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The World Psychiatric Association (WPA)

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EDITORIAL

Psychiatry for the Person: articulating medicine's science and humanism

Juan E. Mezzich

President, World Psychiatric Association

The WPA Institutional Program on Psychiatry for the Person: from Clinical Care to Public Health (IPPP), approved by the 2005 General Assembly, involves a WPA initiative affirming the *whole person of the patient in context* as the center and goal of clinical care and health promotion, at both individual and community levels. This involves the articulation of science and humanism to optimize attention to the ill and positive health aspects of the person.

Ancient Greek philosophers and physicians, like Socrates, Plato and Hippocrates, advocate holism in medicine (1). Socrates taught that "if the whole is not well it is impossible for the part to be well". It is striking that these perspectives are re-emerging with renewed vigor in today's world through assertions that there is no health without mental health and by focusing local and international health efforts on the totality of the person (2-4).

And here the person is to be thought of in a contextualized manner, in the words of the philosopher Ortega y Gasset, *I am I and my circumstance*. In addition, evidence is growing for the value of integrating mental health in general health and public health practice (5). These concerns are emerging in response to many deficiencies in health care including neglect of the needs of real people (6-9). A major perspective to deal with these limitations emphasizes a comprehensive and holistic concept encompassing ill and positive health as well as a biological, psychological, social, cultural and spiritual framework (10-13). The mental health care field in many countries is being stimulated by a recent movement emphasizing *recovery* and *resilience* (14,15) which promotes the fulfilment and empowerment of patients as active participants in their own health care. Also, increasing interest is appearing towards clinicians applying themselves as whole human beings (16). All these perspectives reflect growing aspirations towards meeting scientifically, humanistically and ethically our responsibilities as psychiatrists and health professionals (17-19).

Given the early programmatic achievements and responses received from throughout WPA and initial contacts with external organizations (World Federation for Mental Health, World Medical Association, World Federation for Neurology, etc.) it is becoming clear that Psychiatry for the Person (and eventually a Medicine for the Person) has to be seen as a long term initiative aimed at innovatively refocusing the objectives of the psychiatric and medical fields in consonance with their fundamental soul.

CONCEPTUAL COMPONENT

Several key concepts underlying the IPPP are being analyzed with the expectation that they will lead to a number of papers and monographs. Planned first is an introductory paper to cover two central concepts: a broad notion of health, including ill or pathological aspects and positive ones such as adaptive functioning, protective factors and quality of life, as well as the notion of person and its key characteristics within the IPPP including autonomy, history, context, needs, values, and life project in addition to illness experience. Of relevance, E.J. Cassel (20) has offered a useful description of the person within a medical framework. Also to be considered is the value and need for comprehensive diagnosis and care as well as for integration of services to achieve a person-centered psychiatry and medicine. Also planned is a set of papers, as follows, for a special issue of an international journal: a) historical perspectives: the evolution of person-centered concepts in psychiatry and medicine; b) philosophy of science perspectives: underlying broad conceptualizations of health and person-centered care; c) ethics and values perspectives: axiological implications of a person-centered psychiatry and medicine, relevant to the *reason d'etre* of the field and the profession (this may offer a valuable approach to deal with stigmatization against persons in psychiatric care); d) biological perspectives: the genetic, molecular and physiological bases of a psychiatry and medicine for persons including an individualized understanding of illness, health, and care processes; e) psychological perspectives: the phenomenological, learning and other psychological bases of person-centered care; f) socio-cultural perspectives: the contextual framework of a broad concept of health and the plural meaning of a person in the medical field; g) perspectives from health stakeholders: engaging interactively all stakeholders in the health field for the development and implementation of person-centered concepts and procedures, including persons and families in health care, health professionals and planners, industry and social advocates. Other papers in the set would cover Psychiatry of the Person in literature, in art, and in films. Additional journal papers and books relevant to the conceptual bases of the IPPP are anticipated.

CLINICAL DIAGNOSIS COMPONENT

There are two work objectives in this component. The first

is collaboration with WHO and various WPA components towards the development of the WHO ICD-11 Classification of Mental Disorders. A preliminary background phase principally involving the WPA Classification Section and the WHO Classification Office has resulted in the publication of two monographs (21, 22). A full development of the ICD-11 Mental Disorders Chapter has started in early 2007 under the direction of the WHO Mental Health Department.

The second and main work objective of the IPPP Clinical Diagnosis Component is the development of a provisionally termed Person-centered Integrative Diagnosis (PID). At its heart is a concept of diagnosis defined as the description of the positive and negative aspects of health, interactively, within the person's life context. PID would include the best possible classification of mental and general health disorders (expectedly the ICD-11 classification of diseases and its national and regional adaptations) as well as the description of other health-related problems, and positive aspects of health (adaptive functioning, protective factors, quality of life, etc.), attending to the totality of the person (including his/her dignity, values, and aspirations). The approach would employ categorical, dimensional, and narrative approaches as needed, to be applied interactively by clinicians, patients, and families. A starting point for the development of PID would be the schema combining standardized multiaxial and personalized idiographic formulations at the core of the WPA International Guidelines for Diagnostic Assessment (IGDA) (23-25).

An introduction to this IPPP component's work is being published as an invited editorial in *Acta Psychiatrica Scandinavica* (26). Another planned background publication is an IGDA Case Book.

The development of PID, including its theoretical model and its practical guide or manual, will proceed in three main phases: a) design of the PID Model, encompassing a review of the pertinent background and the most suitable and promising domains and structures for the diagnosis of a person's health; b) development of the PID Guide, through the preparation of a first draft, its evaluation, and preparation and publication of a final version; c) PID Guide translations, implementation, and training.

CLINICAL CARE COMPONENT

While many may argue that personalized care is already mainstream, the fact is that in many settings in both the developing and developed worlds the focus of attention is just illness (and frequently ineffectual at this) with minimal if any attention given to the positive aspects of health (adaptive functioning, resilience, supports, quality of life) and its totality (thus neglecting the bases for health promotion) as well as to the dignity of the persons being cared for.

The main work of this component involves preparing and publishing curricula for graduate, post-graduate and continuing education and training levels in both specialty and primary care. The curricula will promote the development of knowledge, skills and attitudes relevant to person-centered care. Cultivation of the clinician-patient relationship is central to this effort and small group learning and intense supervision will be emphasized. Input from psychiatrists across the world will be sought through workshops at various regional congresses. Networks to enhance and monitor implementation and follow-up will be organized.

An introductory paper on the place, content, and prospects of Psychiatry for the Person in Clinical Care will be prepared at the outset. Each one of the curricula will be presented in due course through a monograph. In addition to educational activities, attention will be paid to the organization of person-centered clinical services and procedures. Some of the key activities in the public health component outlined below are relevant to this aim.

PUBLIC HEALTH COMPONENT

Psychiatry for the Person is a basis for advocacy that emphasizes the value and dignity of the person as essential starting points for public health action. Public health action includes development of policies and services, and the research and evaluation supporting these. Failure to recognize the humanity and dignity of citizens living with mental illness as well as the value of mental health to the individual and community have resulted in abuse and neglect of the former and lost opportunities to improve mental health through population-based and person-based initiatives. Public health actions to promote mental health, prevent illness and provide effective and humane services benefit from and contribute to the conceptual and clinical development of psychiatry for the person.

The proposed program of work aims to foster research and evaluation related to both ill and positive health and the consideration of the totality of the person in society. It will include: a) the design of public policy initiatives aimed at promoting population mental health and b) the development, introduction and monitoring of person- and community-oriented health services in a culturally appropriate manner. The potential scope includes mental health promotion, mental illness prevention, and policy and service development. An introductory paper on the IPPP initiative on public health is being prepared.

Initially three IPPP Public Health Projects will proceed as follows: a) the person's involvement as user and citizen in creating policy and planning and delivering services; b) the person in non-consensual treatment situations and c) psychodynamic essentials for a person-centered psychiatry. Topics for later development may include translating "data" to "policy" and "policy" to "data", using indicators for positive mental health, matching types of needs with levels of care**,** advocating for rural mental health, community-based rehabilitation and recovery, reviewing the importance of private and public sectors in poorly resourced

countries, disaster planning and mental health, national and local planning for suicide prevention, and mass violence and mental health.

WORK STRUCTURES AND PROGRESS

IPPP Workgroups and an Advisory Council will respectively carry out and support the work of the program. An internet platform is in development. Research organizations, foundations and industry are being approached to cover the costs of work meetings, teleconferences, field trials, evaluations, and the preparation of documents and publications. Major institutions such as the UK Department of Health and several US University Departments of Psychiatry have expressed interest to participate in and support the Program.

Two volumes have been recently published, i.e., *Psychiatry and Sexual Health: An Integrative Approach* by Jason Aronson/Rowman & Littlefield, and *Recovery: Das Ende der Unheilbarkeit* by Psychiatrie-Verlag, under the IPPP logo. Two Presidential Symposia on the IPPP have been organized at the 2006 and 2007 annual meetings of the WPA member societies in the US and the UK, respectively. The concept of psychiatry for the person is present in the overall themes of WPA World and International Congresses as well as Regional Congresses and Conferences across continents. Editorials on IPPP are invited in several major international journals.

CONCLUDING REMARKS

The positive responses being received from throughout WPA and external organizations as well as the stimulus from early contributions are encouraging. High are the IPPP aspirations to refocus our field and profession at the service of persons, providing within this framework tools to address collaboratively health problems and health promotion. We are, thus, committed to psychiatry's and medicine's fundamental soul.

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The vision of recovery today: what it is and what it means for services

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In the past, practice in mental health was guided by the belief that individuals with serious mental illnesses do not recover. The course of their illness was either seen pessimistically, as deteriorative, or optimistically, as a maintenance course. Research over the past thirty to forty years has indicted that belief and shown that a vision of recovery can be achieved for many individuals. People with serious mental illnesses have themselves published accounts of their own recovery as well as advocated for the development of recovery promoting services. In North America and other regions, policies have been developed to make recovery the guiding vision of services. Today, particularly in the United States, much effort is going into the transformation of services and systems to achieve recovery outcomes. Despite these trends, the idea of recovery remains controversial and, some say, even illusory. This article clarifies the meaning of the term "recovery", reviews the research and first person accounts providing a rationale for recovery, and sets out implications for developing recovery oriented services.

Key words: Recovery, recovery research, recovery oriented services, serious mental illnesses

(World Psychiatry 2007;6:4-10)

For many years, the conventional wisdom in the field of mental health has been that severe mental illnesses, particularly schizophrenia, inevitably result in progressive deterioration. Professional practice has then understandably focused on managing psychopathology and its symptoms. Research efforts in the 1960s, 1970s and 1980s documented the heterogeneity of outcomes, particularly for individuals with schizophrenia (1-3), including often regaining functioning over the long term, developing friendships and reporting satisfying lives (4-7). The practice field, however, continued to be organized to fend off relapse and deterioration (8,9).

It is unfortunate but not surprising that it has taken the practice field so long to adopt this forty year old understanding of the possibility of recovery. The large gap between research findings and adoption in practice has been often cited as a major barrier to innovation in mental health (10-13). In fact, recent analyses of the state of mental health systems in the United States have concluded that mental health care in America fails a wide variety of individuals, but particularly fails those with serious mental illnesses (14), because it is "not oriented to the single most important goal of the people it serves, that of recovery" (15). Furthermore, the U.S. President's New Freedom Commission report strongly urged the adoption of the notion of recovery as possible for all and as the guiding vision for the system. Bringing the vision of recovery into the practice field requires an understanding of what is meant by recovery, the research findings that provide a rationale for recovery and the implications of these findings for the delivery of services (15).

WHAT IS RECOVERY?

Even though there is no explicit consensus about the meaning of the term, the notion of recovery is guiding policies and practices in many American state mental health systems as well as those of other countries, such as Canada and New Zealand (16-21). Consumer researchers have examined how systems can facilitate or hinder recovery and identified systems performance indicators (22). Recovery is also listed as a performance indicator to monitor and improve the outcome of individuals served by American state mental health systems (23).

Recovery has been the subject of debate among advocates, providers, family members and other stakeholder groups over the past few decades. Some who view mental illnesses as primarily biological in etiology have questioned whether recovery is even possible and have argued that using the term will give false hope both to those diagnosed and those who care about them (24). On the other side of the debate, former patients and other critics of biological approaches have questioned whether mental illnesses even exist as medical entities and prefer to think of life crises as normal parts of human existence (25). From this viewpoint, there can be no "recovery" because there has been no illness. In addition to such controversy, most stakeholders agree that the term itself can be confusing and seem illusory. For example, words such as "recovery", "rehabilitation", and "reintegration" have often been confused one for the other (26). "Rehabilitation" is a field or a service designed to facilitate success and satisfaction in a specific valued role chosen by the individual (27). "Reintegration" into society is an outcome which can be achieved using mental health treatment services, such as community psychiatry and rehabilitation among others, as well as political action and community organizing to promote solidarity and openness to individuals with serious mental illnesses. "Recovery", on the other hand, is neither a service nor a unitary outcome of services. Researchers, providers and, most importantly, individuals with serious mental illnesses themselves have contributed to the meaning of the term as it has evolved over the past few decades.

Some clinical research groups have identified recovery as the alleviation of symptoms and a return to premorbid functioning (28). Working definitions by several groups (6,29) have operationalized variables such as symptom remission, vocational functioning, independent living, and peer relationships. Consumer and psychiatric rehabilitation literature, however, does not hold the view that either symptom remission or a return to premorbid functioning is necessary for recovery to occur (8,30).

Individuals with mental illnesses have long written about their experiences of recovery (31-33). Approximately fifty years ago, the ex-patient movement identified the language of recovery to help to make sense of their own experiences and to develop an alternative vision of mental illnesses (34). The ideas of the Independent Living Movement (i.e., centers established and managed by people with physical disabilities) (35) heavily influenced mental health consumers' views that recovery remains possible, even if a person's functional limitations may not change. In the area of physical disabilities, consumers and rehabilitation specialists have long known that it is possible to regain employment, go back to school, or regain a valued position in society despite never having regained the use of one's limbs or senses (8,36,37). As Anthony and colleagues (8,38) point out, the experience of recovery from mental illnesses includes not only regaining a valued role, but also recovering from the effects of having been diagnosed with a mental illness (e.g., discrimination, disempowerment, negative side effects of unemployment, crushed dreams) as much as from the effects of the illness itself. Like trauma survivors, individuals with serious mental illnesses may experience these effects as having changed their lives irrevocably (39) and thus feel simply unable to return to their lives prior to the onset of illness, but endeavor rather to incorporate the illness experience into a new identity. Deegan (30) eloquently makes this point when she says: "The goal of the recovery process is not to become normal. The goal is to embrace our human vocation of becoming more deeply, more fully human". First-person accounts and consumer advocate descriptions of recovery then underscore the fact that recovery was the personal journey of an individual in taking back control of his or her life, or the lifelong process of "becoming more fully human", even with functional limitations and deep traumas.

The Center for Psychiatric Rehabilitation at Boston University has developed a working definition of recovery, derived from an analysis of first-person narratives and the views expressed by members of the consumer/psychiatric survivor movement. Recovery from mental illnesses has therefore been defined as "the deeply personal process of changing one's attitudes, feelings, perceptions, beliefs, roles, and goals in life". It was further conceptualized as "the development of new meaning and purpose in one's life, beyond the impact of mental illness" (8,38,40). This definition includes and/or implies some of the most common elements of many other definitions that have emerged over the past fifteen years: the importance of renewing hope and meaning (7,18,30,41,42); overcoming stigma and other sources of trauma associated with serious mental illnesses (7,30,43) and assuming control over one's life (28, 41,44-47). Empowerment which closely accompanies the element of assuming control over one's life and, by extension, the notion of regaining citizenship are additional elements which are, perhaps, more implied than stated in Anthony and colleagues' definition, but have certainly been identified as a critical factor by the Center for Psychiatric Rehabilitation and others (7,8,41,47,48).

RECOVERY RESEARCH

As pointed out by Rogers et al (49), it is somewhat difficult to classify the research that has a direct bearing on recovery, given the historical lack of clarity about the term. Traditionally, this research includes longitudinal studies of individuals with schizophrenia, qualitative studies, and first-person accounts of individuals with major mental illnesses. In addition to these traditional sources, developments in other fields of study, such as positive psychology and behavioral science research, have also begun to be seen as contributors to knowledge about recovery.

Recovery research is somewhat unusual in the field of mental health in that it has placed a high value on researchers who are themselves exemplars of recovery (i.e., researchers who are also ex-patients). This focus has contributed to broadening the kinds of questions under study. For example, it was consumers themselves who first recommended the investigation of issues related to success by individuals who had achieved meaningful lives rather than focusing only on issues related to relapse and deterioration, a shift in focus which contributed to the momentum of the recovery vision (8).

Longitudinal studies

Studies designed to examine the long-term outcome of individuals with schizophrenia have been recently summarized by Harding (50). These include studies from Switzerland (51,52), Germany (53), Japan (54) and the United States (1,2,55). Moreover, the World Health Organization recently conducted a multinational study in which outcomes among diverse cultural groups were examined (56). The follow-up period in all of these studies ranged from 22 to 37 years, with sample sizes ranging from 186 to 269 individuals, mainly those hospitalized with a diagnosis of schizophrenia. In the aggregate, one half to two thirds of the subjects were reported as recovered or significantly improved. The outcome indicators for recovery in these studies included: no further symptoms, no use of psychotropic drugs, living independently in the community, working, and relating well to others with no behaviors displayed that others

considered unusual. The designation of "significantly improved" was given when all recovery outcome indicators but one were present (50). These findings have largely held up over time. Despite variations across studies, it is clear that, when viewed through the lens of several decades, significant improvement has been reported for a substantial number of individuals with major mental illnesses.

Qualitative studies

The richness of the experience of recovery has been captured in several qualitative studies and analyses of first-person accounts. They have shown that individuals with serious mental illnesses have achieved recovery both using mental health services and without professional intervention. While it is clear that some do achieve a meaningful life (57,58) without professional intervention, we currently do not have sufficient data to explain or understand which individuals recover on their own or how this occurs.

Several authors (59-62) conducted qualitative studies to describe elements in the course of the recovery journey. In their in-depth interviews of small numbers of individuals over time, they were able to describe common challenges in the recovery process, including elements such as coping with a sense of loss, a loss of power and valued roles (such as parent, worker), a loss of hope, struggles to prevent relapse and to redefine oneself and one's social identity. In addition, they identified processes that appeared to be important to the experiences described, such as discovering a more active sense of self, for example, taking stock of strengths and weaknesses and fostering empowerment.

A number of researchers recently conducted meta-analyses of first-person accounts and narratives of the process of recovery (7,50,63,64), which have provided information on the explanatory frameworks used by individuals to understand the cause of their mental illnesses. For example, some individuals view their condition as the result of a spiritual crisis, others see it as biological, others as environmental or political, while others view it as the result of specific trauma.

Researchers have also examined the processes, coping factors and tasks identified as important to accomplish for recovery to occur (63,65). Examples of categories of the recovery process include those identified by Jacobson (63): recognizing the problem, transforming the self, reconciling the system, reaching out to others. Recovery experiences have also been categorized as being overwhelmed by the disability, struggling with the disability, living with the disability and living beyond the disability (58). Coping factors suggested by Ralph (64) include personal factors (e.g., insight), external factors (social supports), self-managed care (e.g., participating in one's own health care) and empowerment (e.g., sense of self efficacy). Tasks or themes to accomplish recovery suggested by Ridgway (7) include reawakening of hope, achieving understanding of disability, engagement in life, active coping, reclaiming a positive sense of self and regaining a sense of meaning and purpose. The power of a person who believes in the individual, even when the individual cannot believe in him or herself, has been cited, almost universally, as critical to recovery (8,31,50).

Contributions of positive psychology and behavioral science

The fields of positive psychology and behavioral science have begun to contribute to our emerging understanding of the factors associated with recovery. Positive psychology argues that psychology and psychiatry, in general, have focused, to their detriment, almost exclusively on the identification and alleviation of disorder (66). Positive psychology, while focused on individuals without disabilities, emphasizes growth, personal accomplishments and success in valued roles (67), which are also identified as recovery outcomes. Rogers et al (49) argue that the dimensions and processes proposed by positive psychology are equally important for individuals with serious mental illnesses. In addition, behavioral and social science research conducted with the general population in the areas of self-esteem, self-regulation, self-judgment and subjective well-being is all pertinent to the process and outcome indicators of recovery. For example, Diener's work (68) on the individual, cultural, and situational effects on subjective well-being furthers our understanding of individual processes for recovery. Moreover, this research is useful to the investigation of other questions, such as whether or not, as people progress toward recovery, their motivation shifts from preventing losses to promoting gains (69), or how to understand the perceived risks of pursuing self-esteem goals (70).

In summary, recovery research has shown that recovery: is possible over time; represents a multidimensional, highly individualized non-linear process that can be described; may be achieved with or without professional intervention; has multiple objective and subjective outcome indicators that reach beyond symptom reduction.

IMPLICATIONS FOR SERVICES

Recovery has been suggested as the critical overarching goal or mission that can serve to integrate the efforts of all services in mental health, including self-help services, basic support, rights protection as well as treatment and rehabilitation services (71).

While recovery is not an intervention that providers can make, all services can contribute (or not) to the outcomes and experience of recovery (e.g., well-being, self-esteem, valued roles, symptom reduction, empowerment, etc.). Intervention research has suggested that, while the picture is not totally clear cut, we are currently able to facilitate or promote some indicators of recovery outcomes.

Psychiatric rehabilitation has been described as a public health strategy in which all stakeholders, including con-

sumers, families, policy makers, researchers and clinicians play an important role (72), including community psychiatrists (73). Rehabilitation has been identified as effective in helping individuals to gain or regain valued roles in domains such as residential/community, vocational or employment and educational or schooling (74-78), outcomes recently reconfirmed as beyond those achieved by medication alone (79). Farkas (27) notes that these outcomes can promote recovery by increasing an individual's social capital, resources, empowerment and full citizenship in society.

In the field of treatment, effective interventions that promote at least one of the recovery outcomes include, among others, cognitive behavior interventions (80), medication management (81,82), integrated mental health and substance abuse treatment, and family psychoeducation (83). Qualitative studies (58) have also reported that support from others, effective medication and symptom management strategies, access to medical and psychiatric services, and basic resources like shelter, are recognized by consumers themselves as making a difference in an individual's recovery.

