in psychopharmacology, it is important not only to know what the issues are, but also how to deal with them. Trainees in psychiatry receive very little guidance in how to resolve ethical dilemmas if and when they arise, despite basic education in general medical ethics. After identifying ethical concerns, the next step becomes ethical decision-making. How is this accomplished? There are several approaches to ethical decision-making, with the final decision differing according to the different modes of decision-making. Although ethical decisions may ultimately differ, it is critical that the process begins, is comprehensive, has some element of peer review and discussion and is open to revisitation.

There are various approaches to ethical decision-making. Wright & Roberts (2009) briefly review various ethical decision-making models and encourage the use of the ‘Four Topics Method’. This particular model, developed by Siegler (1982), proposed that solutions to ethical concerns should arise based on consideration of operant factors and potential outcomes arrived at in a systematic fashion. These would include deliberation over medical indications, patient preferences, quality-of-life factors and contextual features (Wright & Roberts, 2009).

Another more widely disseminated and very useful approach to ethical decision-making of particular relevance to research and clinical psychopharmacology is that of the World Medical Association (Williams, 2005). This method encourages the analysis of ‘rational’ vs. ‘non-rational’ approaches to ethical decision-making; weighing up different factors on each side. Non-rational approaches include obedience, imitation, feeling or desire, intuition and habit, while rational approaches engage concepts of deontology, consequentialism (utilitarianism), principlism and virtue ethics. While very comprehensive, it makes a great deal of sense and is a wonderful tool for teaching and engaging students in discussion and exploration of factors relevant to ethics and psychopharmacology. The principlism method is probably best known and includes the concepts of autonomy, beneficence, non-malefice and justice. Often there are competing arguments within each principle, but it is a useful model for commencing the ethical discussion process.

In order to educate the psychopharmacologist and assist in the prevention and management of ethical problems during research, ethical issues should be considered and anticipated, ideally along with the assistance of an ethicist, at each stage of the research process (Derenzo & Moss, 2005). This includes study design, subject selection/recruitment, consent, data analysis, unexpected events, privacy considerations and issues regarding special populations. These authors recommend that every research protocol should include an ethics section detailing how researchers will ensure that the proposal will uphold the strictest of ethical standards. In this manner, awareness and sensitivity to ethical issues will be maintained and potential ethical problems alleviated.

**The ethical psychopharmacologist: responsibilities and challenges**

To sum up, ethical considerations in psychopharmacology begin with proper education and training and continue with ethical clinical care and research. Training must emphasize ethical mindfulness, most critical to the development and maturation of ethical psychopharmacologists, both research and clinical. This openness in identifying the issues and investigating them must be developed within the context of a good ethics education programme. Furthermore, the concepts of ethical analysis must be included in the rubric of psychopharmacological training and practice. Consideration must be also given to social implications of psychopharmacological practice that allow us to manipulate our own minds (Fuchs, 2006). On the research front, current ethical approaches to research can still be improved, with respect for the patient remaining as the foundation. Safeguards must include minimal risk and serious, systematic IRBs. It is also important to ensure that empirical ethics research is encouraged and developed with the full support of scientific bodies, along with other empirical and clinical research (Tan & Koelch, 2008). Thought should be invested in the inclusion of a research or clinical ethicist in study design as well as in clinical management settings. Moreover, ethical clinicians and researchers must keep pace with technological advances and subsequent ethical challenges. Despite the fact that physicians in the current economically driven climate of medicine are under great time constraints, it remains critical to devote time to comprehensive and careful ethical evaluation, obtaining ethical consent and optimal ethical decision-making.

Given the direction of psychiatry and the central role of medication in many aspects of illness management,
ethical practice in psychopharmacology and consideration of the best interests of patients are essential. The practice of psychopharmacology from both a research and clinical perspective must be implemented with parity, sensitivity and ethical relevance to all – nothing less than the legitimacy of our profession is at stake.

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Statement of Interest
None.

References