Based on the present state of our knowledge about what constitutes recovery, its process and its outcomes, it is possible to identify some key ingredients of a recovery oriented program, regardless of which specific practice is used. When evidence-based practices are developed, described and replicated (84), possible important philosophical elements of a practice may be omitted, because they may not as yet be empirically linked to the traditional outcomes reported. Yet these features may be important, because they can significantly alter the consumer's personal experience of the program and thus his/her unique process of recovery (85,86). Similar recognition has emerged in general medicine of the importance of value based practice in providing not only effective evidence based interventions, but also those interventions which are perceived to be meaningful to the patient (87).

While there are many values that may be associated with recovery-oriented services, there are at least four key values that support the recovery process and that appear to be commonly reflected in the consumer and recovery literature. These values are: person orientation, person involvement, self-determination/choice and growth potential (88). Farkas et al (89) have detailed an initial comprehensive set of recovery standards for program missions, policies, procedures, documentation and staffing, based on these core recovery oriented values. Regardless of the type of services delivered within the programs (i.e., treatment, case management, rehabilitation, crisis intervention, etc.), these values can guide recovery promoting service delivery.

Person orientation

First-person narratives convey that people with psychiatric disabilities appreciate when mental health professionals express interest in them as a person and in roles other than as "patient" (90,91). They may feel damaged by professionals who refuse to connect in a more holistic way (92). Consequently, recovery oriented services encourage the assessment and development of talents and strengths rather than narrowly focusing on deficits. "Person orientation" also guides services to promote access to resources and environments outside the mental health system where meaningful, socially valued roles can be attained, rather than limiting individuals to ghettos created by mental health service programs.

Person involvement

Research data suggest that outcomes are better for people who have an opportunity for meaningful involvement in the planning and delivery of their services (93). Consumer involvement in designing and delivering mental health services (e.g., program planning, implementation and evaluation) is seen as a critical component of a quality management system for any mental health service (94), as well as critical to the development of a sense of empowerment (95) and a shift in self-identity. Actively promoting the hiring of individuals with serious mental illnesses as peer providers and support personnel, as well as in the role of helping professionals and administrators, is becoming an important element in the development of a recovery oriented service or system (8,22,48). The consumer movement's slogan "Nothing about us without us" sums up its expectations of partnership and involvement in a recovery oriented service.

Self-determination/choice

Self-determination and self-choice is the cornerstone of a recovery process. The opportunity to choose one's long-term goals, the methods to be used to get to those goals and the individuals or providers who will assist in the process, are all components of a service acknowledging this value. Several mental health program models, such as psychiatric rehabilitation (78,96), supported housing (97), psychosocial clubhouses (98) and some case management programs (99), articulate the values of choice and partnership.

Davidson and Strauss (100) note, based on their qualitative research, that coercion has the effect of diminishing, rather than strengthening the self. Compliance does not promote the development of meaning and purpose in life and hence is a barrier to recovery. Placing a person in facility, job, school program or prescribing medications without exploring the person's preferences may achieve the outcome of reducing symptoms or gaining a role in society, without promoting the individual's sense of self, empowerment, well being or recovery. Helping an individual take back a meaningful life requires supporting self-determination and, if necessary, actively creating opportunities and providing assistance to develop more experience in making

informed choices. If a person cannot choose a specific type of role because he/she has not, for example, worked in many decades, a recovery oriented service would organize a variety of work experiences to help the individual figure out what his/her preferences might be. A recovery oriented service based on choice also provides individuals with sufficient education about medications, their intended outcomes and side effects to permit the individual to make choices from a menu of possibilities about which medications, if any, he/she wishes to use to support his/her recovery process.

Hope

Hope for the future is an essential ingredient in all recovery oriented services. A commitment to creating and maintaining hopefulness in both service participants and their practitioners is critical to selecting, training and supervising staff as well as developing program activities in recovery oriented services. While research shows that professionals do no better than random chance in predicting success (8), some staff may believe it is unrealistic to expect their patients to recover because they are "too sick" or "too disabled". Because such staff lack hope themselves, they cannot promote a recovery orientation. Services that promote activities focused on simple maintenance or the prevention of relapse, without opportunities and support to move beyond maintenance, are not recovery oriented. For example, services need to be able to support the aspirations of those who wish to go to or return to university or community colleges, as well as those who wish to complete grade school or high school. Services need to be able to facilitate the goals of those who wish to get married, have families, and start their own businesses, as well as those who wish to live in some type of supported residence and work in a more sheltered employment situation.

Hopefulness does not mean using the promise of recovery as a new tool to label or devalue the individual. The impulse to label someone as "unmotivated" should not now be replaced by the label of "recovery failure" because recovery goals are not met in the moment. Hope means remembering, as research has shown, that recovery can be a long-term process with many setbacks and plateaus along the way.

CONCLUSION

While the field is still developing its understanding of the process and meaning of recovery, it is clear that recovery is a reality that is possible to promote. Services should use practices with some evidence base that are reflective of, at a minimum, the four core recovery values (person orientation, person involvement, self-determination/choice and growth potential) in order to remain relevant as well as effective in the lives of the people they serve. Services focusing on people or the full human experience, not "cases", partnership not compliance, choice not coercion, and a commitment to hopefulness, not helplessness hold the promise of more than just survival or maintenance. Such services promote recovery or the realization of a meaningful life for individuals with serious mental illnesses.

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SPECIAL ARTICLE

Other faces in the mirror: a perspective on schizophrenia

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A patient with schizophrenia may generate an action (whether manual or verbal), but not attribute the generation of that action to himself. We distinguish self-monitoring and attribution of agency, relating only the former to forward models and the mirror system. We suggest that alien hand experiences occur when an action progresses through hand control pathways with no record of disinhibition having been kept and is then seen but dismissed as external. Analogously, auditory pathways are active during verbal hallucinations and produce a subvocal verbal process, but since no record is kept of the words being created, they are treated as external. The subject then proceeds to confabulate, to provide an account for the agency.

Key words: Schizophrenia, mirror systems, self-monitoring, attribution of agency, delusions

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The system of the monkey brain for visuomotor control of hand movements has its premotor outpost in an area called F5. This area contains a set of neurons, *mirror neurons*, with the property that each one is active not only when the monkey executes a specific grasp, but also when the monkey observes a human or other monkey execute a more-or-less similar grasp (1). Most writers have noted the adaptive advantage that such a system could have for social interaction, allowing one monkey to "understand" the actions of another, and thus position himself to compete or cooperate more effectively. However, monkey neurophysiology to date shows only that a macaque can "recognize" certain manual and oro-facial actions made by others, in the very special sense that the neural pattern elicited in the F5 mirror neurons by observing those actions is similar to that generated when he performs a similar action himself.

The mirror neuron system model (2) analyzes F5 mirror neurons as part of a larger mirror system, including parts of the superior temporal sulcus (STS) and area 7b of the parietal lobe. Observation of self-generated actions prepares the F5 mirror neurons to respond to hand-object relational trajectories even when the hand is of the "other", because the system processes the movement of a hand relative to the object, not the retinal input, which can differ greatly between observation of self and other. The system can categorize different actions (e.g., precision pinch vs. power grasp), but says nothing about the "binding" of the action to the agent of that action.

The region of the human brain homologous to macaque F5 is Brodmann's area 44 (3), part of Broca's area. This was traditionally thought of as a speech area, but has been shown by brain imaging studies to be active when humans both execute and observe grasps. These findings are the basis for one account of how the human brain changed from, but built upon, that of ancestral primates to make humans "language-ready". This is the "mirror system hypothesis": "The parity requirement for language in humans – that what counts for the speaker must count approximately the same for the hearer – is met because Broca's area evolved atop the mirror system for grasping with its capacity to generate and recognize a set of actions" (4). A brain that can support language needs not be one that evolved for this purpose, any more than our brains evolved under the pressure to ensure success at Web surfing (5). Specifically, the first hominids to have language-ready brains may have had limited protosign and protospeech, but no full language in the sense of a symbol system equipped with a rich syntax that supports a compositional semantics.

A number of papers (4,6-8) have related mirror neurons to internal models. Consider a system that combines circuitry in the brain encoding commands for a motor control task with the musculoskeletal machinery executing the task as well as with the perceptual machinery generating a neural code for the resultant interaction of the body with the external world.

A *forward model* for such a control system computes the neural transformation Command ➛ Response within the brain to provide an expectation of how the current action will turn out – and thus a basis for correcting for unexpected deviations. It is activated by a corollary discharge of the command to the motor system. Conversely, an *inverse model* provides a neural computation of the map Response ➛ Command, and is thus useful in planning how to obtain a desired response.

The mirror system hypothesis suggests that mechanisms similar to those for generating manual actions – with each control system linked to a forward and inverse model – are available for the phonological component of language, with different control systems and paired models for different sound patterns. However (9,10), the action and mirror system for the sound of a word is distinct from, though intimately linked to, the system for understanding the meaning of the word and mechanisms for generating and comprehending sentences.

AGENCY AND SCHIZOPHRENIA

How do we as humans know the agency of actions? In particular, how does one discriminate one's actions from those of another person? If I am a normal adult, when I move my hand, I know I moved it and also know that someone else did not move it. The same goes for speech and thought. Yet, schizophrenic patients hallucinate voices that they attribute to external agents; they also have delusions that other people are causing movement of their bodies; and they also have delusions of influencing others to act (11,12). In addition, patients with schizophrenia have difficulty determining whether they spoke or thought an utterance (13,14).

To understand both what one is doing oneself and what other people are doing, one needs both a notion of *action*, what is being done, and of *agency*, who is doing it. It has been argued that the brain's mirror systems give humans and many other animals a way of placing themselves in the actions of others. In this paradigm, a mirror system supports my ability to imagine myself moving my hands or saying something in the way another person does while I observe that person executing his actions. However, to function effectively, my brain must *in addition* correctly "bind" the various actions to the appropriate agents.

The binding for actions that I make, or actions that are directed to me, may involve processes partially separate from those involved in binding of actions to other agents. An example might be the observation that delusions in schizophrenia seem to be directed at the patient, or from the patient to another actor. If all agents, including the self, were created equal, we would expect that schizophrenics would experience as many third person delusions (actor to actor) as first person delusions (actor to self/self to actor).

Frith (15) offers another view of binding which must not be confused with the binding of action to agent. He starts from experiments of Haggard et al (16) in which subjects are asked to indicate the time at which they initiated an action. When the subject's button press causes an event, the times of action and event are perceived as being closer together than they actually were. However, when an involuntary movement (caused by transcranial magnetic stimulation) is followed by a tone, then the action and the event are perceived as being further apart in time. Frith thus argues that what he calls *intentional binding*, in which the cause and its effect are perceived closer together in time, could be an indicator of self-agency. The flaw in this argument is that, if the subject is unaware of causing the action, he may not monitor the timing of the cause in a way that grounds this judgment.

Impairment of self-monitoring

Daprati et al (17) had subjects perform a requested movement with the right hand while monitoring an image of a hand movement – either a display of the subject's own movement, or a movement started by the experimenter at the same time and from the identical initial position (see 18 for a related study). Once the movement was performed and the screen had blanked out, the subject was asked to answer "yes" if he saw his own hand performing the movement but answer "no" otherwise. One of three possible images could be presented to the subject in each trial: his own hand; the experimenter's hand performing a different movement, or the experimenter's hand performing the same type of movement. Both normals and schizophrenics made virtually no errors except in the last condition, where the median error rate was 5% in the control group, 17% in the non-delusional group and 23% in the delusional group.

However, *the experiment has little to do with attribution of agency*. In each case, the subject knows that he has made a movement and which type of movement it is – it is just a case of monitoring that movement accurately enough to tell whether a slight variant is indeed different. To clarify this, Mundhenk and I (19) distinguished two *different* factors that may affect the symptoms of schizophrenia: *self-monitoring*, which involves maintaining a working memory of one's recent actions as a basis for evaluating their consequences, and *attribution of agency*. The claim, then, is that the experiments of Daprati et al show impairment of self-monitoring, not attribution of agency.

Note that this function of self-monitoring is exactly that ascribed to a forward model. The model creates expectations which allow one to judge whether the ongoing action is indeed proceeding in the intended way. Frith (15) reviews the considerable work that he and his colleagues have conducted (e.g., 20,21) to advance the view that delusions of alien control are associated with abnormalities in the forward model's prediction of the outcome of intended actions. However, as Frith himself notes, some patients with lesions of supplementary motor area (SMA) or anterior corpus callosum exhibit a condition called anarchic hand (22), where the contralesional hand performs actions that the patient did not intend – yet the patient usually reports that there is something wrong with his hand, not that it is being controlled by alien forces. This is further evidence that imperfect self-monitoring is distinct from erroneous attribution of agency.

Frith also provides an accessible overview of literature that complements that discussed here. Other reviews relevant to the present discussion focus on the "social brain" (23) and on "theory of mind" (24). In relation to both these topics, a number of authors have suggested that the role of the mirror system in understanding manual, vocal and orofacial actions extends to support understanding and empathizing with the actions of others (25,26).

Attribution of agency

As Frith (15) notes, a touch we apply to ourselves feels

less intense than the same touch applied by someone else, but patients experiencing delusions of control do not show this attenuation (21). This suggests that corollary discharge does not automatically accompany the prefrontal signal to the motor system. Instead, I hypothesize that the forward model can only be activated by a "willful command" – that when one commits oneself to a movement, one both activates the forward model (grounding self-monitoring) *and* stores the intention of the action in working memory (attribution of agency to the self).

While several authors, as we have seen, suggested a role for extended mirror systems in recognizing the action of others, less attention has been given to the mechanisms whereby the brain can distinguish the "simulation" involved in recognizing the action of another from the actual creation of an action by the self. We do not, generally, attribute agency to movements of a disembodied hand. Rather, we seek to link the hand to a person whose face we can recognize. The binding of agent (whether self or a particular other) to action in working memory plays a crucial role in our behavior and our understanding of behavior.

Note that departure of an action from my expectation (forward model) for that action needs not call my agency into account. For example, if I suddenly swerve while driving, I will not have intended that swerve in advance but will recognize that it was an appropriate (but not premeditated) response to, say, an unexpected obstacle and that it fits within my overall intention.

Although the two processes are separate, self-monitoring may be crucial to my understanding of my agency with respect to certain observed consequences. In the case of a swerving car, I may compare a trajectory with an expected trajectory to decide (consciously or unconsciously) whether the departure was such that I should posit an external cause. But in either case, I know that I am the agent of my primary action, even if it departs from my expectations. Moreover, my brain can take account of feedback both at and below the conscious level of my intentions. For example, when I speak I may be most conscious of feedback on the effect of my communicative intention, yet I am constantly making adjustments at many levels down to the detailed effects of articulation.

In summary, the issuing of any command for action within the brain is accompanied by an expectation of the outcome of that action, and current actions generally unfold within the context of recent actions and ongoing plans which situate potential future actions with respect to current goals. Goals, plans, intentions, actions and expectations all require "working memories", whether the data they contain are accessible to conscious introspection or not.

Back to the delusions of schizophrenia

We may say that an action *m* is intended only if there is explicit prefrontal activity *x* to prime it, and other prefrontal activity *y* to release the inhibition that holds its premotor activity below the threshold for execution.

Arbib and Mundhenk (19) hypothesize, then, that each action is accompanied by a more or less accurate motor working memory of the trajectory of the action. Thus, if the need arises to question the agency of the action, the brain may consult its working memories (the plural is significant) to determine whether there was the *x,y* of priming and disinhibition prior to the action and, if so, whether the working memory of expected outcome of the action sufficiently matches the observed trajectory of the outcome. On this basis, the normal brain can decide "I am the agent", "I was the agent but for some reason the action did not come out as intended", or "I am not the agent".

We relate this to schizophrenia by hypothesizing that the primary deficit is in the lack of adequate control of inhibition. If the brain cannot maintain inhibition at an adequate level to block unintended actions, then an action may be made without need for a disinhibitory signal *y* that represents the decision to execute the action. Lacking any memory of having intended the action, the patient concludes "I am not the agent" and then proceeds to confabulate, to provide an account for the agency of the observed action.

Schizophrenic misattributions of agency are commonly linked to hand movements and language. While delusions of influence are not as common as auditory verbal hallucinations, in most cases they take the form that the schizophrenic hallucinates that another agent is causing his hand to move. This leads us to stress the relevance of the mirror system hypothesis for the study of schizophrenia. Extending the hypothesis, we suggest that the working memories for language production are evolved from, yet still closely related to, those for hand movements. This would explain why the disease does not strike all working memories and all "releasers of intention" equally, but most affects those for hand movements and language.

We suggest that schizophrenia is a disorder of the combined system, but also stress that the disorder leads to an impairment of this working memory system that is statistical in effect, rather than simply excising the whole system. Thus, depending on "where the dice fall", the patient's misattribution of agency may be related more to hands or voices, or may affect both in large part. We thus suggest that auditory verbal hallucinations are accounted for by the observation that auditory pathways are active during hallucinations (27) and produce a verbal process of some internal voice, but, since no record is kept of the voice being created, that voice is treated as external. That is, an utterance is created and progresses through verbal creation pathways, and returns as a vocalization *observed*, only to be dismissed as external, since no record of it being created has been kept. Schizophrenic patients, on this account, then confabulate the agent. The confabulated agent then takes on a strong identity persisting across hallucinatory episodes, even if the fictitious agent is nowhere to be found, or does not even exist.

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SPECIAL ARTICLE

Dimensional models of personality disorder

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There is little doubt that someday the classification of personality disorder will be dimensional. The failures of the categorical model are so many and are so well established that it is difficult to imagine that this model will ultimately survive. This paper provides a brief discussion of the major alternative proposals for a dimensional classification of personality disorder. It is possible that the authors of a future edition of a psychiatric diagnostic manual will simply choose one of these alternative proposals. However, the ideal solution might be to develop a common, integrative representation including the important contributions of each of the models.

Key words: Personality disorder, classification, dimensional, categorical

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Work is now underway toward the revision of the personality disorders sections of the ICD-10 (1) and the DSM-IV (2). There is perhaps little doubt that someday the classification of personality disorder will be dimensional. The failures of the categorical model are so many and are so well established that it is difficult to imagine that this model will ultimately survive. This paper, though, will not be concerned with a further reiteration of these failures, as they have been well specified in quite a number of prior reviews (3). This paper will focus instead on the future of personality disorder classification.

In 1999, a DSM-V Research Planning Conference was held under joint sponsorship of the American Psychiatric Association and the National Institute of Mental Health. The Nomenclature Work Group, charged with addressing fundamental assumptions of the diagnostic system, concluded that it is "important that consideration be given to advantages and disadvantages of basing part or all of DSM-V on dimensions rather than categories" (4). They recommended in particular that initial efforts toward a dimensional model of classification be conducted with the personality disorders. The DSM-V Research Planning Conference was followed by a series of international conferences to further enrich the empirical data base in preparation for the eventual development of the psychiatric diagnostic manual. The first such conference was devoted to reviewing the research and setting a research agenda that would be most useful and effective in leading the field toward a dimensional classification of personality disorder (5).

ALTERNATIVE DIMENSIONAL MODELS

By one count, there are 18 alternative proposals for a dimensional classification of personality disorder (6). This number is itself a testament to the interest in shifting the ICD-10 and DSM-IV personality disorder classifications to a dimensional model. This article will confine its coverage to what might be reasonably considered to be primary alternatives (7,8): a) a dimensional classification of the existing categories (9); b) the 18 scales of the Dimensional Assessment of Personality Pathology (DAPP, 10) and/or the 12 scales of the Schedule for Nonadaptive and Adaptive Personality (SNAP, 11); c) the three polarities of Millon (12); d) the seven-factor model of Cloninger (13); and e) the five-factor model (FFM) (14).

A DIMENSIONAL CLASSIFICATION OF THE EXISTING CATEGORIES

One proposal is to simply provide a dimensional profile of the existing (or somewhat revised) diagnostic categories (9,15). A personality disorder could be characterized as "prototypic" if all of the diagnostic criteria are met, "moderately present" if one or two criteria beyond the threshold for a categorical diagnosis are present, "threshold" if the patient just barely meets diagnostic threshold, "subthreshold" if symptoms are present but are just below diagnostic threshold, "traits" if no more than one to three symptoms are present, and "absent" if no diagnostic criteria are present (9). This proposal was actually made for DSM-IV (15), but was rejected at that time as providing a too radical shift in the conceptualization of personality disorder (16). It is perhaps now the most conservative of proposals and, with Andrew Skodol appointed as the Chair of the DSM-V Personality Disorders Work Group, it is probably the proposal most likely to be implemented for the nomenclature used predominately within the United States (9).

A significant limitation of this proposal is that clinicians would continue to be describing patients in terms of markedly heterogeneous and overlapping constructs. A profile description of a patient in terms of the anankastic, dissocial, dependent, histrionic, anxious and other existing personality disorder constructs would essentially just reify the excessive diagnostic co-occurrence that is currently being obtained (17). The problem of excessive diagnostic co-occurrence would be "solved" by simply accepting it.

A modified version of the proposal has been provided by Westen and Shedler (18). They suggest that the clinician be

provided a narrative description of a prototypic case of each personality disorder (half to full page, containing 18-20 features), with the clinician indicating on a 5-point scale the extent to which a patient matches this description (i.e., 1=little to no match; 2=slight match, only minor features; 3=significant match; 4=good match, patient has the disorder; and 5=very good match, exemplifies the disorder, prototypic case). Westen et al (19) suggest that their version of the prototypal matching procedure addresses the problem of diagnostic co-occurrence. They compared empirically the extent of diagnostic co-occurrence obtained with their prototypal matching to that obtained if the same clinicians systematically considered each diagnostic criterion. They reported considerably less diagnostic co-occurrence with their prototypal matching.

However, their findings in fact indicated that their prototypal matching procedure is "solving" the problem of diagnostic co-occurrence by simply neglecting to provide an adequate recognition of its existence. The fact that diagnostic co-occurrence increases when clinicians are encouraged to consider specific features of other personality disorders suggests that this co-occurrence is actually present but is not being recognized when clinicians are allowed to base their diagnoses on whatever feature or feature(s) they wish. Prior studies have shown that clinicians who do not systematically use diagnostic criterion sets grossly underestimate diagnostic co-occurrence and the extent of maladaptive personality functioning that is in fact present (20).

The prototypal matching of Westen and Shedler (18) can be supported by the Shedler-Westen Assessment Procedure-200 (SWAP-200). The SWAP-200 is a clinician rating form of 200 items, drawn from the psychoanalytic and personality disorder literature (21). Initial research with the SWAP-200 has reported good to excellent convergent and discriminant validity (21,22). The positive results obtained with the SWAP-200 should be tempered though by methodological limitations of the initial research (7,23,24). For example, clinicians who have provided the personality disorder criterion ratings have typically been the same persons who have provided the SWAP-200 rankings. This is comparable to having semi-structured interviewers provide their own criterion diagnoses in a study testing the validity of their semi-structured interview assessments. No such studies have ever been conducted because they would not be particularly informative. An additional methodological concern is that the clinicians in each study have been provided with guidelines for the distribution of their rankings (23,24). For example, in the typical SWAP-200 study, clinicians are required to identify half of the items as being absent, with an increasingly restrictive distribution for higher ranked items. Only eight SWAP-200 items can be given the highest ratings (21), no matter the opinions of the raters or the symptoms present. Convergent and discriminant validity of any semi-structured interview assessment of personality disorder diagnostic criteria would be improved dramatically if interviewers were instructed to code half of the diagnostic criteria as absent and to identify only a few of them as present. A final concern is that in all prior SWAP-200 studies the ratings were provided by persons who already knew the patients very well. It is not at all clear that reliable or valid SWAP-200 ratings would or could be made of persons during an initial clinical or research intake interview, which is precisely when a diagnostic assessment is typically conducted.

REORGANIZATION OF DIAGNOSTIC CRITERIA

Two predominant dimensional models of personality disorder symptomatology are the 18 scales of the DAPP (10) and the 12 scales of the SNAP (11). These two instruments were constructed by factor analyzing personality disorder diagnostic criteria, along with additional features, to yield more distinctive scales of maladaptive personality traits. The DAPP and SNAP scales provide profile descriptions of symptomatology that would be more differentiating and less susceptible to construct and scale overlap than five-point Likert scales of the existing diagnostic categories. Patients could be described more precisely with respect to elevations on such scales as mistrust, manipulativeness, insecure attachment, identity problems, affective lability, and self-harm.

A potential limitation of the DAPP and SNAP approaches is an absence of an explicit coordination with general personality structure. Coordinating the psychiatric manual with general personality structure would be consistent with the research indicating the lack of a distinct boundary between, and the close relationship of, normal and abnormal personality functioning, and would bring to psychiatry a wealth of scientific research on the etiology, course, and mechanisms of personality structure (6,14). The SNAP is coordinated in theory with three fundamental temperaments (i.e., positive affectivity, negative affectivity, and constraint), but factor analysis of the 12 SNAP scales does not generally obtain a corresponding three-factor solution. Joint factor analyses of the DAPP and SNAP have usually yielded four factors, described as negative affectivity, positive affectivity, antagonism, and constraint, which do correspond well with four of the five domains of personality functioning included within the FFM (25).

MILLON'S THREE POLARITIES

Millon hypothesized that each of the personality disorders reflects elevations on one or more of six fundamental dispositions of general personality structure organized with respect to three polarities (12). The three polarities are pleasure-pain, active-passive, and self-other. As suggested by Strack (26), Millon's personality disorder theoretical model is perhaps "one of the most frequently applied personality frameworks of this generation". Millon has been a prominent theorist in the conceptualization of personality

disorder. The inclusion of the avoidant personality disorder in DSM-III is due largely to him. The Millon Clinical Multiaxial Inventory-III (MCMI-III) (27) might be the most favored self-report inventory among practicing clinicians for the assessment of the personality disorders.

His particular theoretical model, however, is among the least studied (28), and the limited amount of research that has been conducted has often been refutative. For example, O'Connor and Dyce (29), using a variety of samples and assessment instruments provided by nine previously published studies, demonstrated that personality disorders do not covary in a manner that is consistent with how they are described in terms of the three polarities.

The Millon Index of Personality Styles (MIPS, 30) is a self-report measure of general personality functioning that includes scales constructed to directly assess the fundamental polarities. Piersma et al (31) reported that the MIPS assessment of the three polarities does not in fact relate to personality disorders in the manner outlined by the theory, even when the personality disorders were assessed with the MCMI-III. A replication of the findings of Piersma et al demonstrated incremental validity for an alternative dimensional model (32).

CLONINGER'S SEVEN FACTOR MODEL

Cloninger (13) has proposed a seven-factor model of normal and abnormal personality functioning. The seven factors consist of four fundamental temperaments, three of which are said to be associated with particular neurotransmitters: novelty seeking (dopamine), harm avoidance (serotonin), reward dependence (norepinephrine), and persistence. In addition, he suggests that there are also three character dimensions of self-directedness, cooperativeness, and self-transcendence, that developed through a nonlinear interaction of temperament, family environment, and life experiences (33).

Cloninger's theory is grand in its effort to integrate humanistic, existential theory with modern neurobiology (33) and his seven-factor model has generated a substantial amount of research. However, efforts to validate the seven-factor structure have raised significant concerns (34-37), and there does not appear to be support for the temperament and character distinction (36,38). The four temperaments do not appear to be well tied to the existing literature on childhood temperaments (39), and current understanding of neurobiology appears to be inconsistent with the model (40).

FIVE FACTOR MODEL (FFM)

An empirical approach for determining personality structure is through the study of the language. Language can be understood as a sedimentary deposit of the observations of persons over the thousands of years of the language's development and transformation. The most important domains of personality functioning would be those with the greatest number of words to describe and differentiate their various manifestations and nuances, and the structure of personality will be evident by the empirical relationship among the trait terms. Such lexical analyses of languages have typically identified five fundamental dimensions of personality: extraversion (or positive emotionality), antagonism, conscientiousness (or constraint), neuroticism (or negative affectivity), and openness (or unconventionality) (41). Each of these five broad domains can be differentiated further in terms of underlying facets. For example, the facets of antagonism versus agreeableness include suspiciousness versus trusting gullibility, tough-mindedness versus tender-mindedness, confidence and arrogance versus modesty and meekness, exploitation versus altruism and sacrifice, oppositionalism and aggression versus compliance, and deception and manipulation versus straightforwardness and honesty (42).

The FFM has considerable empirical support with respect to underlying genetic structure (43), childhood antecedents (39), temporal stability across the life span (44), universality (45) and functional relevance for a wide variety of important life outcomes, including work, well-being, marital stability, and even physical health (46). In addition, a considerable body of research has well documented that personality disorders are readily understood as maladaptive variants of the domains and facets of the FFM (7,14,47-50). Widiger et al (51) outline a procedure for the diagnosis of personality disorder in terms of the FFM. A clinical illustration of this procedure is provided by Widiger and Lowe (52).

A significant limitation of the FFM, as it is currently assessed, is that some of the lower order facet scales focus primarily on the normal variants of personality functioning (e.g., altruism, openness to aesthetics) rather than on the maladaptive personality functioning that would be of most clinical interest.

INTEGRATION OF ALTERNATIVE MODELS

It is possible that the authors of a future edition of a psychiatric diagnostic manual will simply choose one of the above alternative proposals. However, the ideal solution might be to develop a common, integrative representation that includes the important contributions and potential advantages of each of the models (6). Each model does appear to have some flaws and deficits, and each model would likely have at least some useful features. In fact, it is apparent that the alternative dimensional models are readily integrated within a common hierarchical structure (6,53).

The FFM is itself well integrated with the DAPP (10) and the SNAP (11). For instance, the conscientiousness domain of the FFM aligns well with the compulsivity domain of the DAPP and the constraint domain of the SNAP. The

lower order SNAP scales of workoholism and impulsivity, and the lower order DAPP scale of compulsivity, align well with the FFM personality scales of achievement striving, dutifulness, order, self-discipline, deliberation, and competence. Within an integrated dimensional model, one could retain the FFM domain scales (e.g., conscientiousness) but use DAPP and/or SNAP scales for the maladaptive variants. For example, high scores on FFM conscientiousness would lead to a consideration of DAPP compulsivity and/or SNAP workaholism, whereas low scores would lead to an assessment of DAPP passivity and SNAP impulsivity (14).

In any case, it is hoped that the authors of the ICD and DSM will recognize the importance and value of shifting to a dimensional classification of personality disorder, and one that is well integrated with basic science research on general personality structure. An integration of psychiatry's classification of personality disorder with dimensional models of general personality structure would transfer to the psychiatric nomenclature a wealth of knowledge concerning the origins, development, mechanisms, and stability of personality (14), and provide a bold and innovative paradigmatic shift that would help advance and reinvigorate a seriously troubled field.

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Rethinking psychosis: the disadvantages of a dichotomous classification now outweigh the advantages

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Emil Kraepelin would clearly recognize his 19th century dichotomy within current operational classifications of psychosis. However, he might be surprised at its survival, given the extent to which it has been undermined by the weight of currently available empirical evidence. The failure of this evidence to influence diagnostic practice reflects not only the comfortable simplicity of the dichotomous approach, but also the fact that this approach has for many years continued to receive support from some areas of research, particularly genetic epidemiology. This, however, is changing and findings from genetic epidemiology are being reappraised. More importantly, the potential of molecular genetics to indicate biological systems involved in psychopathology has been recognized, and with it the potential to develop diagnostic classifications that have greater biological validity. Crucially, this will facilitate diagnostic schemes with much greater clinical utility, allowing clinicians to select treatments based on underlying pathogenesis. Recent molecular genetic findings have demonstrated very clearly the inadequacies of the dichotomous view, and highlighted the importance of better classifying cases with both psychotic and affective symptoms. In this article we discuss these issues and suggest ways forward, both immediately and for DSM-V and ICD-11. If psychiatry is to translate the opportunities offered by new research methodologies, we must move to a classificatory approach that is worthy of the 21st century.

Key words: Nosology, classification, diagnosis, schizophrenia, bipolar disorder, psychosis, schizoaffective disorder, genetics

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Theoretical constructs in science, including diagnoses in medicine, have a finite lifespan and should be discarded when the weight of research data against them becomes critical and when more satisfactory alternatives become apparent. In this paper we summarize the evidence that such a tipping-point has been passed with regard to the traditional dichotomous approach to diagnosis of the functional psychoses. We argue that reliance on 19th century approaches to classification will impede translation of powerful 21st century research tools into benefit for psychiatric patients, and that we need new, more appropriate approaches to diagnosis and classification.

Emil Kraepelin is rightly regarded as one of the most important figures in the history of psychiatry. His writings remain rewarding to this day and his clinical descriptions are amongst the very best we have (1). He continued to develop and refine his ideas about psychiatric diagnoses, and his thinking had in many ways moved on from the dichotomous classification by the end of his life (2). However, it is not the goal of this article to consider Kraepelin's views in relation to modern nosological practice. A discussion of this sort, although of historical interest, is not of direct relevance to contemporary clinical psychiatry. Rather we wish to highlight the failure of the dichotomous classification, which originated with Kraepelin, to account for key research data and to consider alternative approaches.

A LONG HISTORY OF DISSENT FROM THE DICHOTOMOUS VIEW

Although the dichotomous view has dominated clinical psychiatry for over 100 years, there has been a long history of dissent (2,3). Many nosologists have developed their own models and approaches. Important recent examples include Crow's continuum model (4), the spectrum models of bipolarity of Angst and Akiskal (3,5), Marneros' focus on schizoaffective (6) and brief psychotic illnesses (7), and the polychotomous Leonhardian diagnostic system (8). Furthermore, a minority of practicing clinical psychiatrists have continued to recognize one or more distinct illness categories in addition to the two Kraepelinian prototypes (e.g., cycloid psychoses, psychogenic psychoses, bouffée délirante).

WHY HAS THE DICHOTOMY SURVIVED SO LONG?

In the absence of "laboratory" tests based on a solid understanding of pathogenesis, the criteria used in psychiatry for validating nosological categories have usually been restricted to clinical features, outcome and family history (9). These tools were used by Kraepelin in formulating his ideas and by more recent nosologists in shaping the modern operational classifications. One of the key scientific observations supporting the Kraepelinian dichotomy was that the prototypical disorders tend to "breed true". Thus, a consistent finding has been a substantially increased risk of schizophrenia but not bipolar disorder in the relatives of probands with prototypical schizophrenia and vice versa in corresponding studies of bipolar disorder. It is also true that groups of individuals classified as having typical schizophrenia can be dis-

criminated from sets of individuals classified as having typical bipolar disorder on the basis of a variety of clinical features and outcome.

As well as having some empirical support, the Kraepelinian view holds attractions for clinicians: it is conceptually simple and allows psychiatrists to demonstrate diagnostic expertise by exercising judgment over an often complex clinical picture and to reach a clear diagnosis. However, most experienced psychiatrists, whilst willing to make use of these advantages, are fully aware of the limitations and operate under conditions of dissonance in which management decisions are made based on a personal model of illness that has evolved from their own clinical experience. Although cogent arguments for abandoning an essentially dichotomous approach in favour of alternative formulations (categorical, dimensional or continuous) have been advanced, these have failed to gain widespread support, in part because of lack of robust scientific data, but possibly also because of the practical complexity of applying alternative classifications in clinical practice and research settings.

WHY SHOULD WE CHANGE OUR DIAGNOSTIC APPROACHES NOW?

Given that psychiatry has continued for many years to use a diagnostic approach that most nosological researchers have known provides an unsatisfactory model of mental illness, why should we make changes now? We consider two broad domains of rationale: a) the compelling research data that challenge the validity of the dichotomy, and b) problems with the general properties of the current approach to classification.

Research data are inconsistent with the dichotomy

There is now an overwhelming body of research data that challenge the validity of the dichotomous classification. Any psychiatrist with experience of functional psychotic illness knows that many patients do not have disorders that conform to either prototypical dichotomous category. Many individuals receive one diagnosis at one time or from one team and the alternative diagnosis at a different time or from another team. This clinical reality is supported by formal studies of symptom profiles that have typically failed to find a clear discontinuity between the clinical features of the two categories (what nosologists refer to as a "point of rarity") (10). Further, findings emerging from many fields of psychiatric research, such as neuroimaging, neuropathology and neuropsychology, do not fit well with the traditional dichotomous model (11). Of crucial relevance to our arguments are findings from recent genetic studies.

Evidence has been gradually accumulating over 10-20 years from genetic epidemiology that is inconsistent with the dichotomous view. Recent molecular genetic findings are most persuasive. Key pieces of evidence include the following:

- *Family studies*. Recent family studies point to the existence of a non-trivial degree of familial co-aggregation between schizophrenia and bipolar illness and between schizoaffective disorders and both bipolar disorder and schizophrenia (reviewed in 12-15).
- *Twin study*. A recent twin study – the only one that used an analysis unconstrained by the diagnostic hierarchy inherent in current systems of classification – demonstrated an overlap in the genetic susceptibility to mania and schizophrenia (16) and provided evidence that there are genes that confer susceptibility across the Kraepelinian divide.
- *Linkage studies of schizophrenia and bipolar disorder*. Systematic, whole-genome linkage studies of schizophrenia and bipolar disorder have implicated some chromosomal regions in common. This is consistent with shared susceptibility genes (reviewed in 12,17).
- *Linkage studies of schizoaffective disorder*. The only linkage study to date that has selected families through a proband meeting criteria for schizoaffective disorder strongly supports the existence of loci that provide specific susceptibility to psychosis with both schizophrenic and bipolar features (18).
- *Association studies*. Most recently, and most convincingly, genes have been identified whose variation appears to confer risk to both schizophrenia and bipolar disorder (reviewed in 17).

We, and others, have reviewed these recent genetic findings in detail elsewhere (17,19-21) and have considered their implications for psychiatric nosology (22). Here we will provide some examples of findings that demonstrate very clearly the shortcomings of the dichotomous classification.

Neuregulin 1 (NRG1)

The NRG1 gene was first implicated in studies of schizophrenia in the Icelandic population (23). A set of DNA variants, which we will collectively refer to as the "risk haplotype", showed association with susceptibility to illness. Meta-analyses confirm the strong evidence from several studies that genetic variation in NRG1 confers risk to schizophrenia (24,25). NRG1 has not yet been extensively studied in bipolar disorder. However, we found significant evidence for association of the risk haplotype with susceptibility to bipolar disorder with a similar effect size to that seen in our schizophrenia sample (26,27). Unlike other studies of NRG1, we undertook further analysis to search for evidence of phenotypic specificity of the effects of the NRG1 risk haplotype. In the bipolar cases, the effect of the NRG1 risk haplotype was most marked in cases with predominantly mood-incongruent psychotic features. In schizophrenia cases, the effect was greatest in the subset which had experienced mania. Our findings suggest that NRG1 plays a role in influencing susceptibility to a subset of functional psychosis that has both manic and mood-incongruent psychotic features; there is little effect in cases without such "dual" features. We would, therefore, expect that in any

sample the ability to detect the effect of the risk haplotype will be dependent on the proportion of cases with these dual features. Uncritical application of the dichotomy as if it captures homogeneous disease entities leads to the erroneous and unhelpful conclusion that there is a small, non-specific effect in both categories and that the only way to increase chances of replication is to increase sample size. In reality, by far the best way to increase the chances of replication will be to select a *smaller* sample from the total available – namely, the subset that has dual features.

G72/G30(D-amino acid oxidase activator, DAOA) locus

This locus was first implicated in studies of schizophrenia (28) and association was later reported also in bipolar disorder (29). Meta-analysis supports significant association in both diagnostic categories (30). We have reported the largest study to date, which included 2831 individuals: 709 who met criteria for DSM-IV schizophrenia, 706 with DSM-IV bipolar I disorder, and 1416 ethnically matched controls (31). We found significant association with bipolar disorder but failed to find association with schizophrenia. Analyses across the traditional diagnostic categories revealed significant evidence for association in the subset of cases (N=818) in which episodes of major mood disorder had occurred. A similar pattern of association was observed both in bipolar cases and in schizophrenia cases who had experienced major mood episodes. In contrast, there was no evidence for association in the subset of cases (N=1153) in which psychotic features occurred. This finding suggests that, despite being originally reported as a schizophrenia susceptibility locus, variation at the G72/G30 (DAOA) locus does not primarily increase susceptibility for prototypical schizophrenia nor psychosis. Instead, it appears that this variation influences susceptibility to episodes of mood disorder across the traditional bipolar and schizophrenia categories.

Importantly, the findings at the G72/G30(DAOA) locus also imply that whether or not significant associations are seen in schizophrenia samples will depend upon the proportion of cases that have suffered from episodes of mood disorder. As with NRG1, using the dichotomous view leads researchers to assume that increasing sample size is the way to replicate the small, apparently non-specific effects, whereas the most effective way forward will be to select a subset of the schizophrenia sample that has the specific clinical features that are influenced by the G72/G30 (DAOA) locus.

We could give other examples but will here mention briefly just one other locus, the 1q42 region of chromosome 1. This is strongly implicated in susceptibility to functional psychosis by observations in an extended Scottish pedigree, in which both schizophrenia and major affective illness co-segregated with a translocation that disrupts this part of chromosome 1 (32). In the only linkage study of schizoaffective disorder undertaken to date, we found genome-wide significant evidence for linkage at this same locus in 35 affected sibling pairs identified through a proband with DSM-IV schizoaffective disorder, bipolar type (18). That this reflects a phenotype-specific effect rather than some general effect in both schizophrenia and bipolar disorder is demonstrated by the absence of evidence for linkage at this locus in our much larger samples of sib-pairs selected through probands with schizophrenia (N=353) (33) or bipolar disorder (N=400) (34) from which these 35 sibling pairs were selected.

The molecular genetic findings at NRG1 and the 1q42 locus demonstrate a phenotypic specificity for mixed "mood" and "schizophrenia" features and, thus, provide evidence of biological validity for one or more subsets of cases of "schizoaffective" illness that may represent useful disease entities. These findings also suggest that it is important to take a longitudinal approach to diagnosis and to consider the nature and occurrence of psychotic and affective symptoms across the patient's illness history.

"Schizoaffective" illness: the importance of recognizing cases with mixed features

The term "schizoaffective" disorder is applied to cases with a mix of clinical features associated with prototypical schizophrenia and prototypical bipolar disorder. Such cases are common, but definitions have varied substantially (35-38). Within the context of neo-Kraepelinian operational classifications such as the DSM-IV (39) and ICD-10 (40), "schizoaffective disorder" tends to be used only when cases cannot be fitted to definitions of schizophrenia or bipolar disorder. Thus, in clinical practice and the vast majority of research, the diagnosis is treated like a "not otherwise specified" category that represents supposedly atypical cases. As a result, although some excellent work has been undertaken, cases with a rich mix of psychotic and bipolar features have not received the same attention as schizophrenia and bipolar disorder in research into treatment and pathogenesis. Indeed, the approach has often been to treat schizoaffective cases as a "nuisance" and to either exclude them from analysis or combine them with one or other of the dichotomous categories. For example, in molecular genetic research on schizophrenia, it is common for researchers to undertake a "narrow" analysis with only DSM-IV schizophrenia and a "broad" analysis that includes also schizoaffective disorder.

This approach to schizoaffective spectrum cases is highly problematic if such cases actually reflect the expression of one or more relatively specific underlying disease processes. As noted in an earlier section, some clinicians and researchers have certainly believed that at least some schizoaffective cases represent distinct clinical entities and have continued to apply minority diagnostic concepts, such as "bouffée délirante" (France; e.g., 41), psychogenic psychoses (Scandinavia; e.g., 42) and cycloid psychoses (43) – the latter being part of the rich but complex classification of endogenous psychoses of Leonhard (8). Further, the existence of one or more relatively discrete nosological entities

with mixed features is supported by latent class analyses (44-47). Genetic epidemiology supports a strong genetic component to schizoaffective illness (48-53). Indeed, the effect size may be higher in this phenotype than in prototypical schizophrenia or bipolar disorder (52). As we have already discussed, there is now molecular genetic evidence for the existence of at least two loci that specifically influence susceptibility to this phenotype.

One of the criticisms of "schizoaffective disorder" by clinical and research psychiatrists is the lack of reliability and temporal stability that has been reported using current definitions (54). However, this is an almost inevitable consequence of the overly restrictive nature of current definitions of "schizoaffective disorder", together with the tendency of clinicians to make diagnoses "cross-sectionally" rather than longitudinally. We know that the precise clinical presentation of any individual with psychosis varies over time and, given the very restrictive definition of the schizoaffective category compared with the much broader definitions of schizophrenia and mood disorder, it is inevitable that the latter categories will seem much more reliable and stable than the schizoaffective category. If cases with "schizophrenic" and affective symptoms do indeed represent a group with shared underlying pathogenesis and strong genetic loading, then the neo-Kraepelinian dichotomous approach, with its narrow definition of schizoaffective disorder, will simply serve to impede aetiological research.

General properties of the classification system

Current operational diagnostic systems: the theory and the practice

The neo-Kraepelinian operational classification systems that were developed in the latter part of the 20th century in response to concerns over poor diagnostic reliability were an important advance for clinical and academic psychiatry. The theorists who developed these systems to provide descriptive categories acknowledged their uncertain validity (55). However, despite the clear caveats within the diagnostic guidelines (39,40), there has been a strong tendency for the categories to be reified and credited with properties of homogeneity and validity that were never intended. This tendency is arguably most marked amongst individuals who do not have direct experience of mental illness, such as non-clinical researchers, medical managers, politicians, etc. However, it is also surprisingly common amongst clinical psychiatrists, particularly those whose training post-dated the requirement to use operational diagnostic classification for clinical work and research. This must serve as a lesson for future classifications: we need to ensure, perhaps by the structure of the classification, that all users are completely aware of the limitations as well as benefits.

Practical and organizational problems that result from continued use of the dichotomy

The thinking and actions of those involved with mental illness is shaped and constrained by "official" classifications. If psychotic illness is not really separable into two major categories with distinct pathologies and treatment responses, there can be negative consequences to continuing to act as if it were. We provide some examples:

- *Clinical services.* Many clinical services, particularly but not exclusively in the US, are divided according to the dichotomy. For example, clinics serving schizophrenia and bipolar disorder are often staffed by different clinicians and even located on different floors of a hospital.
- *Scientific meetings.* Sessions at scientific meetings and often whole meetings are divided according to the dichotomy.
- *Drug licenses*. Typically, legal approval of a drug is restricted to a specific diagnostic category with a license granted only for one of the dichotomous categories.
- *Therapeutic research*. Clinical trials are conducted according to diagnostic category. Many studies of individuals meeting criteria for schizophrenia find effects in some but not all individuals; likewise for mood disorder. It is entirely possible that specific, predictable effects may fail to be recognized if analyses are not undertaken that take account of clinical variation within a diagnostic category and across diagnostic categories.
- *Research into causation*. The vast majority of psychiatric research studies report findings according to operational diagnostic categories and do not consider more detailed clinical descriptors.
- *Understanding by non-professionals*. When the terms "schizophrenia" and "mood disorder" are used by individuals without clinical training and experience (such as politicians, lawyers and health service managers), there is a strong tendency for them to be used as robust categories without any of the caveats required. Further, much of the neuroscience research in psychiatry is carried out by non-clinical scientists, and many of these have a faith in the diagnostic categories that is completely unjustified by the evidence.

Practical problems with applying current operational diagnostic classifications to real patients

Clinicians and researchers experience several major problems in using the current systems for making *lifetime* diagnoses (Table 1) (56). We need to minimize such difficulties in our future classifications.

THE WAY FORWARD FOR CLASSIFICATION: WHAT VALIDATORS TO USE?

The most useful validators for diagnosis of a given group of disorders will vary over time according to a) what techniques are available, and b) the over-riding aim of diagnosis. In Krae-

Table 1 Major limitations of current operational categorical approach to diagnosis

- The focus is on episode rather than lifetime experience of psychopathology
- Hierarchies lead to loss of information
- Boundaries between diagnostic categories are often arbitrary
- Boundaries between categories often require substantial subjective judgement
- Available diagnostic categories are relatively unhelpful in distinguishing severity
- Sub-clinical cases are usually not accommodated usefully
- "Not Otherwise Specified (NOS)" categories are highly heterogeneous

pelin's time, with no effective treatments available, the practical aim of diagnosis was mainly to predict prognosis. It was, thus, entirely logical that Kraepelin developed his dichotomy on this basis, and it performs relatively well against this validator. Given that the main goal of modern psychiatrists is (or should be) to provide effective treatment, it is our view that the ultimate validator for our diagnostic systems must be *treatment response* (57). Over the half century that effective psychotropic drugs have been available, it has become clear that they do not respect diagnostic boundaries. Perhaps the most elegant demonstration of this comes from the landmark Northwick Park study (58), which found that, in patients with functional psychosis, psychotic symptoms responded to a neuroleptic and mood symptoms to a mood stabilizer (lithium); there was no diagnostic specificity.

We now have at our disposal powerful molecular genetic tools that should allow us to identify the biological systems that are involved in disease pathogenesis. These techniques allow us to study biological systems in large numbers of individuals whilst they are alive. For the first time in psychiatry, this provides the opportunity to validate our diagnostic concepts and procedures against biologically relevant criteria that in many cases will relate to the effectiveness of treatments. In time the impressive developments in neuroimaging are likely to provide us with the power to study the functioning of specific, relevant brain systems *in vivo* in individuals during differing phases of illness and in response to varying environmental situations. These approaches will, we imagine, be complemented by developments in many other fields. This will facilitate the bringing together of diverse domains of research evidence that can be synthesized into models of brain function and dysfunction and their relationship with psychopathology. We must now grasp this opportunity and develop approaches to classification that are explicitly designed to take advantage of the new research tools.

THE WAY FORWARD FOR CLASSIFICATION: WHAT NEEDS TO HAPPEN IMMEDIATELY?

There are some relatively simple changes to our thinking and general approach that could be taken immediately and would be of great benefit for research, clinical practice and improving lay understanding of mental illness (Table 2).

The key practical issue is, of course, how we can start to better recognize and describe the cases that share relevant clinico-pathological features and facilitate their grouping close together in "classification space". One approach is to use quantitative, ordered descriptions of key domains of psychopathology and to apply these longitudinally. Such clinical dimensions can be used alongside categories (existing or novel) as a way of providing a richer representation of individual psychopathology and allow individuals with similar lifetime experiences of psychopathology to be recognized and grouped. We have used this approach for our own research on psychosis by developing the Bipolar Affective Disorder Dimension Scale (BADDS) (56). This provides a description of an individual's lifetime experience of psychopathology using four ordered integer scales (0-100), or "dimensions": mania; depression; psychosis; incongruence of psychosis. It is important to stress that this is a descriptive-classificatory tool that may help in moving from the current classification towards classifications that are anchored in an understanding of pathogenesis. It is not driven by any particular model of illness and does not presuppose that psychopathology is distributed continuously.

Table 2 Steps that need to be taken immediately

1. Change our thinking to accept that:
   a) we must move towards a classification offering greater clinical utility
   b) this will be an iterative process and the first steps must facilitate this
   c) clinical utility requires biological validity
2. Change our practice to ensure that:
   a) clinical psychiatrists are supported in treating across diagnostic categories
   b) researchers routinely use and report more sophisticated clinical phenotypes
   c) the diagnostic utility of schizoaffective spectrum illness is better recognized
3. Change our organization such that:
   a) clinical service provision is not constrained by invalid diagnostic boundaries
   b) research is encouraged across the functional psychosis spectrum

Recognizing schizoaffective illness

As we have seen, current data demonstrate that, amongst illnesses with mixed features of the dichotomous prototypes, there are likely to be one or more subsets of cases that may constitute relatively distinct disease entities. To facilitate the research necessary to explore this, it is essential that such cases are recognized, classified together and acknowledged as worthy of at least as much attention as is given to cases of "schizophrenia" and "mood disorder". In our own research, based on our genetic findings to date, we adopt one simple approach that uses DSM-IV lifetime diagnosis supplemented by some additional information about lifetime psychopathology (which comes from our BADDS scores). We also use the concept of "schizoaffective spectrum phenotype" (SASP) to denote an illness meeting one of the following criteria: a) DSM-IV schizoaffective disorder, bipolar type, or b) DSM-IV schizophrenia with at least one episode of DSM-IV mania during lifetime or c) DSM-IV bipolar I disorder with psychotic features in at least half of all episodes of major mood disorder. We make no claims that our definition is somehow

"correct". Rather, we have taken a simple pragmatic approach informed by our data (18,59,60).

We believe that this approach, or similar, would provide immediate benefits at minimal cost and would facilitate a transition from our current state to the first iterations of the new classifications that we need.

THE WAY FORWARD FOR CLASSIFICATION: WORKING TOWARDS CLASSIFICATIONS THAT WILL BE OF GREATER BENEFIT FOR PSYCHIATRIC PATIENTS

Those charged with the responsibility of developing DSM-V and ICD-11 are well aware of the shortcomings of the current approach (61), and the process of considering options has already been under way for several years. Data from the ongoing large scale molecular genetic studies (particularly, but not exclusively, whole genome association studies), together with data from other areas of neuroscience, offer the opportunity of starting to put psychiatric classification on a robust framework that has biological validity. Although it is too soon to know the details of such classifications, it is already possible to identify several important properties that are highly desirable and should be used to inform the development of new biologically valid, clinically useful classification systems (Table 3).

Table 3 Desirable properties of a classification system

1. Uses measures that are likely to map onto biological systems
2. Uses multiple descriptors of an individual's psychopathology:
   - Symptomatology, severity, course, impairment, etc.
   - Categorical and dimensional measures
3. Explicitly recognizes that the scheme will develop in response to new data:
   - Forward and backward compatibility with other classification systems
4. Can accommodate sub-clinical psychopathology
5. Facilitates grouping together of individuals likely to share similar pathology
6. Is flexible for different needs:
   - Allows different versions for different uses (clinical, research, service, etc.)
7. Is longitudinal rather than cross-sectional
8. Is developmentally sensitive:
   - Provides continuity across the lifespan

Phenotype boundaries

Here we have focussed our discussion on the need to move from the traditional dichotomous approach to diagnosis of mood-psychotic disorders and towards approaches that have demonstrable biological validity and greater clinical utility. We do not have space here to consider the various other phenotypic boundaries relevant to mood-psychotic disorders. However, in general, similar considerations apply. For example, we anticipate the need to consider improved approaches to representing the interfaces between bipolar spectrum illness and attention-deficit/hyperactivity disorder. We think it extremely likely that there will be an important overlap in the biological systems involved in the pathogenesis of the psychopathology experienced by individuals who meet criteria for these diagnoses (specifically those systems involved in attention and motor activity) (62). Likewise, we anticipate the need to refine our thinking about the distinction between "illness" and "personality". For example, it is highly likely that there will be remarkable overlaps in the systems and dysfunctions contributing to the substantial mood instabilities seen in individuals meeting criteria for borderline personality disorder and some individuals meeting criteria for rapid cycling bipolar disorder (63).

CONCLUSIONS

Kraepelin himself fully recognized the difficulties in applying the dichotomy he had suggested. He was a clinical scientist capable of major feats of synthesis and demonstrated an ability and willingness to modify his thinking in response to new data. We suspect that, had he lived, he would have abandoned the dichotomous view completely at some point during the 20th century. Further, we think he would have been surprised and disappointed at the failure to move forward in any significant way.

We now have a large body of research data that are inconsistent with the dichotomy and powerful tools at our disposal that allow us to start developing a biologically valid framework for classification that is likely to offer much improved clinical utility. We do not claim that the current genetic findings are sufficient to decide on precise alternatives to the current classifications. Neither do we claim that every current finding will turn out to be robustly replicated. Rather, our argument is that they are sufficient to show that there is an urgent need to change our approach *now*.

Changing to definite distinct systems of psychiatric classification every few years is confusing and wasteful. What we need is an approach that is not misleading about the current level of understanding, is clinically useful, and helps, rather than hinders, researchers to unravel the biological basis of disorders. Typically, "physical" disease classifications include mixtures of defined pathological entities and more or less well-defined clinical syndromes according to the state of understanding of each disease entity. Thus, it is to be expected that this will be the case in psychiatry as our knowledge develops. Therefore, we might find some relatively discrete syndromes that have discrete biology but others that are better conceptualized on a continuum. We should be prepared for this.

Given the lowly status accorded to "schizoaffective" cases in our current official classifications, it would be an embarrassment if genetic and other biological risk factors turned out to have the greatest impact on schizoaffective spectrum illness. That this might be so is hinted at by studies of familiality and the striking linkage findings at 1q42. Should this turn out to be the case, it will be a sobering academic exercise to estimate how many patients will have suffered from the delay to progress in psychiatry caused by continuing to apply a classification that, instead of carving nature at the joints, has ensured that we have been "sawing through bone" (64).

We summarize the key points of our article in Table 4. Finally, we note that, as a general rule, human beings do not like change and tend to treat proposals for change with suspicion and resist-

Table 4 Key messages

- Valid diagnostic classification is crucial for clinical research and practice
- Data, rather than opinion or tradition, must inform classification
- Research data from many fields are inconsistent with a dichotomous classification
- Powerful new research tools provide biological validators for classification
- Current classifications are inhibiting progress in research and clinical practice
- Simple steps can, and should, be taken immediately as "first aid" measures
- Development of biologically valid classification will be an iterative process
- Key desirable properties can already be identified for new classification systems

ance. However, as responsible clinicians, we owe it to our patients to take action urgently.

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Deconstructing and reconstructing illness syndromes associated with psychosis

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Craddock and Owen summarize evidence supporting a movement away from the Kraepelinian dichotomy. They are correct in the assessment of evidence, but breaking down old boundaries does not establish new boundaries. One approach, however, is well suited for current application: the domains of pathology paradigm. I will briefly illustrate application with work from our group, and suggest where we may be headed with the DSM-V Schizophrenia and Related Disorders Work Group that I will chair.

Schizophrenia is a clinical syndrome. It has not been documented as a single disease entity. Nonetheless, most study designs during the 20th century investigated schizophrenia as a class. This may be analogous to studying dementia rather than specific entities such as Alzheimer's disease. Since specific disease entities had not been identified within the schizophrenia syndrome, we proposed using domains of pathology to reduce syndrome heterogeneity. This was based on the tripartite model that we published in 1974 (1), viewing schizophrenia as comprising positive psychosis, negative symptoms, and impairments observed in interpersonal relations. These domains were found to be rather independent of each other in our studies. Implementation of this model would be a paradigm shift, as we advocated the study of each pathologic domain as the independent variable allowing for differences in etiology, pathophysiology, and treatment between pathologic domains within the syndrome boundaries. However, at that time, the concept of nuclear schizophrenia was dominant and only recently has the domains of pathology paradigm received wide attention.

The 1982 type I/II (2) and positive *vs.* negative (3) proposals attempted to move the domains paradigm forward, but the dominant paradigm held sway. Cognition impairment and negative symptoms are now the focus for drug discovery, with the assumption of relative independence between these pathologies and psychosis (4,5). The failure of the schizophrenia as a disease entity model is seen in the porous boundaries addressed by Craddock and Owen, and is also evident in fifty years of producing antipsychotic drugs and complete failure to develop pharmacotherapy for cognition and negative symptoms.

At our center we focused on negative symptom pathology and advocated application of this domain to reduce heterogeneity in study samples (6,7). We studied schizophrenia, dividing subjects with primary negative symptoms (the deficit schizophrenia group) from subjects with a schizophrenia diagnosis but without primary negative symptoms (8). A series of studies supported the hypothesis that deficit schizophrenia was a separate disease within the syndrome (9). These studies addressed the 100-year challenge of determining whether Bleuler was correct in referring to the "group of schizophrenias".

What is the relevance of this work, which identifies multiple boundaries within schizophrenia, to the breakdown of boundaries between the major diagnostic classes associated with psychosis? I believe that the domains of pathology paradigm provides the best current method for addressing similarities and differences between classes. More importantly, domains of pathology will cut across diagnostic boundaries. Not all cases in any class will have a specific domain unless the domain is a required diagnostic criterion. This will go a long way in the current implementation that Craddock and Owen advocate. Restricted experience and expression of affect may occur in many patients with a schizophrenia diagnosis and few with a bipolar diagnosis. But genes that convey vulnerability to restricted affect pathology may be associated only with those schizophrenia subjects who have this pathologic domain, but also may be found in the few cases of bipolar illness where this pathology is observed between episodes of manic and depressive symptoms. Similarly, etiologic factors associated with hallucinations may be restricted to patients with hallucinations within each class, but be similar across classes. It would be surprising, indeed, if genes associated with vulnerability to depressive episodes in the general population were not also associated with depression in a subgroup of schizophrenia patients.

DSM-V is scheduled for 2011, and the Work Group for Schizophrenia and Related Disorders is being formed at the time of this writing. The DSM process will be a critical opportunity to see how far we can travel along the road outlined by Craddock and Owen. My prediction is that we will retain the major diagnostic classes with extensive similarity to DSM-IV and ICD-10. We simply do not have sufficient new knowledge to radically revise nosology for these illnesses. However, I believe that the shortcomings of the current classification will be substantially addressed by developing a parallel system based on domains of pathology. If a case meets criteria for schizophrenia, for example, it will be essential to also determine if the case meets criteria for certain dimensions. This will include symptomatic domains such as negative symptoms, disorganization, reality distortion, depression and anxiety. It may also include assessment of cognition and, should any have sufficient sensitivity and specificity, biomarkers. General dimensions such as social and occupational function may also be considered. In any case, such a two-step diagnostic approach will address four important problems: a) that domains of pathology cut across syndrome boundaries; b) that developing and applying new knowledge will be more decisive at the level of specific domains; c) that clinicians plan

treatment based on an individual patient's actual pathologies, not a syndrome designation; and d) that our ability to relate pre-clinical models to clinical phenomena is weak at the syndrome level, stronger at the domain level.

The field has much work to do on the roadmap provided by Craddock and Owen.

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The right answer for the wrong reasons?

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The Kraepelinian dichotomy has been challenged by evidence from many fields of psychiatric research (1-3). Following on from the pioneering critique by Tim Crow (4) fifteen years ago, Craddock and Owen now examine the dichotomous approach from a molecular genetics perspective. They introduce the beguiling prospect of certain candidate genes such as neuregulin 1 having phenotypic specificity for psychopathological features, in this case mixed "mood" and "schizophrenia" features. However, as Kendler, one of the leading American psychiatric geneticists, has so eloquently reviewed recently (5), the effect of individual genes on susceptibility to different psychiatric disorders is likely to be too small to be useful in drawing up a novel classificatory system.

Furthermore, while it is certainly true that evidence against the validity of the Kraepelinian dichotomy is mounting, it is premature to argue the case using molecular genetic data, because of their inconsistency. Different methods of meta-analysing whole-genome linkage scans of bipolar disorder and schizophrenia have yielded different results. For example, using the technique of multiple scan probability, Badner and Gershon (6) found common loci for both disorders on chromosome 22q, as well as two distinct susceptibility loci. On the other hand, Craddock and Owen were co-authors of a rank-based meta-analysis of schizophrenia and bipolar disorder, which showed significant evidence for linkage to several chromosome regions in schizophrenia (7), whereas no region achieved genome-wide statistical significance in bipolar disorder (8).

Maziade et al (9) undertook a genome scan of schizophrenia and bipolar disorder in multigenerational families affected by schizophrenia, bipolar disorder or both. Their work was based on the hypothesis that susceptibility genes may be shared by the two major psychoses (the common locus phenotype). Their results showed convergence in some regions, but suggested that other susceptibility genes may be specific to each disorder.

Our group's previous twin study also supports the idea that schizophrenia and bipolar disorder may share some common genes, while others may be specific to each condition (10). We have used these data to argue elsewhere that developmental and dimensional perspectives are likely to throw the greatest light on the relationship between schizophrenia and bipolar disorder (3,11). Thus, neuropsychological and grey matter deficits are much more noticeable in schizophrenia than bipolar disorder (12,13), as are neurological soft signs. Indeed, children who later develop bipolar disorder do not share the excess of subtle neuromotor and cognitive impairments of their pre-schizophrenic counterparts and often appear superior to the normal population in motor development and school examinations (14).

Furthermore, the risk-increasing effect of obstetric complications appears to be confined to schizophrenia (15). Exposure to perinatal hypoxia is known to result in smaller volume of the amygdala and hippocampus, which are reduced in schizophrenia but not in bipolar disorder. These findings suggest that one distinction between schizophrenia and bipolar disorder is that there exists a gradient of neurodevelopmental impairment which is much more important in the former than the latter.

We accept that the neo-Kraepelinian view that schizophrenia and bipolar disorder are totally discrete entities is not supported by the available scientific evidence. However, in our opinion, what is needed is not a rush from one invalid system to another. Rather, we require careful and systemic enquiry and large scale empirical studies. Already, such studies have shown that the symptom dimension model as proposed by van Os (16) adds substantial information to Kraepelin's system. Dikeos et al (17) suggest that the categorical and dimensional approaches

are complementary, and that the use of both maximizes the potential of available information. We now need to carry out comparable studies using external validators, such as neuroimaging, neuropsychology and developmental epidemiology, as well as molecular genetics (11), to establish the extent to which incorporating these measures adds value to our ways of describing patients.

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Psychiatric diagnoses: the weak component of modern research

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Kraepelin's dichotomy is built on Kahlbaum's large monograph (1) on the history and principles of the classification of psychiatric disorders. Kahlbaum proposed a classification based on symptoms, course and good vs. bad outcome (vecordia vs. vesania). Kraepelin's classification owes its enormous success to the clarity of his concepts and his lively and literary language. Later Kraepelin himself had doubts about a clear distinction between schizophrenia and manic-depressive insanity, stressing in 1920 (2) that "no experienced diagnostician would deny that cases where it seems impossible to come to a clear decision are unpleasantly frequent. Therefore the increasingly obvious impossibility of separating the two illnesses satisfactorily should arouse the suspicion that our approach to the question was wrong".

Kraepelin's concept was seriously shaken by Zendig's follow-up study of Kraepelin's own patients diagnosed as schizophrenic, a substantial number of whom were found to have a good prognosis (3). Zendig's interpretation that the diagnosis had been made incorrectly proved to be wrong, as shown by Lange's diagnostic check (4), and the dichotomous distinction was later disproved by Kick's reassessment of Kraepelin's cases, which documented a continuum at the symptom level between the two groups (5).

Multiple studies subsequently confirmed the existence of a group of conditions between schizophrenia and affective disorders, which were named intermediate psychoses (6), mixed psychoses (7), atypical psychoses, schizo-affective psychoses. Kretschmer (8) assumed that about half of psychotic patients suffer from mixed psychoses. Important longitudinal studies, starting with that conducted by Schüle (9), demonstrated the existence of cases beginning as manic-depressive and later turning into schizophrenia, as well as cases initially schizophrenic and later turning into manic-depressive disorder (10-13).

Many follow-up investigations demonstrated that schizo-affective patients can manifest, over their lifetime, manic, depressive, catatonic, hebephrenic and other psychotic (mainly delusional) syndromes, the course and outcome of which take an intermediate position between schizophrenia and affective disorders (14). In addition, clinical-genetic findings confirmed the continuum hypothesis by comparing the morbid risk ratio for schizophrenia vs. affective disorders among first-degree relatives of probands with a diagnosis of affective, schizo-affective (affect-dominant and schizo-dominant) or schizophrenic disorder (15).

It is highly probable that Kraepelin would have changed his dichotomous concept had he lived longer. Hence, those who still believe in that concept today may be called archeo-Kraepelinians rather than neo-Kraepelinians. There may be several reasons why Kraepelin's dichotomy has survived until now despite findings disproving it: a) Kraepelin's nosology was for a while the counterpart to the psychoanalytical view; b) by nature we prefer to think dichotomously; c) for obvious practical reasons, the important and influential diagnostic and statistical manuals (ICD, DSM) develop slowly, have to stick to discrete diagnostic classes and have to be conservative.

An early fundamental critique of the dichotomy was based on serious doubts about the existence of psychiatric entities defined by symptoms, course and outcome. The great antagonists of Kraepelin, Hoche (16) and Bumke (17), preferred a pure, descriptive *syndromal approach* and assumed that identical syndromes can have multiple causes (18), a concept which is of great relevance today. Mundt suggested a transnosological psychopathology (19) and van Praag proposed a functional psychopathology based on biological mechanisms, pointing out that "nosologomania" is a "disorder of psychiatry" (20). It is also an old story that drugs act on target symptoms or syndromes across disorders (21), although they are licensed for the latter. A book on psychopharmacology with such a syndromal approach was published in 1979 (22).

The great danger of the present operational diagnoses is that they are misperceived as well-established "natural" entities and that clinicians restrict their examinations and even their research to them. Examples are the widely used standardized interviews in epidemiology, which do not describe psychological and somatic symptoms comprehensively, but identify only whether or not symptoms meet a diagnostic scheme, with a serious inherent loss of information. This approach cannot question the diagnostic criteria themselves and is therefore unsuitable for developing the system further. Better measurements, as mentioned by Craddock and Owen, are badly needed and one can only agree with all their recommendations.

If treatment utility should be a main goal of classification, as Craddock and Owen suggest, therapeutic studies have to be much more sophisticated and more independent from the pharmaceutical companies' proximal interests. The minimized assessment and measurement of psychopathology in therapeutic studies has to be replaced by much more comprehensive symptom inventories, like those which were used some decades ago. Currently the goal and methods are usually set by the minimum requirements of the European Agency for the Evaluation of Medicinal Products (EMEA) or the Food and Drug Administration (FDA) for the marketing of new drugs and not by scientific or realistic practical targets. As a consequence, the results of many studies, especially those which are placebo-controlled, cannot be generalized and transferred into practice.

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Rethinking psychosis

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I was glad to read Craddock and Owen's paper on the classification of the psychoses. There is much to admire

in their work: not only their genetics but their clinical methodology is "state of the art". In contrast to many earlier investigations, they recognise that, in nosological research, one must use course (longitudinal, "lifetime") data, not just episode symptomatology. They employ a detailed abstract of all clinical records, the best source for longitudinal psychopathology. They use multiple raters, not only for diagnoses, but also for symptoms and course: the raters review a typed narrative synopsis, there is regular training and review, and generating a consensus reduces error and enables reliability to be measured for actual ratings, not borrowed from those made long ago by co-trained experts. Their rating schedules cover many aspects of the natural history, as well as key symptoms. They use polydiagnosis for diagnostic categories with disputed definitions. The huge series needed for genetic studies makes more data available for nosological analysis than was available for earlier studies.

I am also in complete agreement about the need to rethink the classification of the psychoses, and jettison the Kraepelinian framework. In their work on schizoaffective psychosis, I was disappointed that acute polymorphic (cycloid) psychosis was not included in the polydiagnostic analysis, but I appreciate that this is just another taxon to be melted down. The strategy is no longer to search for genes matched with conventional categories. Rather the whole genome is to be related, by a giant canonical correlation, to all that can be identified and measured in psychopathology. The nosology of the psychoses qualifies for Sir Keith Peters' "area of medicine in which everything that is worth knowing has yet to be discovered". This generation of researchers will make these discoveries and bury the 19th century dogmas.

I need to take issue with the statement that "studies of symptom profiles …have failed to find a clear discontinuity between …the two categories". The source of this conclusion is a paper written by Kendell in 1987 (1). Four years later, we published an analysis of "lifetime" psychopathology (10 years, 3 episodes on average) in more than 300 patients. We condensed the psychopathology by maximum likelihood factor analysis, and searched for discontinuities by canonical variate analysis, deriving functions in one randomly selected half, and testing them in the other. We used a variety of criterion groups and found that the bipolar group was always distinct (2). Thus, it is not the "two entities principle" that needs revision. One entity (bipolar disorder) is a concept "worth knowing", and deserves an ICD and DSM rubric of its own. This would include mania and schizo-affective mania; cyclothymia and hyperthymia; hypomania provoked by electroconvulsive therapy and drugs; some catatonia; some recurrent familial endogenous depression; seasonal affective disorder; puerperal, menstrual, steroid and postoperative psychoses; perhaps cycloid psychosis, and the rare but quintessential 48-hour cyclers. Its boundaries need clearer definition, and no doubt genetics will identify a variety of antecedents, but bipolarity must be a final common path, based on a localised or biochemically specific brain phenomenon. It is the other category, "schizophrenia", that needs rethinking.

The discovery of genes that increase the risk of both "schizophrenia" and bipolar disorders is challenging. There is probably a mismatch between the number of genes involved, and the limited keyboard of psychopathology and temporal patterns. Symptoms can be condensed to delusions, auditory hallucinations, passivity experiences, depression, states of excitement (not all of which are "manic") and various forms of defect and social handicap; the temporal patterns are equally restricted. The number of genes has yet to be determined, but, if it is large, discords will inevitably be struck. But what does this predict for future genetic classifications? If there are no genes of major effect, but, instead, there are many which make a small contribution, it will not be possible to link a disease picture to a gene. What, then, will be the basis of the classification? Bipolarity, and perhaps delusional disorders, will survive, each with complex antecedents and with their biological basis clarified. But it is impossible to guess what kind and what level of brain dysfunction will define the chronic polymorphic psychoses. Will it be an anatomical dysfunction, or pathology at the micro-anatomical level – such as ideo-motor feedback loops (3) – or perhaps specific anomalies in the neurotransmitters themselves? Once the pathogenesis has been clarified, how will this be translated into clinical diagnosis and therapeutics? I look forward with fascination to the evolution of research and ideas in this area.

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Physis does not take leaps, neither does Psyche

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Emil Kraepelin did not think dichotomously, but his epigones did. Kraepelin (1) tried to classify mental disorders systematically, bringing a more or

less unsystematic period to an end. The classification of the so-called endogenous psychoses in two categories, namely dementia praecox (schizophrenia) and manic-depressive insanity (mood disorders), was one of his attempts to systematization. But Kraepelin warned about dichotomous thinking, especially in one of his most important papers, published in 1920: "No experienced psychiatrist will deny that there is an alarmingly large number of cases in which, despite the most careful observation, it seems impossible to arrive at a reliable diagnosis. …We therefore will have to get used to the fact that the symptoms we have used so far are not sufficient to always reliably distinguish between manic-depressive insanity and schizophrenia, but that there are overlaps based on the origin of these symptoms from given preconditions." (2).

It is obvious that Kraepelin described "prototypes" rather than straight entities having impermeable borders. He accepted the idea of an "overlap of affective and schizophrenic spectra" (3) or a "psychotic continuum" (4), just to use the modern nomenclature. According to Kraepelin, the most important parameters for the distinction between schizophrenia and mood disorders are the course and the outcome. But even the research carried out by himself and his fellows and pupils showed that there is an "alarmingly large number" (2) of cases having the course and outcome of the opposite group. Moreover, when observing patients with a long-term course of more than one decade, we realize that schizophrenic, manic, melancholic, schizodepressive, and schizomanic episodes as well as any other psychotic episodes can change into one another (5,6).

The clinical research of the last 50 years (3) and the genetic research of the last decades (7,8) make obvious that there is no gap between the two prototypes "schizophrenia" and "mood disorders", but bridges and overlaps. Many efforts have been made to identify the overlaps. And so many concepts have been created, like those of schizoaffective disorders (9), bouffée délirante (10), cycloid psychoses (11,12), atypical psychoses (13), reactive psychoses (14), acute and transient psychotic disorders (6), etc. Irrespective of the reliability and validity of such concepts, all of them reflect clinical realities. A great number of patients all over the world suffer from these clinical realities, which are so difficult to classify. Exactly these clinical realities oblige us to think undogmatically and pragmatically.

That is what Craddock and Owen do in their paper. They consider the clinical, but also scientific, reality and try to eliminate the nosological nuisance. Their conclusion – that we now have a large body of research data which are inconsistent with the dichotomy and powerful tools allowing us to start to develop a biologically valid framework for classification which is likely to offer much improved clinical utility – is basically correct. But we also have to be aware – which is compatible with Craddock and Owen's conclusions, I think – that even the prototypes cannot be defined biologically and genetically as yet. The biological purity of the prototypes "schizophrenia" and "mood disorders" is not clear (15), but the limitations of monolithic categories and of current operational categorical approaches to diagnosis, as demonstrated by Craddock and Owen, are quite evident.

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When the paradigms languish

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Craddock and Owen start their cogent, thought-provoking analysis and bold vision of the future of psychiatric classification of major psychoses by inserting, not surprisingly, a Kuhnian reminder of the fate of theoretical constructs in science (1). It is, indeed, impressive that the "dichotomous view", underlining the apparent clinical independence between schizophrenia and bipolar disorders, has survived for almost a century. On the other hand, it seems evident that DSM-III and DSM-IV have contributed decisively to the advances that substantiate the authors' proposals. The progress in research, particularly on molecular genetics, has

now set the stage for the development of a new classification. It will have to offer clear validators that, according to the authors, "should allow us to identify the biological systems that are involved in disease pathogenesis".

The debates in the field of psychiatric diagnosis are among the most lively and productive, both theoretically and heuristically. It is rather predictable that they will continue for years and decades to come. The etiological insufficiencies are echoed by phenomenological insufficiencies. The categorical versus dimensional debate thrives in the realm of terminological ambiguities, gray areas in the clinical ambit, or the impact of demographic variables, developmental cycles, comorbidities, and cultural variations (2). Nowadays, with DSM-V in the horizon, there is no question that the dimensional view will gain ground, and that genetic concepts will have a stronger impact. Yet, issues such as a multiaxial approach, physical concomitants, disability, quality of life or sociocultural environment will have to be considered as well. Therefore, a purely neurobiological approach to psychiatric diagnosis would still be incomplete. The complexity of human beings suffering from mental illnesses surpasses the lofty aspirations of clinicians and researchers.

The authors suggest – and rightly so – that family, twin linkage and association studies have demonstrated the shortcomings of the dichotomous classification. Bipolar disorder and schizophrenia are but two components of a spectrum that apparently can be more carefully and elegantly delineated on the basis of genes, loci and haplotypes, coding specific susceptibilities, or explaining unique clinical characteristics. A big part of the argument is the existence of "mixed features" in many patients. Polypharmacy, in the treatment of not only major psychoses but practically all types of psychiatric conditions, is a contemporary phenomenon that deserves more studies. Craddock and Owen stop short of suggesting that practically all those conditions, and not only the "major" psychiatric disorders, should be included in a "mixed" space. And this is one of the most fascinating features of their work.

Schizoaffective disorder was the first American contribution to psychiatric nosology (3). It embodied a bold break from the hierarchical principle sponsored by Jaspers as a perpetuation of the Kraepelinian creed. In turn, the schizoaffective disorder is one vivid example of the trials and tribulations of psychiatric nosologies. Its existence as a valid diagnostic entity is questioned even by Craddock and Owen. They advocate a finer phenomenological approach to detect clinical nuances that can justify not only the use of the term, but the validity of the concept. This goes beyond the "mood incongruent delusions" model (4), the exclusion of depressive states in established schizophrenia, or the mood incongruence "explainable" in the context of a bipolar mood psychosis (5). Yet, some would still rather readily embrace the idea that schizoaffective disorder represents a "heterogeneous collection of interforms" (6). It may be wishful thinking to consider it as a "lifetime diagnosis", particularly considering its well-known instability (7).

We all want new psychiatric classifications possessing all the advantages that Craddock and Owen postulate. Presumably, they agree with the resurgence of concepts such as endophenotype (8). More explicitly, they agree with concepts such as spectrum, syndrome, or even dimensions. By the same token, they recognize the value of a descriptive-classificatory approach, as they used it to develop their Bipolar Affective Disorder Dimension Scale (BADDS). Would it not be more conceptually sound and clinically pragmatic to think of a behavioral continuum going from being "just different" to the most severe psychotic pictures? That is, essentially, a Popperian approach (9), opposite to Kuhn's life and death of paradigms. This eclectic view would tell us that, together with "unraveling the biological basis of disorders," we should accept, like Craddock and Owen state in their paper, that there may be "syndromes" with a discrete biological basis, but also conditions that are better conceptualized on a continuum.

Paradigms die, but they don't die acute deaths, they languish. It is rather a long-term, step-by-step process. Comprehensiveness, balance, and harmony are essential ingredients of a good psychiatric (and medical) diagnosis. Clinical usefulness requires not only biological validity. From Kandel (10), we have learned that genetic expressiveness can be changed by external factors, such as psychotherapy. From Eisenberg (11), we know that learning more about biology will hopefully allow more specific non-biological interventions. From Kendler (12), that there is something called "explanatory pluralism". And, from Popper, we know that a continuous search for the truth, away from dogmas, is the only guarantee of individual and collective freedom.

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Classifying psychosis: when is the time ripe for changes?

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The question about whether psychotic symptoms have an underlying taxonic (categorical) or dimensional structure is not an easy one. Even though diagnostic categories are widely used and form the basis of current classifications, it can be argued that a dimensional conceptualization of psychosis has more powerful empirical support, since there is evidence that symptom dimensions predict treatment response and outcome better than categorical diagnoses (1-3). However, even if the explanatory power of dimensions were better than what it is, there would still be a problem with their use in epidemiology, where the interest is in counting, and certainly in their use as robust phenotypes for biological studies. It would therefore seem that a parsimonious approach to the classification of psychosis is what can be supported by current evidence (4). Combining categorical classification with dimensional assessment offers the possibility of improving management of the individual patient, but the parsimony offered by categories is likely to be attractive for a long time to come.

Kraepelin's dichotomy was developed on the basis of what he saw among patients in asylum. Suggestions for revision of the dichotomy are being made on the basis of what we can see among clinical samples which are more varied and diverse than those seen by Kraepelin. Given the common occurrence of psychotic symptoms in the community, with several people experiencing them not making clinical contacts, can we be sure that whatever revision of our current classification we carry out will be applicable across the totality of the psychotic experience? Many previous studies of schizophrenia spectrum disorders (5-9) have proceeded from the standpoint of their symptoms being qualitatively and quantitatively different from common experience. If we conceive of the psychotic experience as a dimensional one or a continuum (10), then it may be necessary to measure the symptoms as a continuous phenomenon. That would require the study of a much broader profile of psychotic symptoms than are presented in clinical settings. The same sort of suggestions has often been made for dealing with the continuity controversy in depression (11).

Nevertheless, several of the properties of a classification system identified by Craddock and Owen are indeed desirable. For example, the development of clinical, research and primary care versions of ICD-10 would seem to have been done in order to make the classification flexible for different needs (12). The multiaxial format was an attempt to use multiple descriptors to capture the clinical status of the individual patient. However, the suggestion that "clinical utility requires biological validity" is probably a futuristic goal for psychiatry. If utility is defined mainly by what the clinician can do for the patient that waits for treatment in front of him, then it is difficult to see how current biological validations of the different types of schizophrenia spectrum can affect treatment choice. Isn't it the case that antipsychotics remain the treatment of choice for these disorders? And isn't it the case that current knowledge suggests that there are more similarities than differences between those medications, irrespective of the claims made by pharmaceutical companies? Indeed, the difficulty in following recent lines of evidence suggesting a re-classification of psychotic disorders, as competently reviewed by Craddock and Owen, is the fact that clinical utility, that is, the here-and-now management of patients, is not necessarily influenced by that evidence.

The controversy over whether to "lump" or to "split" is not going to be resolved until psychiatry has more than the blunt instruments it currently has to cut "nature at its joints" (13). Any classification that is based on aggregation of symptoms and signs without a validating set of biological features will be prone to arbitrary shifting of the "points of rarity", because such points will be defined in so many different ways by people with different needs for classification. Still, there is a recognized and subsisting need to derive phenotypes to aid in the search for susceptibility genes and in the identification of robust biological features that could help in identifying risk, targeting treatment, and offering more reliable prognosis. That process will be along the path of identifying specific neuropathologic processes underlying specific clusters of symptoms and signs. The process is likely to be greatly enhanced by the identification of endophenotypes which are likely to have better discriminating power than the phenotypes we currently employ.

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A dimensional and categorical architecture for the classification of psychotic disorders

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Craddock and Owen's insightful review convincingly summarizes the many problems that have arisen by using a dichotomous classification of the psychotic illness. They go beyond simply identifying problems by also proposing realistic solutions based on the existing evidence, and conclude that there is an urgent need to change the current approach. We would add that this change needs to be a radical one.

An important and rather controversial feature of all psychiatric disorders, including psychotic disorders, is whether they are dimensional or categorical in nature. May be that this is a false debate, in that every psychiatric disorder is both, and the main question is not whether diagnosis is categorical or dimensional, but whether it should be categorical or dimensional in order to yield the best clinical and research results (1). In fact, there exists compelling evidence that past and current categorical classifications of psychotic disorders are the result of arbitrary class distinctions being imposed along a continuum of risk factors, neurobiological mechanisms, frequency and severity of symptoms and outcome (2-5). Furthermore, both schizophrenic (6) and affective (7) symptoms do not have a taxonic structure, and studies specifically comparing the validity of dimensional and categorical models to classify psychotic disorders have consistently shown the superiority of the former in several domains (6-9).

Organizing a dimensional approach, however, is a complex task. A dimensional model to describe psychotic disorders needs to be developed on a systematic and stepwise basis. First and foremost, because dimensional models involve a continuum by definition, it is imperative to develop new scales that can assess the entire range of the dimensions of interest. Item selection is perhaps the most important decision in the whole process (10). Particular attention should be paid to including items in a comprehensive and balanced way. For example, there has been an excessive emphasis on the assessment of reality-distortion and negative symptoms to the detriment of other psychotic manifestations such as cycloid, affective, motor and behavioral features, and this bias should be avoided in future developments.

The second level is represented by the natural grouping of symptoms into dimensional syndromes. There is some consensus about the existence of at least six nuclear syndromes within the psychoses: reality distortion, disorganization, negative, catatonia, mania and depression. However, depending on the number and type of symptoms considered, the number and composition of the resulting dimensions will vary accordingly. Comprehensive rating scales with many fine-grained symptoms typically result in complex dimensional structures of the psychotic illness, which may be organized in a tiered hierarchical way, from lower-order dimensions that are closer to the symptoms to higher-order dimensions that are closer to the prototypical diagnostic categories of schizophrenia and manic-depressive illness (11). The question would arise as to the relative importance of the higher- vs. lower-order dimensions, in tandem with the caution that the future nosology should not become overly reductionistic. For example, although psychomotor poverty and asociality might be coherently integrated within a higher-order negative syndrome, differentiation may still be important, because these constructs provide more information about treatment planning regarding neurocognitive or psychosocial rehabilitation.

Given that classes and dimensions of psychotic disorders are highly dependent on the period considered to assess symptoms (9), there is also a need for taking into account a longitudinal perspective to rate dimensional syndromes. This can be done by making successive assessments across the different stages of the psychotic illness. Particularly relevant assessments would be those conducted at the height of the psychotic state and during a stabilization period, in order to maximize diagnostic and outcome value, respectively. Furthermore, a lifetime assessment should be ideally conducted for each dimension on the basis of the presence, frequency and severity of each constituting item. Of particular importance would be to rate the relationships between psychotic and mood symptoms by means of one or more scores reflecting their relative frequency, severity and temporal link, as exemplified by the Bipolar Affective Disorder Dimension Scale (12).

The third step consists of determining at what level dimensional syndromes are best incorporated into categorical diagnoses. The dimensional approach would help to generate the data needed to formulate a "bottom-up" structural organization for the diagnostic system,

in which categories of psychotic disorders can be derived from dimensions by setting some cutpoint to particular dimensions, or combination of them, forming a mixed categorical and dimensional nosology. In addiction or alternatively to this dimensional-based categorization of psychotic disorders, other mixed approaches could be employed. For example, the existing classifications (historical, empirical or consensus) may be combined with the multidimensional approach, to examine relationships between alternative nosologies and dimensions and their differential validity.

Adopting a dimensional formulation of nosology is not necessarily inconsistent with subsequently generating a typology or with existing alternative categorizations of psychotic disorders, including the Kreapelinian one. Interestingly, the highly differentiated Leonhard's nosology (13), by separating five big classes of psychotic disorders which in turn are further subdivided into subtypes, has provided us with a system that is very close to the dimensional approach, in that dimensions of psychopathology (negative, disorganization, catatonia, reality-distortion, affective) can be traced across the subtypes of the major classes.

Indeed, categorical and dimensional models are two sides of the same coin, and thus they are not incompatible but complementary. Their integration is of particular relevance to the complete understanding of psychotic disorders.

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Validity of the bereavement exclusion criterion for the diagnosis of major depressive episode

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Since the publication of DSM-III in 1980, the official position of American psychiatry has been that the presence of bereavement is an exclusion criterion for the diagnosis of a major depressive episode (MDE). However, the empirical validity of this exclusion has not been well established. As DSM-V is now being planned, it is timely to reexamine the bereavement exclusion, particularly in the light of new evidence since the last reviews of this subject. This paper evaluates the relative validity of two competing hypotheses: 1) the bereavement exclusion for the diagnosis of MDE is not valid because, using validating criteria, bereavement related depression (BRD) within the first two months after the death of a loved one resembles non-bereavement related depression (SMD); 2) the bereavement exclusion for the diagnosis of MDD is valid because, using validating criteria, BRD within the first two months after the death of a loved one does not resemble SMD. The prevailing evidence more strongly supports Hypothesis 1 than Hypothesis 2. Thus, the bereavement exclusion for the diagnosis of MDE may no longer be justified.

Key words: Major depression, bereavement, DSM-V, diagnostic validators

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Consider the following cases:

1) *Allen is a 49 year old man who has been sad and unhappy for the past 5 weeks. In addition, he has lost interest in normally enjoyable activities, sleeps four hours less than usual, has lost 10 pounds, has difficulty concentrating, limited energy, and no zest for life. These symptoms began within days of being fired from his job of 25 years due to down-sizing of the work force.*

2) *Beth is a 49 year old woman who has been sad and unhappy for the past five weeks. In addition, she has lost interest in normally enjoyable activities, sleeps four hours less than usual, has lost 10 pounds, has difficulty concentrating, limited energy, and no zest for life. These symptoms began within days of her husband filing for divorce.*

3) *Cole is a 49 year old man who has been sad and unhappy for the past five weeks. In addition, he has lost interest in normally enjoyable activities, sleeps four hours less than usual, has lost 10 pounds, has difficulty concentrating, limited energy, and no zest for life. These symptoms seemed to come out of the blue when everything was going well.*

4) *Diane is a 49 year old woman who has been sad and unhappy for the past five weeks. In addition, she has lost interest in normally enjoyable activities, sleeps four hours less than usual, has lost 10 pounds, has difficulty concentrating, limited energy, and no zest for life. These symptoms began within days of her husband's death from pancreatic cancer.*

Now consider the following question: which of the four individuals described above does not have a major depressive episode (MDE)? If you answered "Diane", you are correct according to the DSM-III, DSM-III-R, DSM-IV and DSM-IV-TR. But is Diane's depressive syndrome really different from the others? Is it less likely to be associated with impaired health or functioning, or with a chronic or recurrent course than the others? Is she less deserving of treatment or less likely to respond to standard treatments for MDE? This paper examines the available empirical data to help answer these important questions. The answers will help determine the validity of the DSM's nosological convention to isolate recent bereavement as the one life event that may exclude the diagnosis of MDE.

Since publication of DSM-III in 1980, the official position of American psychiatry has been that the presence of bereavement is an exclusion criterion for the diagnosis of MDE. However, the empirical validity of this exclusion has not been established. In addition, the other major psychiatric nosological system, the ICD-10, does not recognize this exclusion (2). According to the ICD-10, all of the cases described above would be diagnosed with MDE. As work toward DSM-V has begun, it is timely to re-examine the DSM's bereavement exclusion, particularly in the light of new evidence since the last reviews of this subject (3-5).

According to DSM-IV-TR, the "bereavement" exclusion criterion "can be used when a focus of attention or treatment is a *normal* reaction to the death of a loved one". The manual further states that a full depressive syndrome is a *normal* reaction to such a loss, with feelings of depression and such associated symptoms as poor appetite, weight loss and insomnia. To more carefully differentiate bereavement from MDE, the DSM-IV-TR identifies several features more characteristic of one than the other: 1) a bereaved individual typically regards the depressed mood as "normal", although the person may seek professional help for relief of associated symptoms such as insomnia or anorexia; 2) the diagnosis of MDE is generally not given

unless the symptoms are still present at least 2 months after the loss; and 3) MDE should be considered in the presence of certain symptoms that are not characteristic of a "normal" grief reaction, such as *guilt* about things other than actions taken or not taken by the survivor at the time of the death, *thoughts of death* other than the survivor feeling that he or she would be better off dead or should have died with the deceased person, morbid preoccupation with *worthlessness*, marked *psychomotor retardation*, prolonged and marked *functional impairment*, and *hallucinatory experiences* other than thinking that he or she hears the voice of, or transiently sees the image of, the deceased person.

We recently reviewed the literature bearing on the question "Does bereavement related depression (BRD) resemble standard, non-bereavement related depression (SMD)?". We concluded that the predominance of the published literature supported the similarity of BRD to SMD (1). Since most of the studies reviewed did not describe or follow individuals with BRD specifically within the first two months of bereavement (the period of time the DSM-IV-TR demarcates as excluding the diagnosis of MDE), we were unable to draw definitive conclusions about the validity of the bereavement exclusion. In the present paper, we focus on evaluating the validity of the bereavement exclusion by examining published data on predictors, course, clinical characteristics, consequences, biology and treatment of depression syndromes occurring within the first two months of bereavement. The central question addressed is: "Is BRD occurring within the first two months following the death of a loved one the same as or different from SMD on key validators?".

METHODS

We evaluated the relative validity of two competing hypotheses: 1) the bereavement exclusion for the diagnosis of MDE is not valid because, using validating criteria, BRD within the first two months after the death of a loved one resembles SMD; 2) the bereavement exclusion for the diagnosis of MDD is valid because, using validating criteria, BRD within the first two months after the death of a loved one does not resemble SMD.

We examined three classes of potential validators (6,7), with subclasses as follows: 1) antecedent validators (family studies; past history of MDE; demographic factors); 2) concurrent validators (health; social support; associated clinical features; biological variables); 3) predictive validators (diagnostic consistency over time; treatment outcome).

Articles were located with Medline searches up to December 2006, English language only. Exploded searches, using "grief or bereavement" and "depression" as key words, were employed. Bibliographies of located articles were searched for additional studies. Publications were selected if they included individuals diagnosed with MDE or meeting threshold levels for clinically significant depression based on validated depression interviews or scales. One or more systematic comparison groups were included in most of the selected studies. If the same sample was presented in more than one publication, only the most relevant or inclusive one was considered. The only exception to this general rule is in the categories of family and past history studies, where two different studies from Paula Clayton's series of widowhood investigations were included because of the different control groups used (8,9).

While it would have been ideal to conduct a formal meta-analysis of the literature, this was not feasible. Very few primary reports provided confidence intervals (or standard errors) of the estimates or primary data (i.e., contingency tables or correlations).

RESULTS

Antecedent validators

Two of the most consistently noted predictors of SMD are family history (10) and past personal history of SMD (11). The demographic factors most strongly associated with risk for SMD are female gender and young adult age (12).

Of the two studies that evaluated family history and past personal history of MDE, one supported Hypothesis 1 (that the bereavement exclusion is not valid because early BRD resembles SMD) (13), and one supported Hypothesis 2 (that the bereavement exclusion is valid because early BRD does not resemble SMD) (14).

One of four studies that evaluated gender supported Hypothesis 1 (15) and three did not (3,9,16). In contrast, each of the three studies that evaluated age provided support for Hypothesis 1 (3,5,15).

Overall, then, it does not appear that the antecedent validators of family and past personal histories of MDE or gender or age provide consistent evidence for or against the bereavement exclusion.

Concurrent validators

A number of environmental, clinical and biological features characterize SMD. Two important concurrent risk factors for SMD are poor physical health (17) and low social support (18). Some of the clinical features that are associated with SMD are characteristic symptoms (19), dysfunction and disability (20), and suicidality (21). Biological factors that often are seen in SMD include adrenocortical dysregulation (22), immune dysfunction (23) and sleep architecture disruption (24).

In studies assessing BRD within two months of the death of a loved one, BRD was associated with poor health (25,26) and low social support (25,27,28). In addition, compared to bereaved individuals without BRD, those with BRD had significantly more suicidal thoughts, feel-

ings of worthlessness and psychomotor disturbances, suggesting that these symptoms are not common manifestations of normal early bereavement (3,29-31). Instead, these symptoms are similar to those found in hospitalized patients with SMD (32). Thus, BRD resembles SMD more than it resembles "uncomplicated bereavement".

The four studies that evaluated biological parameters within the first two months of bereavement mostly supported the similarity of BRD with SMD. Two found immunologic changes in BRD to resemble those reported in SMD (33,34). Importantly, in the former study, immunologic changes were seen in bereaved women with BRD but not in a matched bereaved control group without MDE. One study in adults with BRD (33) and another in children with BRD (32) found non-suppression on the dexamethasone suppression test (DST) in recently bereaved individuals to correlate with depression symptom severity, while one study found DST non-suppression more associated with anxiety than with depressive symptoms in recently bereaved widows and widowers (35). In no case does it appear that DST non-suppression is commonly seen in uncomplicated bereavement.

Predictive validators

One of the hallmark characteristics of SMD is that it tends to be a chronic and/or recurrent illness (20,36-39). Another is that about 50-70% individuals with SMD respond to antidepressant medications (40,41).

Each of the studies that assessed BRD at or within two months of bereavement found that the rate of persistence of BRD was high and virtually identical to persistence rates of SMD (5,13,25,31,42-45). The only treatment study focusing exclusively on individuals who met criteria for MDE during the first two months of bereavement found a high rate of response to antidepressant medication, similar to that seen with SMD (46).

DISCUSSION

Normal grief is a highly dysphoric state, characterized by intense sadness, a variable mix of other negative emotions (e.g., anxiety, guilt, anger) and a tendency to turn inward and withdraw from the outside world. The fact that these symptoms resemble those of MDE has caused confusion regarding whether and when MDE should be diagnosed in a bereaved person. However, people experiencing normal grief, even when very intense, often have a full range of affect and are capable of warm joyous feelings, even if transient. Dysphoria often occurs in waves of "pangs of grief". Most do not meet criteria for MDE. These observations raise questions about the validity of excluding all people bereaved less than two months from the diagnosis of MDE. Furthermore, accumulating evidence suggests that early treatment of depression may be vitally important. For example, a recent study demonstrated that both lack of a partner and time in depression were significant predictors of suicidality among people meeting criteria for MDE (21). These findings, along with data indicating that early depression responds well to antidepressant medication, underscore the fact that the validity of the bereavement exclusion for the diagnosis of MDE is not an academic issue.

We reviewed studies assessing antecedent, concurrent and predictive validators. Although none of these studies was designed specifically to answer the question of whether the bereavement exclusion is valid, their data do at least address its validity empirically, albeit indirectly. We attempted to organize the available information to evaluate two competing hypotheses: Hypothesis 1 (that the bereavement exclusion is not valid because early BRD resembles SMD) and Hypothesis 2 (that the bereavement exclusion is valid because early BRD does not resemble SMD). Table 1 summarizes the results of this empirical literature review from the perspectives of these two hypotheses.

As might be expected given a range of methodological differences across the studies, results were not entirely consistent. However, a clear and relatively impressive trend is observed. Hypothesis 1 receives considerably more empirical support than Hypothesis 2. From the perspective of multiple validators, early BRD appears to be closely related to SMD. Like SMD, BRD is particularly frequent in bereaved individuals who are young, have past personal or family histories of SMD, and have poor social supports and compromised health. In addition, BRD has clinical characteristics reminiscent of SMD, including impaired psychosocial functioning, comorbidity with a number of anxiety disorders, and symptoms of worthlessness, psychomotor changes and suicidality. Moreover, the latter symptoms, mentioned in the DSM-IV-TR as unlikely to occur in nor-

Table 1 Summary of evidence for Hypothesis 1 (the bereavement exclusion is not valid because early BRD is similar to SMD) vs. Hypothesis 2 (the bereavement exclusion is valid because early BRD is not similar to SMD)

Antecedent validators	
Family history of MDE	±
Past history of MDE	±
Gender	±
Age	H1
Concurrent validators	
Health	H1
Social support	H1
Clinical features	H1
Immunologic studies	H1
Predictive validators	
Persistence over time	H1
Treatment	H1

BRD - bereavement related depression; SMD - non-bereavement related depression; MDE - major depressive episode; ± - data are inconclusive; H1 - data support Hypothesis 1

mal bereavement, can be long lasting and do not predict which individuals with BRD develop chronic or recurrent depression. BRD also has biological characteristics that reflect similarities with SMD: increased adrenocortical activity and impaired immune function. Like SMD, early BRD is common, long-lasting and recurrent. Finally, BRD appears to respond to antidepressant medication.

One can argue that early BRD is not the same as SMD in that it is often mild, may remit spontaneously, is not self-perceived as an illness, and shares many symptoms with uncomplicated bereavement. But those features often characterize community samples of depressed individuals, as well (37,39,47). The diagnosis of MDE may be difficult to make, especially soon after the death, as many symptoms of normal grief overlap with those of MDE. Nevertheless, all such diagnostic challenges are also present in other instances of MDE and should not mitigate diagnostic precision.

Why should bereavement be singled out as the only stressful life event that excludes the diagnosis of MDE when all other features are present? With all substantial stressors, including the death of a loved person, one may experience the onset or exacerbation of depression (47-50). Thus, a variety of other serious stressors, like divorce (51), illness and disability (52), to name a few, have been found to increase the risk for MDE in vulnerable or sensitive individuals. Kendler et al (53) reported high rates of the onset of MDE following the death of a close relative (OR=16.0), and comparably high rates for several other stressful life events, such as assault (OR=15.0), serious marital problems (OR=12.3) and divorce/break-up (OR=12.3). But in none of these cases, other than death of a loved one, does the presence of the stressor negate the diagnosis of MDE. If someone has met the criteria for MDE for more than two weeks after assault, divorce or myocardial infarct, we do not say that he is not depressed or call his depressive syndrome a "normal stress response"; instead, we make the diagnosis of MDE and consider the most appropriate treatment options (54,55). With one exception, a post-hoc study suggesting that divorce-related depression is similar to SMD but BRD is not (8), it is not clear why bereavement has become the one stressor that negates the diagnosis of MDE (17).

The major limitation of this paper is that so few studies examined depressive syndromes restricted to the first few months after bereavement, the period identified by the DSM to exclude the diagnosis of MDE. The "bereavement exclusion" was instituted to prevent clinicians from diagnosing MDE when the individual was instead experiencing a "normal" grief reaction. Recognizing that true MDE could be triggered by the loss of a loved one, guidelines were given to allow a MDE to be diagnosed following the loss of a loved one if certain features were present: duration of more than two months and/or the presence of specific symptoms characteristic of a true MDE (suicidal ideation other than wishes to join the lost loved one, morbid preoccupation with worthlessness, beyond remorse related to the relationship to the loved one, and psychomotor retardation). Thus, the ideal study to test our hypotheses would simultaneously compare: a) individuals meeting criteria for MDE beginning less than two months after the death of a loved one; b) early bereaved individuals who do not meet criteria for MDE and c) individuals with MDE of similar duration whose onset is unrelated to the death of a loved one. Unfortunately, we found no such studies in the literature. Early BRD, as conceptualized in this paper, is likely a mixture of cases including: those with "bereavement" as defined by the DSM-IV; those that start out with DSM-IV "bereavement" and evolve into true MDE; and others whose onset may precede the actual death of a loved one or be delayed for several months after the death. Although this paper suggests that bereavement-associated MDE is probably quite similar to MDE beginning in other contexts, definitive work clarifying the relationship between "normal grief" and MDE remains to be done.

Several additional caveats are important to note. First, the majority of studies reviewed here dealt with widowhood and included a preponderance of mid-life and older participants. Only two of the studies involved children (losing parents) or adolescents (losing friends to suicide). Data on individuals throughout the life span, experiencing bereavement following loss of different close relationships under a range of circumstances, are needed to fully examine our hypotheses. Second, the primary source of studies included in this paper was a Medline search followed by searching the bibliographies of identified manuscripts. Abstracts, posters, reviews and non-data based chapters were not included. This method may not have captured all relevant information. Third, some subjectivity may have influenced which studies were included and how some of the data have been interpreted. Few of the available studies used structured interviews, and even fewer incorporated the most appropriate control groups to answer our key questions. Only one small study of what might be the most interesting perspective – directly comparing MDE after bereavement with MDE after other kinds of severe events – was identified, and the results of that study support Hypothesis 2. Finally, few studies used control groups ideally suited to test our hypotheses: matched groups of persons with SMD or groups experiencing stressors other than bereavement. With these caveats in mind, our conclusions must be interpreted with caution.

In summary, this paper evaluated studies that bear on the validity of the "bereavement" exclusion for the diagnosis of MDE. Although the definitive study has yet to be completed, the preponderance of available data suggests that excluding recently bereaved individuals from the diagnosis of MDE, when all other symptomatic, duration and functional impairment criteria for MDE are met, may no longer be justified. Given the highly heterogeneous nature of both BRD and SMD, the most propitious conclusion may be that, on average, these two syndromes appear to be closely related. Neither is a true "natural kind", but, with

the very rough kind of syndromal data available, it looks as if these categories are both examples of the same broad syndrome.

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A prospective study of delayed sleep phase syndrome in patients with severe resistant obsessive-compulsive disorder

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There have been relatively few studies examining sleep in patients with obsessive-compulsive disorder (OCD) and these have produced contradictory findings. A recent retrospective study identified a possible association between OCD and a circadian rhythm sleep disorder known as delayed sleep phase syndrome (DSPS). Patients with this pattern of sleeping go to bed and get up much later than normal. They are unable to shift their sleep to an earlier time and, as a result, suffer considerable disruption to social and occupational functioning. In this study, we examined the sleep of patients with OCD prospectively. We aimed to establish the frequency of DSPS in this population and any associated clinical or demographic factors which might be implicated in its aetiology.

Key words: Obsessive-compulsive disorder, delayed sleep phase syndrome, circadian rhythms

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Obsessive-compulsive disorder (OCD) is a common, chronic disorder which results in marked distress and impairment of social and occupational functioning. Sleep disturbance often accompanies mental disorders, but there have been few studies of sleep disturbance in OCD. These have produced contradictory findings, with some reporting sleep disruption, and others a normal sleep pattern (1-3).

In a study by Bobdey et al (4), the sleep patterns of non-depressed OCD patients did not differ significantly from controls. There was, however, a small subgroup of patients who went to bed and arose much later than normal. This delayed pattern of sleeping, known as delayed sleep phase syndrome (DSPS), results in daytime sleepiness and major disruption of work and social functioning (5). It is the commonest form of circadian rhythm sleep disorders (6), which are defined as a mismatch between the usual daily schedule required by the individual's environment and his or her endogenous circadian sleep-wake system (7,8).

In a recent retrospective study, we identified a possible association between OCD and DSPS (9). The present study aims to examine sleep patterns in OCD prospectively, to establish the frequency of DSPS in this population, and to explore its clinical impact and any associated factors which might be implicated in its aetiology.

METHODS

The study was granted clinical approval by Wandsworth ethics committee, and all subjects gave informed consent. Consecutive admissions with a DSM-IV diagnosis of OCD to the inpatient unit of the Behavioural Cognitive Psychotherapy Unit at Springfield Hospital, London from August 1, 2003 to July 31, 2005 were invited to enter the study. This unit offers specialist treatment for patients with severe resistant OCD using predominantly psychological methods (10). To be accepted by the unit, patients must have already failed at least one trial of outpatient cognitive behavioural therapy (CBT) plus two trials of a serotonin reuptake inhibitor (clomipramine or a selective serotonin reuptake inhibitor, SSRI).

Within a week of admission, prior to commencing any treatment, subjects were assessed using a range of validated instruments. Symptoms and severity of the OCD were measured using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) checklist and severity scale (11), the Padua Inventory (12) and the Compulsion Activity Checklist (CAC) (13). Comorbid depression was assessed using the Montgomery-Asberg Depression Scale (MADRS) (14) and the Beck Depression Inventory (BDI) (15). The Sheehan Disability Scale (16), a self-rated instrument measuring impairment in work, family and social functioning during the past month, was used to assess the degree of disability. All subjects provided both retrospective and prospective data on their sleep using the sleep measures outlined below. In addition, the patients' sleep patterns were observed and recorded by nursing staff over five consecutive nights. Demographic data, alcohol and medication use were also recorded.

Patients with comorbid DSM-IV major depressive disorder, schizophrenia or serious physical illness were excluded, as these are known to interfere with sleep.

The sleep measures included the Pittsburgh Sleep Quality Inventory (PSQI, 17), the St. George's Hospital Medical School Insomnia Questionnaire (18), and objective assessment of sleep. The PSQI is a retrospective self-report questionnaire covering the previous month's sleep. It comprises nineteen self-rated items, which combine to seven component scores, measuring subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleeping medication and daytime dysfunction. The St.

George's Hospital Medical School Insomnia Questionnaire is a self-report questionnaire on the previous night's sleep, which patients were asked to complete over five consecutive nights, after a two-night "settling in" period. For the objective assessment of sleep, settling and rising times plus time asleep were recorded by nursing staff who checked the patients hourly over the same five-night period.

We used DSM-IV criteria for circadian rhythm sleep disorder, delayed sleep phase type (307.45), except item C, which excludes concurrent mental illness. In addition, we operationally defined DSPS as regularly falling asleep later than 1.00 am and awakening after 10.00 am. The choice of timing was based on previous research (19). Non-phase shift (NPS) was defined as falling asleep before midnight and awakening before 9.00 am. Subjects were categorised as DSPS or NPS on the basis of their sleep pattern over the five-night observation period and the history of usual sleep pattern obtained from the PSQI. Some patients who did not persistently display either DSPS or NPS patterns were excluded from the analysis.

Patients with DSPS were compared to their non-phase shifted counterparts on measures of illness severity, symptom profile and standardized parameters of sleep. Age, sex, ethnicity, duration of illness, concomitant medication, hypnotic use and alcohol or substance misuse were also compared. The Y-BOCS symptom checklist was used to establish if rituals occurred around bedtime. Patients with DSPS were asked to evaluate if their bedtime was delayed because of rituals, if they were happy with their sleep pattern and whether this pattern pre- or post-dated the OCD.

The two groups were compared with respect to age variables and standardized measures using unpaired t-tests, as despite the relatively small sample size the data did indicate a normal distribution. They were compared with respect to categorical variables using chi-squared tests.

RESULTS

Thirty-one out of 36 consecutive admissions consented to participate in the study. Of these, 13 fulfilled criteria for DSPS, 15 had a normal sleep phase and three fell into neither category and thus were not included in the analysis (Table 1). Compared to the NPS group, patients with DSPS were significantly more likely to be male, were significantly younger and had more severe OCD based on significantly higher scores on the Y-BOCS, Padua Inventory and CAC. DSPS patients were also more disabled than patients with a normal sleep phase based on significantly higher scores on the Sheehan's Disability Scale. Levels of depression based on scores on the MADRS and BDI were not significantly different between the two groups.

With regard to previous treatment, all patients had received at least one trial of outpatient CBT. All but one patient, who was in the DSPS group, had received two trials of clomipramine or an SSRI. This individual refused all medication based on obsessional fears. Augmentation with an antipsychotic had been given to seven patients with normal sleep phase and four with DSPS. Three patients in the NPS group had received augmentation with a mood stabilizer, two with sodium valproate and one with carbamazepine. One patient in the DSPS group had been given lithium augmentation. All four patients remained on mood stabilizers throughout the study. No patient had previously had psychosurgery.

Table 1 Characteristics of OCD patients with phase-shifted sleep compared to those with a normal sleep phase

	Phase-shifted (N=13)	Non-shifted (N=15)
Sex (% males)	76.9*	40.0
Ethnicity (% Caucasian)	92.3	86.7
Age (years, mean ± SD)	29.3 ± 12.2**	41.4 ± 13.4
Age at onset (years, mean ± SD)	16.4 ± 9.2	22.4 ± 10.8
Score on CAC (mean ± SD)	48.5 ± 19.4***	26.1 ± 16.7
Score on Padua Inventory (mean ± SD)	108.7 ± 30.8***	55.1 ± 25.4
Total score on Y-BOCS (mean ± SD)	32.4 ± 3.5***	24.3 ± 3.7
Score on BDI (mean ± SD)	25.4 ± 13.2	18.4 ± 10.7
Score on MADRS (mean ± SD)	14.2 ± 2.1	12.9 ± 2.7
Global score on PSQI (mean ± SD)	7.8 ± 2.6	6.0 ± 2.8
Global score on Sheehan Disability Scale (mean ± SD)	22.2 ± 2.0***	17.9 ± 4.0

*p<0.05; **p<0.02; ***p<0.01

OCD - obsessive-compulsive disorder; CAC - Compulsion Activity Checklist; Y-BOCS - Yale-Brown Obsessive Compulsive Scale; BDI - Beck Depression Inventory; MADRS - Montgomery-Asberg Depression Scale; PSQI - Pittsburgh Sleep Quality Inventory

At the time of the study, the majority of patients in both groups were taking an antidepressant, most commonly an SSRI. Prescribed hypnotics (temazepam 10 mg or zopiclone 3.5 mg) were being taken by two patients in the DSPS group. One patient was taking zopiclone 7.5 mg in the NPS group. Four patients in each group were also taking an antipsychotic (olanzapine, risperidone, sulpiride or quetiapine). Two patients with DSPS and one with normal sleep phase were on no medication. There was no difference in reported alcohol use between the two groups and no illicit drug use was reported.

Subjective sleep quality, based on scores on the PSQI, was worse for patients with phase-shifted sleep, but this failed to reach significance. There was also no significant difference between the two groups for subjective sleep latency, sleep duration, sleep efficiency, sleep disturbance and daytime dysfunction. Mean objective sleep latency, i.e., time taken to fall asleep as measured by nursing staff, was 33 minutes for patients with phase-shift compared to 43 minutes for their non-phase shifted counterparts. Again, this difference was not significant.

All but one patient from each group had rituals which occurred around bedtime. Of the patients with DSPS, none believed rituals to be the cause of their delayed sleep pattern. They also reported that they were unhappy with this pattern and that the onset of the shifted sleep phase was after the onset of OCD.

Of the three patients who had neither a normal or delayed sleep phase, two went to bed at a normal time (i.e., around 11.00 pm) but slept for a prolonged period (average 12 hours) and the third had no discernable pattern. Both patients with prolonged sleep described having a normal length but delayed sleep phase pattern in the past.

DISCUSSION

In this study, 42% of patients with severe resistant OCD had DSPS. Patients with DSPS were significantly more likely to be male, were younger and had more severe OCD than those with a normal sleep phase. Apart from the timing of sleep, there was no significant difference on any other parameter of sleep as measured by the PSQI or the objective nursing assessment. This concurs with Weitzman's (5) finding that sleep is essentially normal in DSPS, albeit at a later time. The delayed sleep phase was not due to patients taking longer to fall asleep, as there was no significant difference in sleep latency as measured by nursing staff. Those with DSPS were also no more likely to have bedtime rituals, and patients themselves denied this as the reason for going to bed late. Use of hypnotics and other medications was also similar between the two groups. All the patients with a phase-shifted sleep pattern expressed dissatisfaction with the timing of their sleep and were unable to explain why the shift had occurred. Patients with DSPS were significantly more disabled in their social and occupational functioning than those with a normal sleep. It is uncertain whether this is due to the shifted sleep pattern itself or reflects the fact that this group had more severe OCD.

DSPS is uncommon in the general adult population: estimates of 0.17-0.72% have been reported (20). However, a prevalence of 7.3% has been found among adolescents (7) and up to 10% of otherwise normal children (21). Onset of DSPS is usually in childhood or adolescence. No difference between the sexes has been found and a familial trait has been noted in 44% of patients (6).

There are relatively few studies examining DSPS in patients with mental disorders. An association between OCD and DSPS has not previously been reported. However, patients with OCD are notoriously secretive about their problems, which they often conceal for many years. An OCD diagnosis may thus often be missed. This study suggests that DSPS is a common problem in patients with chronic severe OCD. A retrospective study of similar OCD patients found a prevalence rate of 17% with DSPS (18).

In Weitzman's series (5) of 30 patients presenting to an insomnia clinic with DSPS, 17 were found to have no mental disorder; two had chronic schizophrenia; one manic-depressive disorder; four chronic depression and six personality disorder. In a study of 33 patients with DSPS referred to a sleep disorders clinic, Regestein and Monk (19) reported that 75% were, or had been, depressed. This assertion, however, was only based on current or previous antidepressant use. In 14 of 22 adolescents with DSPS, Thorpy et al (22) found symptoms of depression and suggested a primary psychiatric cause for the sleep disturbance. Weitzman (5) turns this suggestion around and claims psychological symptoms are not the cause, but a product of the problem, quoting the evidence that many DSPS patients show a dramatic improvement in psychological functioning after treatment of the sleep disorder. Other authors support the suggestion that DSPS precedes and may contribute to the development of mental disorder. Dagan et al (23,24) found a high incidence of personality disorder in patients with DSPS and suggested that a mismatch between the individual's biological clock and the environment leads to emotional and social problems. Patients in our study, however, reported that sleep phase shift developed after the onset of OCD.

From early childhood, the cycle of wakefulness and sleepiness is regulated by a circadian "clock" in the suprachiasmatic nucleus of the hypothalamus. A typical adult's endogenous sleep-wake cycle is slightly more than 24 hours and hence must be reset daily to keep it aligned with the external 24-hour day. The circadian clock is regulated by various cues, such as the light-dark cycle of day and night. Bright light presented early during the wake period tends to produce a phase advance of sleep but, if presented late, produces a phase delay. Social cues such as mealtimes and activity also play a role in the regulation of the sleep-wake cycle, either acting in conflict or helping to stabilize phase relationships. Interference with normal regulation can occur as a result of consumption of caffeine, alcohol or drugs.

The effect of light on the sleep-wake cycle is mediated via melatonin. The secretion of melatonin is stimulated by the dimming of light in the evening and is suppressed by bright light during the day. The evening rise in melatonin precedes the onset of sleepiness by approximately 1.5-2 hours (25). Serotonin is involved in the resetting process both indirectly via melatonin and through direct action on the suprachiasmatic nucleus. It follows that any medication acting on the serotonergic system could influence the sleep-wake cycle. In a study by Hermesh et al (26), 10 patients with OCD developed DSPS after starting fluvoxamine. All patients were taking only fluvoxamine and, in 9 out of 10, DSPS disappeared on withdrawal of the drug. The authors also noted that 7 out of 10 patients had taken fluoxetine and/or clomipramine in the past and had not developed this sleep disturbance. The authors concluded that the DSPS was attributable to fluvoxamine rather than OCD itself. A possible mechanism for the differential effect of fluvoxamine and fluoxetine is the different impact these drugs have on melatonin levels (26, 27). In our study, of the patients with DSPS, none was on fluvoxamine and just one was taking fluoxetine.

It has been suggested that people who develop DSPS do so because they are unable to adequately reset their biological clocks (5). One explanation for difficulty in producing the necessary phase advance of sleep is that indi-

viduals with DSPS have an unusually long endogenous circadian period. In studies of the spontaneous circadian rhythms of young adults living in temporal isolation, most developed sleep-wake cycles of around 25 hours, but in some subjects the cycle extended to up to 50 hours (19). Differences between individuals are partly accounted for by genotype. Several genes are involved in the regulation of human circadian rhythms, and familial forms of DSPS are associated with mutations in one or other of the clock genes. Age is also a factor: the endogenous cycle is longer in early life and tends to shorten in middle and old age. This may account for the overrepresentation of DSPS in adolescents and young adults (19) and for our finding of significantly younger age in patients with DSPS.

With an understanding of how the sleep-wake cycle is regulated, we can hypothesize about the mechanisms by which DSPS might develop in our patients with severe OCD. Lengthy or complex rituals can render patients housebound, resulting in inadequate exposure to morning light that in turn produces a phase delay of sleep. Social isolation, lack of activity and difficulty preparing regular meals, also common in severe OCD, would compound the problem by impeding the daily resetting of the biological clock. There is also some evidence for abnormalities in the circadian secretion of melatonin in patients with OCD. In a study of circadian rhythms in 13 medication-free OCD patients, Monteleone et al (28) found the night-time peak of melatonin levels was significantly lower than in controls and occurred 2 hours later. This difference was more pronounced in patients with more severe OCD based on higher Y-BOCS scores. A later peak melatonin time would typically produce a phase delay of sleep.

The importance of light and melatonin in the regulation of the sleep-wake cycle suggests a possible role for treatment with exogenous melatonin and/or light therapy in OCD patients with this disabling sleep disturbance. Further research examining biological processes in DSPS and OCD are warranted, which may lead to future pharmacological treatments for both conditions.

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Psychoactive substance use among medical students in a Nigerian university

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The study was aimed at determining the prevalence, pattern and factors associated with psychoactive substance use among medical students in the University of Ilorin, Nigeria. All consenting medical students were requested to compile a 22-item modified, pilot-tested semi-structured self-report questionnaire based on the World Health Organization's guidelines for student substance use survey. It was found that the most currently used substances were mild stimulants (33.3%), alcohol (13.6%), sedatives (7.3%) and tobacco (3.2%). Except for tobacco, the use of these substances seemed to be only instrumental. Substance use was directly associated with male gender, living alone, self-reported study difficulty, being a clinical student, and being aged 25 years or more. There was an inverse relationship of substance use with religiosity and good mental health.

Key words: Psychoactive substance use, medical students, Nigeria

(World Psychiatry 2007;6:48-50)

Substance use is becoming increasingly widespread in many African countries (1-3). In Nigeria, a substantial percentage of the national budgetary health allocation is utilized for treatment and rehabilitation of people with substance use problems (2). In this country, industrialization, urbanization and increased exposure to Western life style have contributed to the spreading of substance use, with alcohol and tobacco acting as "gateway drugs" to the use of other substances like cocaine, heroin, amphetamine, inhalants and hallucinogens (4). Factors like unhealthy family background, high social class, peer-group influence, desire to remain awake at night, pressure to succeed in academic work, self-reported poor mental health, and easy accessibility of drugs have also been implicated (4-7).

Several studies have reported alarming rates of substance abuse in student populations (2,8-13). The university experience is unique as it provides students with the first opportunity to be part of a larger group of peers without parental supervision. It also represents the perceived (by students) last period of freedom before taking on the responsibilities of adulthood. This makes them more vulnerable to try novel, previously prohibited and sometimes illicit experiences (14,15). Furthermore, it has been suspected that the use of substances like cannabis, heroin, cocaine and to some extent alcohol may have to do with the spreading of secret cults among university students (5,16).

In Nigeria, there are only a few published studies focusing on substance use among medical students (17-19), none of which has been carried out in the area covered by the present investigation.

METHODS

The study was carried out between February and March 2004 at the University of Ilorin, a federal institution which mainly admits students from its government designated catchment states (Kwara, Kogi, Benue and Niger), although students from other parts of the country may also be admitted. Following permission from the University authorities, the students were informed about the purpose of the study and also assured that their responses would be kept confidential. Those who were unwilling to partake were reassured of no negative consequences.

All consenting medical students were requested to compile a modified pilot-tested semi-structured self-report questionnaire based on World Health Organization's guidelines for student substance use survey (20). The instrument had been previously used and found reliable and valid among Nigerian students (21). The questionnaire consists of 22 items covering demographic characteristics (6 items), frequency and age of first use of 14 types of substances, including alcohol and tobacco (14 items), and the honesty with which the questions are answered (2 items). The modified semi-structured questionnaire was pilot-tested among 20 non-medical students from the same university and was found quite understandable and usable for this study.

Data was analysed using the Epi Info version 6.02 software. Frequency tables were generated and relevant cross tabulations made. Means were compared using Student's t-test, while proportions were compared using the chi-square test.

RESULTS

Of 1,420 registered medical students on campus during the study period, 961 (68%) participated in the survey. Questionnaires from 906 (94.3%) students were considered valid for analysis. Six hundred and twenty five respondents (69%) were males. Age ranged from 16 to 43 years (mean 22.4±3.2 years). Forty five percent of respondents were clinical students. More than half (52%) of the respondents were from families with 5-9 living children. About 26% of respondents reported to be the eldest child

of the family, and about 14% the last; less than 1% reported to be the only child of the family. The majority of respondents had parents belonging to a middle class occupational status, according to the International Labour Organization's classification (56.2% of fathers and 70.2% of mothers). About 25% of respondents' fathers had more than one wife. More than 32% of respondents lived alone or with friends while at school. Six hundred and seventy one (74.1%) respondents claimed they were very religious. About 68% of respondents were Christians, 32% were Moslems, and less than 1% practiced other religions.

Tobacco was the substance most heard of (99.4%), while anabolic steroids were the least heard of (48.9%). Almost all respondents had seen cigarettes and reported that they are freely available locally. The majority of respondents had heard of cannabis (92.5%), but only 37.6% of them had ever seen it; about half (48.8%) of the respondents were aware of its local availability. Of the substances ever being offered to respondents, mild stimulants ranked first, with about 78% respondents admitting that they had been offered in the past; alcohol ranked second (43.2%) and sedatives (sleeping tablets) ranked third (27.4%). Only few respondents (8.2%) admitted they had been offered cannabis in the past. Cocaine and heroin were the least offered psychoactive substances, with only 1.7% and 1.3%, respectively, admitting being offered.

Current use of one or more psychoactive substances was reported by 40.4% of all respondents, 35.6% of whom were using more than one substance. The overall lifetime prevalence of substance use was 78%. The most frequently used substances (both currently and lifetime) were mild stimulants, followed by alcohol, sedatives and tobacco (Table 1). No subject reported current use of cocaine or heroin. The vast majority of the users of mild stimulants, alcohol and sedatives (82.0%, 82.8% and 93.9%, respectively) reported using them only monthly. Of 29 tobacco users, 51.7% used it monthly, 31.0% weekly and 17.2% daily.

About 44% of male and 33% of female respondents reported current use and 69% of males and 31% of females reported lifetime use of one or more psychoactive substances. A significantly higher proportion of males than of females were current (17.6% vs. 4.7%, χ^2=26.06, p<0.001) or lifetime (42.8% vs. 27.0%, χ^2=19.84, p<0.001) users of alcohol; lifetime users of tobacco (14.3% vs. 2.1%, χ^2=28.91, p<0.001); lifetime users of cannabis (3.1% vs. 0.4%, χ^2=5.20, p=0.023); lifetime users of mild stimulants (70.1% vs. 62.7%, χ^2=4.53, p=0.033); and lifetime users of sedatives (29.1% vs. 22.6%, χ^2=3.77, p=0.052). Current use of cannabis and anabolic steroids was only reported among the males.

Table 1 Prevalence rates of psychoactive substance use

Substance	Current use (%)	Lifetime use (%)
Alcohol	122 (13.6)	341 (38.0)
Tobacco	29 (3.2)	95 (10.5)
Cannabis	5 (0.6)	20 (2.3)
Mild stimulants	300 (33.3)	612 (67.9)
Strong stimulants	6 (0.7)	19 (2.1)
Sedatives	66 (7.3)	244 (27.0)
Anabolic steroids	4 (0.4)	13 (1.4)
Cocaine	-	5 (0.6)
Heroin	-	6 (0.7)
Sniffing agents	6 (0.7)	26 (2.9)

Current use of alcohol was significantly associated with living alone during school period (χ^2=20.18, p<0.001), self-reported study difficulty (χ^2=10.39, p<0.001), being a clinical student (χ^2=9.28, p<0.01) and age 25 years or above (χ^2=4.75, p<0.05). Respondents with self-reported good mental health were less likely to be current users of alcohol (χ^2=7.29, p<0.05). Respondents who claimed they were very religious were less likely to be current users of alcohol (χ^2=76.01, p<0.001), tobacco (χ^2=90.64, p<0.001) and mild stimulants (χ^2=3.07, p<0.01).

There was a significant association between lifetime alcohol use and that of tobacco (χ^2=107.9, p<0.001), mild stimulants (χ^2=60.7, p<0.001), sedatives (χ^2=37.9, p<0.001), sniffing agents (χ^2=12.6, p<0.001) and cannabis (χ^2=10.28, p<0.001). Similarly, there was a significant association between lifetime use of tobacco and that of cannabis (χ^2=59.0, p<0.001), mild stimulants (χ^2=12.2, p<0.001), sedatives (χ^2=16.8, p<0.001), sniffing agents (χ^2=25.4, p<0.001), and anabolic steroids (χ^2=8.27, p<0.01). Lifetime cannabis use was significantly associated with lifetime use of stimulants (χ^2=11.39, p<0.01) and anabolic steroids (χ^2=17.47, p <0.01).

DISCUSSION

In our sample, the most currently used psychoactive substances were mild stimulants (33.3%), followed by alcohol (13.6%), sedatives (7.3%), and tobacco (3.2%). This seems to differ from an earlier study among medical students in Enugu, Nigeria, which found alcohol to be the most currently abused substance (18). The difference might be due to increased proliferation of religious groups/activities on campuses between 1988 and the time of study, national economic downturn, and discouragement of sales of alcohol on campus. Mild stimulants are largely socially tolerated, accessible and affordable, which may be responsible for their relatively higher prevalence in this study. They are mainly used while preparing for examinations (4,6).

The current use of sedatives ranked third, with about 7.3% of respondents being users. This is consistent with earlier reports among all undergraduates (medical and non-medical) of the same university (12). Less than 1% of respondents admitted current use of strong stimulants, cannabis, anabolic steroids and sniffing agents. No current use was reported of cocaine and heroin, which is in keeping with previous studies among medical students in Enugu (18) and Ogun state (19). This may be related to the good knowledge of the risks of cocaine and heroin use among the respondents, as perceived harmfulness had been shown to have an inverse relationship with substance use (22). Lifetime use of all substances was relatively low

when compared with previous studies among medical students within and outside the country (18,19,23).

The observation that significantly more males were users of alcohol and tobacco is in keeping with previous studies in Nigeria (17,24). That respondents living alone were more likely to use alcohol may be contrary to reports that substances are usually taken in company of peers: this pattern of alcohol use may represent a strategy for self-medication associated with social exposure anxiety rather than a ritualized social behaviour.

It is also noteworthy that clinical students were significantly more likely to be current users of alcohol. This finding, supporting previous reports of highest prevalence of substance use among clinical students in Enugu, Nigeria (18), may be explained by the fact that most clinical students stay alone and off-campus during school terms, due to insufficient accommodation on campus. In addition, previous studies have reported that, since clinical students tend to have more access to funds, they may be more predisposed to substance use (19).

The presence of self-reported study difficulty was found to be significantly associated with current use of alcohol, mild stimulants and sleeping tablets. This is in keeping with previous findings that students with study difficulty tend to use mild stimulants to remain awake for long periods (4,6,25). Such students may then need to use sleeping tablets to reverse or step down the effect of mild stimulants. Respondents with self-reported good mental health were also found to be less likely to use alcohol and sleeping tablets. This is in keeping with previous report of a significant association between current use of alcohol and self-reported poor mental health (25).

The finding that lifetime use of substances such as alcohol, tobacco and cannabis was significantly associated with the lifetime use of substances such as mild stimulants, sedatives and sniffing agents is in keeping with the "gateway theory" (4,26). We suggest that, where there is shortage of resources (fund, manpower, etc), efforts aimed at controlling substance use or abuse should be directed at "gateway drugs".

Planners of medical education should lay more emphasis on the risks of psychoactive substance use in medical curriculum right from preclinical schools, while governmental and non-governmental bodies should focus increased attention on medical students in campaigns against substance abuse. These efforts might increase the chance of producing more drug-free future doctors.

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Reform of mental health care in Serbia: ten steps plus one

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Disastrous events in the country and the region caused a 13.5% increase in the prevalence of mental and behavioral disorders in Serbia in the last few years, thus making them the second largest public health problem. Due to prolonged adversities, the health system has deteriorated and is facing specific challenges. However, the reform of mental health care has been initiated, with a lot of positive movements such as the preparation of a national policy for mental health care and a law for protection of mentally ill individuals. The transformation of mental health services has started, with an accent on community care, antistigma campaigns and continuing education. Based on an assessment carried out by the National Committee on Mental Health, service provision, number of professionals working in services, funding arrangements, pathways into care, user/carer involvement and other specific issues are reported.

Key words: Mental health care, service provision, community care, policy, destigmatization

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In the past decade, Serbia has been exposed to many stressors, such as civil war in the surroundings, United Nations (UN) sanctions which have lasted for 3.5 years, and a collapse of the former state. There are approximately 500,000 refugees and internally displaced persons in the country. In addition to this, many Serbian people live in either forced or voluntary exile: about 100,000 of them in European Union member states and about 200,000 in other countries.

The mental health care system has been seriously affected by the above events. The overall quality of services has deteriorated. On the other hand, the prevalence of mental disorders has increased by 13.5% from 1999 to 2002, so that they are now the second largest public health problem after cardiovascular diseases.

The incidence of stress-related disorders is high, but also that of depression, psychosomatic disorders, substance abuse and suicide, as well as that of burnout syndrome among physicians who shared adversities with their patients (1,2).

The economic situation of the country can be briefly described by the following indicators: the gross domestic product (GDP) per capita is US$ 1,400; the national debt is US$ 9 billion; the percentage of the GDP spent on health care is 5.1%. According to the UN data, 29.0% of the population was unemployed in 2002. Most likely the percentage is even higher this year, considering the serious transition problems that the country is facing. A lot of people lose their job in the prime of their lives; many are socially deprived and frequently lack the essential resources necessary to fulfill basic survival needs. Recently, the suicide rate increased among people who had lost their jobs.

Another issue is the lack of appropriate information of the general public and the widespread stigma related to mental disorders, as well as a lack of interest by the media in mental health issues, unless they serve their sensationalistic purposes.

PSYCHIATRIC SERVICES

There are 46 inpatient psychiatric institutions in Serbia (specialized hospitals, psychiatric institutes, psychiatric clinics, clinics for child and adolescent psychiatry, and psychiatric departments in general hospitals). Furthermore, there are 71 outpatient services in the municipal health centers. The entire mental health sector has a total of 6,247 beds at its disposal, 50% of which are in large psychiatric hospitals. There are 12.6 psychiatrists, 2.3 psychologists, 1.6 social workers and 21.6 nurses/technicians per 100,000 population. The total number of psychiatrists (neuropsychiatrists) in the country is 947. However, 336 psychiatrists work in the capital. In addition to that, most of the specialists in the provinces deal with neurological, in addition to psychiatric problems (3). General practitioners seldom treat patients with severe mental disorders. Only 39.5% of patients treated in psychiatric institutions have been seen by a general practitioner.

There are a lot of non-governmental organizations, both international and national, dealing mainly with refugees and internally displaced persons, gender problems, torture victims, domestic violence and human rights.

Health care is free of charge. The services are financed by the state through the Republic Office of Health Care. Every institution signs a one-year contract with the Office, and the remunerations are received monthly (for medication, medical supplies, food for the patients, energy consumption, employees' salaries, etc.). The funds depend on the number of beds and provided service. Preventive and psychotherapeutic activities are not funded.

TOWARDS SOLUTIONS

Since 2000, eight countries entered the Stability Pact for South-Eastern Europe (SEE): Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Macedonia (FYROM), Moldova,

Serbia and Montenegro (4). The international community decided to take a proactive attitude rather than intervening during crises only, and initiated the mental health project entitled "Enhancing social cohesion through strengthening community mental health services". The project started in 2002 and is supported by donor countries, such as Greece, Italy and Belgium. The World Health Organization (WHO) is closely involved in the project.

A National Committee for Mental Health was established in January 2003 by the Ministry of Health of the Republic of Serbia, which has become the research team of the SEE mental health project. The Committee prepared the national policy and action plan (3), and drafted the law on the protection of rights of persons with mental disorders. Both documents were discussed in public debates in 16 towns and reviewed by distinguished international experts. The national strategy was approved by the government in January 2007 and the law is expected to be approved by the parliament soon. The strategy is based on the WHO recommendations as stated in the World Health Report (5). It is in accordance with the WHO Helsinki Declaration and harmonized with the mental health policies of the region.

The national policy and action plan for the next decade has ten steps plus one and incorporates several domains: legislation and human rights; organization of services; prevention of mental disorders and mental health promotion; work force development; research; evaluation of services; improvement of quality; information system; intersectoral cooperation (partnership for mental health); advocacy and public representation; reform of psychiatry and psychiatrists (6). The reorganization of services, such as reducing the length of hospitalization especially in the old-fashioned psychiatric institutions, has started and some hospitals are being slowly downsized. Prevention of mental disorders and mental health promotion have been marginalized, but still there are many preventive programs, especially for vulnerable groups, such as refugees and torture victims (3).

There is only one pilot independent community mental health centre, which was opened last year in Nis, a university town in the South of Serbia, as part of the SEE mental health project. Residential facilities in the community are lacking. However, in most of the health centres throughout the country, there is a mental health team, integrated in primary care.

Mental health reform entails workforce development and continuing education of professionals, especially of general practitioners, which is what we have been doing for the last five years. We have developed packages for continuing education in mental health care of general practitioners, which were applied in Sarajevo and Belgrade, supported by the Norwegian Medical Association. However, it is not easy for primary care physicians to accept taking care of psychiatric patients, since they are already overburdened with a high daily number of patients.

The involvement of patients and their families in decision making process is not developed. However, in Belgrade there are clubs of treated alcoholics, the first one of which was established 44 years ago, which function quite well.

Multicentric studies that include several countries of the region are of particular importance, and might serve as tools for reconciliation. We are involved in two international multicentric studies of post-traumatic stress in refugees and in general population supported by the European Commission (7,8).

Destigmatization of psychiatric patients is a significant step in our reform of mental health care. This process already began two years ago, when we organized the campaign "United colours of soul". The campaign included psychiatrists, general practitioners, non-governmental organizations and patients. The "Wednesday culture circle" has been organized for our patients at the Institute of Mental Health in Belgrade as an important antistigma activity: once a month concerts and meetings with public figures are regularly organized for our inpatients.

The reform of psychiatric services and mental health care is not easy in countries facing social transition, due to many problems such as economic difficulties, as well as resistance and marginalization of psychiatry in the society (9). The implementation of the new national policy will take time. It needs competent workforce development, evaluation of services and interventions, as well as a long-term investment and commitment by government (10).

The reform implies transformation, and the transformation should start within our profession and ourselves, not from outside. Individualization and humanization of treatment could be reached even without huge resources. Integrative treatment, good clinical practice based on values and not only on evidence as demanded by modern science, is essential, and it does not need a lot of money. Psychiatrists and other mental health professionals should treat persons and not diseases, following the ancient Aristotle's medicine of personality and in accordance with the WPA Institutional Program on Psychiatry for the Person (11).

This is not easy and might sound unfeasible when low motivation of staff is prevailing due to apathy, chronic stress, poor conditions of work, and low salaries. Many professionals left the country and found shelter in developed countries; some have established non-governmental organizations or opened private services. In addition to that, many show resistance to changes and reform, which is a natural reaction.

Therefore, we believe that, in addition to transformation of services, the reform of mental health care requires another step – the reform of psychiatry and psychiatrists, which involves restoring the dignity of our noble discipline. Destigmatization of psychiatrists, who are often stigmatized together with their patients, is one of the important steps in this direction.

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Doping in sports and its spread to at-risk populations: an international review

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Doping is now a global problem that follows international sporting events worldwide. International sports federations, led by the International Olympic Committee, have for the past half century attempted to stop the spread of this problem, with little effect. It was expected that, with educational programs, testing, and supportive medical treatment, this substance-abusing behavior would decrease. Unfortunately, this has not been the case. In fact, new, more powerful and undetectable doping techniques and substances are now abused by professional athletes, while sophisticated networks of distribution have developed. Professional athletes are often the role models of adolescent and young adult populations, who often mimic their behaviors, including the abuse of drugs. This review of doping within international sports is to inform the international psychiatric community and addiction treatment professionals of the historical basis of doping in sport and its spread to vulnerable athletic and non-athletic populations.

Key words: Doping, sport, steroids, EPO, hGH, adolescents, performance enhancement

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The creed of the Olympics states: "The important thing in the games is not winning but taking part. The essential thing is not conquering, but fighting well". As noble a goal as this is, it has little to do with the reality of the modern sports world. Athletes are rewarded for winning at virtually every level of competition. Second place is viewed as the "first loser". A coach's job security is directly related to his team's success, not that they are simply "fighting well". Given this reality, it is not surprising that athletes and coaches will sacrifice and risk a great deal in order to obtain a competitive edge and enhance performance at all costs. Performance enhancement in olympic and professional sport has now become a medical, ethical, and legal problem for modern athletes and athletic organizations. This is primarily due to the amount of money associated with winning in today's sports industry. Multimillion dollar contracts, appearance fees, international endorsement and sports merchandising represent a billion dollar industry that offers today's athletes, their sponsors and entourage previously unheard of financial gains. When Sports Illustrated interviewed a cohort of elite olympic athletes, one of the questions was: "If you were given a performance enhancing substance and you would not be caught and win, would you take it?". 98% of the athletes responded "Yes". The more chilling question was: "If you were given a performance enhancing substance and you would not be caught, win all competitions for 5 years, then die, would you take it?". More than 50% said "Yes" (1).

Athletic performance enhancement can be gained using various diets, training routines and hard work. However, it can and has been achieved since ancient competitions by using a wide variety of physiological, mechanical and pharmacological doping techniques. As prize money and endorsement rewards increased, so did the science and abuse of performance-enhancing techniques. Today no sport is spared the cloud of cheating using illegal performance enhancement. Driven by the millions of dollars now routinely available for winning a sporting event, unethical pharmacists, medical professionals, trainers and sports organizations have worked secretly, and at times without their athletes' consent, to develop sophisticated doping programs where performance is optimized, often at the risk of the athletes' health. Now, these same doping programs are moving out of the professional sports market to our youth and other at-risk populations at alarming rates.

There are several hundred forms of known and potentially more unknown doping substances and techniques abused by professional athletes worldwide. This review will provide a summary of the history of doping in sport, and focus on the most commonly abused substances: anabolic androgenic steroids, human growth hormone (hGH) and erythropoietin (EPO).

HISTORICAL OVERVIEW OF DOPING

Performance-enhancing drugs are not unique to modern athletic competition. Mushrooms, plants and mixtures of wine and herbs were used by ancient Greek olympic athletes and Roman gladiators competing in Circus Maximus dating back to 776 BC. Various plants were used for their stimulant effects in speed and endurance events as well as to mask pain, allowing injured athletes to continue competing (2-4).

In the 1904 Olympics, marathon runner Thomas Hicks used a mixture of brandy and strychnine and nearly died.

Mixtures of strychnine, heroin, cocaine, and caffeine were used widely by athletes, and each coach or team developed its own unique secret formulae. This was common practice until heroin and cocaine became available only by prescription in the 1920s. During the 1930s, it was amphetamines that replaced strychnine as the stimulant of choice for athletes. In the 1950s, the Soviet Olympic team first used male hormones to increase strength and power. When the Berlin Wall fell, the East German government's program of performance enhancement by meticulous administration of steroids and other drugs to young athletes was exposed. These well-documented and controlled hormonal doping experiments on adolescent athletes by the East German Sports Medical Service yielded a crop of gold medalists (mostly young females as they responded more dramatically to male hormones). These athletes suffered severe medical abnormalities, including premature death (5).

The world became acutely aware of the extent and benefits of doping in sport when Ben Johnson's gold medal was stripped in the 1988 Seoul Olympics for using the steroid stanazalol. The International Olympic Committee (IOC) medical commission had established a list of prohibited substances in 1967 and introduced anti-doping testing of athletes in the 1972 Munich Games. It was clear at this point that doping did work and, if gone undetected, would win gold medals. East German scientists from the state-run doping programs at Kreischa and Leipzig, who were disgraced in their own country, where now in demand in Asia, former Soviet Block nations and sports organizations worldwide that wanted to promote their status. Doping became so prevalent in Olympic sport that some argued that all records should be discarded or put on hold until all forms of doping could be detected and stopped. Through the 1980s and 1990s, clandestine doping programs spread from sport to sport guided by modern, albeit unethical, pharmacists and sports medicine professionals. In 1999, the IOC organized a World Conference on Doping in Sport in response to a shocking discovery of massive amounts of performance enhancing drugs and paraphernalia by French police at the 1998 Tour de France. It was at this meeting that an independent global agency was founded, the World Anti-Doping Agency (WADA). Its mission was to work independently of the IOC, sports organizations and governments to lead the fight against doping in sport (6).

Despite years of aggressive anti-doping testing by international sports federations such as those for cycling, athletics and soccer, steroid abuse scandals involving high profile athletes continue to be front page news across the globe. Professional sports in the United States are not subject to extensive anti-doping programs, as players' unions and collective bargaining agreements prevented such extensive testing to be put into place. However, they did establish limited anti-doping programs, as the professional sports organizations recognized the potential of doping to harm athletes and their sport. In 1998, when Mark McGuire, an American baseball player, broke Roger Marris' home run record, it was revealed that he had been taking a supplement containing a precursor to nandrolone, a steroid. At that time Major League Baseball did not ban steroids and did not believe that steroids were a problem within the league. However, subsequent government investigations and former players revealed that steroid abuse was a problem in the League, which resulted in a limited steroid testing program.

In 2003, another significant event in the understanding of the institutional nature of doping occurred. A syringe was anonymously sent to a WADA-accredited laboratory in Los Angeles that contained tetrahydrogestrinone (THG), a "designer" steroid that was not known and not on the current WADA prohibited list, made specifically to avoid detection by modern anti-doping technologies. This led to a series of investigations resulting in the indictment and subsequent conviction of individuals running a performance-enhancing program for professional athletes at the BALCO pharmacy in San Francisco.

In May 2006, Spanish police arrested five people and seized a variety of banned performance-enhancing drugs and blood-doping supplies at a Madrid doping clinic. Here, professional athletes would receive medically-supervised injections of hormones and other performance-enhancing drug regimes. The 40-page police report included a clear paper trail of doping procedures on at least 50 professional cyclists. The report was given to the International Cycling Union, which led to the disqualification of 23 professional cyclists, virtually all the top contenders from the 2006 Tour de France. The final of the 2006 Tour was also tarnished, as the champion, Floyd Landis, was found to have a positive anti-doping test for steroids. Landis was stripped of the championship and discharged from his team. At this writing the result is being challenged by Landis and his legal and medical experts, claiming that the test was invalid since several errors were made in the collection, analysis and reporting of the results.

In a separate investigation in Paris in 2006, 23 individuals were sentenced to 4 years in jail for trafficking a cocktail of amphetamines and other performance-enhancing drugs known as "Belgium Pot" to professional cyclists. Making this problem even more complex, in the June 2006 issue of the Journal of Applied Physiology, an article from Stanford University reported that Viagra can be used to increase by approximately 45% the performance of cyclists in high altitudes, suggesting a whole new class of performance-enhancing drugs not restricted to cycling (7). In October of that same year, the cricket world was shocked to learn that two Pakistani fast bowlers, Shoaib Akhtar and Mohammad Asif, tested positive for the steroid nandrolone.

This brief overview suggests not only the historical and institutional nature of doping by athletes, but also the international development of a clandestine and sophisticated distribution network of black market doping programs that follows the modern sports industry. Today perform-

ance-enhancing programs and drugs are not the exclusive province of elite athletes, but have spread to health clubs, high schools and other at-risk populations, creating an over $1.4 billion US dollar industry that is growing daily as new compounds are synthesized and marketed (8).

KNOWN DOPING SUBSTANCES AND TECHNIQUES

There are literally hundreds of known doping substances and an equal number of designer, veterinary, and yet to be identified drugs and techniques abused in sports today. The 2006 WADA list of prohibited substances includes the following major categories: anabolic agents (i.e., exogenous anabolic androgenic steroids such as androstendiol, boldenose, closterbol and danazol; endogenous anabolic androgenic steroids such as dihydroxytestosterone and testosterone, and other anabolic agents such as clenbuterol and tibolone); hormones and related substances (i.e., EPO, hGH, insulin-like growth factors, mechno growth factors, gonadotropins, insulin and corticotrophins); beta-2 agonists (i.e., terbutaline, salbutamol, etc.); agents with anti-estrogenic activity (i.e., anastrozole, letrozole, clomiphene, etc.); diuretics (furosemide, hydrochlorothiazide, etc.) and other masking agents (such as epitestosterone, probenecid, plasma expanders, etc.); stimulants (amphetamines, ephedrine, cocaine, etc.); narcotics (morphine, oxycodone, etc.); cannabinoids (marijuana, hashish), and glucocorticosteroids (allowed externally but not internally). WADA also lists prohibited methods, including enhancement of oxygen transfer (blood doping, efaproxial, etc.), chemical and physical manipulation (tampering or substitution of sample) and gene doping. In addition, WADA prohibits alcohol and beta-blockers (in specific sports: archery, billiard, etc.) (6).

Testing for the above list of compounds is technically challenging, expensive and only performed by about 35 WADA-accredited laboratories worldwide. Steroids are still the most detected performance-enhancing drugs by WADA laboratories. However, because of the limitations of laboratory technology and sophistication of doping athletes to avoid detection, they may not be the most abused.

Anabolic androgenic steroids

Anabolic androgenic steroids are naturally occurring male hormones involved in a wide range of physiological functions. Simply referred to as "steroids", they fall into two categories: endogenous or naturally occurring, like testosterone, and exogenous or synthetic, like danazol.

In 1923 Bob Hoffman formed the famous York Barbell Company in the United States. A dominant figure in US weightlifting, he published the *Strength and Health* magazine and sold health and food supplements in his gym. As a weightlifting coach, his success led to him being named the head coach of the US Olympic weightlifting team. At the 1954 World Championships in Vienna, he met with a Soviet colleague who told him of a synthetic form of testosterone developed by the Nazis which produced dramatic improvements in strength and power. He and his colleagues contacted Ciba Pharmaceuticals in pursuit of synthetic testosterone. Ciba had conducted a number of studies on the use of synthetic testosterone in pain patients and the physically disabled. This resulted in the development of danazol, which rapidly became a doping substance abused by weightlifters (9).

Although steroids were first reported to be abused in Olympic sports in the 1950s, the abuse of steroids in young male non-Olympic athletes was not reported until the 1980s (10). As demand increased, trafficking steroids at schools and gyms became common and the use of steroids was seen in younger and younger populations (11). Steroid sources included doctors, trainers, friends, the black market and foreign suppliers. In the United States, the Anabolic Steroid Enforcement Act of 1990 brought anabolic steroids under the record-keeping, reporting, security, prescribing, import and controls of the Controlled Substances Act. All manufacturers and distributors of steroids were required to register with the Drug Enforcement Agency. Other countries have similar laws on the manufacture and dispensing of steroids. However, the amount of illegal steroids entering the United States and distributed to athletic and at-risk populations has increased dramatically. It is now estimated to be an over 100 million US dollar black market for steroids in the US alone, with more than 80% manufactured in Mexico. Projecting these figures internationally suggests that the illegal steroid market alone approaches a billion US dollars annually, clearly making it a public health concern, especially for at-risk groups.

The serious side effects of steroids described in the medical literature include liver function abnormalities, liver and kidney tumors, endocrine and reproductive dysfunctions, testicular atrophy, lipid and cardiac effects and psychiatric symptoms (12). These consequences are exaggerated with the common doping practices using ten times or more the recommended medical dose, and multiple drugs or "stacking", e.g., steroids and EPO or hGH. Added to this, a new problem has emerged with the manufacture of "counterfeit" drugs by unregulated pharmacies, which are tainted with impurities, contain no medication, or are potentially harmful. Now, more so than in the past, when an athlete buys performance-enhancing drugs from a friend or at the gym, he will never know exactly what is being bought or taken. Steroids are sold on the internet ranging in price from $50 to $200 per regime, depending upon the type of steroid and doping program selected. These black market steroids may or may not contain any medication at all or may contain harmful material. Testing for steroids in urine is available at a few commercial clinical laboratories in the United States and can be obtained in the price range of $100-$200/test, depending upon the number of steroids screened.

Human growth hormone (hGH and rhGH)

hGH is a naturally occurring hormone produced by the anterior pituitary gland and is one of the major hormones influencing growth and development. Harvey Cushing discovered the hormone in 1912 and isolated it from human and monkey cadaver brains in 1956. Two years later it was used to treat dwarfism in children by injection. The unfortunate development of Creutzfeldt-Jakob disease, a degenerative brain disorder, in boys who were treated with cadaver growth hormone led to the discontinuation of all products derived from the human pituitary gland. Because of this ban, the abuse of hGH was rare in sport until the middle to the end of the 1980s. In 1985 Genentech received approval from the US Food and Drug Administration (FDA) to market Protropin for children with growth hormone deficiency. This was the first recombinant DNA form of growth hormone (rhGH) that was safer than cadaver extracts used in the past. Recombinant DNA technology made the production of pharmaceutical grade growth hormone easier and cheaper. Genetically engineered rhGH is now marketed as Nutropin, Humatrope, Genotropin, Norditropin, Saizen, and Tev-Tropoin. Most human growth hormone used in medicine and diverted to sports doping is now obtained by recombinant technology, and is simply referred to as hGH (but it may also appear as rhGH or HGH). Unfortunately, cadaver extracts of pituitary hGH may still be in circulation. It has been reported that a Russian coach was arrested and, upon searching his apartment in Moscow, over 1000 cadaver pituitary glands were found preserved in a large container (13). Moreover, the problem of counterfeit drugs also exists with hGH: illegal pharmaceutical manufacturers are now flooding the black market with hGH vials of unknown quality and safety. It is estimated that an eight-week performance enhancement regime of pharmaceutical grade rhGH will cost about $2000, well out of the range of an adolescent and the majority of weekend athletes. However, the increased trafficking of low cost counterfeit rhGH will create interest and experimentation in these at-risk populations. hGH is marketed on the internet in many forms: pills, drops and aerosol formulations; most are ineffective and shams. The normal route of administration of hGH is injection, posing an additional health risk of infection from non-sterile counterfeit drugs and the risk of HIV and hepatitis transmission caused by shared needles.

Olympic, professional and weekend athletes abuse hGH because of unsubstantiated reports that it is as effective as anabolic steroids with fewer side effects. They often abuse hGH as a steroid substitute to prevent loss of muscle after discontinuing the use of steroids. Ben Johnson admitted to using hGH along with steroids during investigations after his disqualification in Seoul. According to some controlled scientific studies, hGH does not increase muscle strength. Nevertheless, the abuse of hGH in sports is escalating, with large caches of needles and vials of hGH being confiscated at sporting events worldwide. Six months prior to the 2000 Olympic Games, a pharmacy in Sydney was broken into and 1,575 multiple dose vials of hGH were taken while nothing else was touched. Also, on their way to Australia, the Chinese swimming team were detained, as needles, syringes, and vials of hGH were found by customs officials in their baggage.

Using hGH may lead to life-threatening health conditions, especially since some estimates report that athletes who use hGH to enhance performance are taking 10 times the therapeutic dosage. Some reported side effects of hGH are abnormal bone growth, hypertension, cardiovascular disease, cardiomyopathy, glucose intolerance, colonic polyps, decreased life span, and cancer (14).

Since hGH is a naturally-produced hormone and rhGH is similar in structure, testing for doping with rhGH has been a technical challenge only recently solved by WADA-certified laboratories. Routine blood tests for hGH available at clinical laboratories will not differentiate hGH from rhGH and are of no value in determining if an adolescent or weekend athlete is doping.

Erythropoietin (EPO)

EPO is a naturally occurring hormone produced by the kidney that stimulates red blood cell production in the bone marrow in response to low circulating oxygen levels. It was not until 1977 that it was identified and extracted from human urine. This was concurrent with the development of recombinant DNA technology, and in 1989 Epogen was released in the United States and approved for the treatment of anemia. Procrit was licensed in 1991 for the treatment of chemotherapy-induced anemia. European formulations include Aranesp, Eprex and NeoRecorman.

EPO abuse in sport was believed to start as soon as the drug was available as a replacement for the older, more complex and dangerous doping technique referred to as "blood doping". In this technique an athlete donates his own blood several months before a competition, stores it and transfuses it back into himself prior to competing. This technique is fraught with problems and health risk. EPO accomplishes this same effect by increasing red blood cells, which results in more oxygen in circulation. It was in 1998 at the Tour de France that French customs arrested Willy Voet, a physiotherapist of the Festina cycling team, for the illegal possession of needles, syringes and over 400 bottles containing EPO, hGH, steroids, amphetamines, narcotics and stimulants.

EPO used for medical treatments can cost thousands of US dollars a month and is administered by intravenous or subcutaneous injection. As with steroids and hGH, doping with EPO is often injected in supernormal doses that could cause increased blood viscosity, deep vein and coronary thromboses, cerebral thromboses, pulmonary embolism, arrhythmias, stroke and death. It has been estimated that 20 European cyclists have died since 1987 due to abuse of

EPO, making it one of the most deadly doping agents. The genetically engineered form of EPO is indistinguishable from naturally occurring EPO, making routine blood testing useless to determine if an athlete is doping. At the 2000 Olympic Games in Sydney, the Australian WADA-certified laboratory first launched a sophisticated anti-doping test for EPO that required both urine and a blood sample. Over 300 tests were performed for EPO for the first time in Olympic history and no positives were reported. This could be due to the fact that the technology for the test was new and questions still existed about the assay.

OTHER AT-RISK POPULATIONS FOR DOPING

Given the above history and current state of knowledge, it is not difficult to understand why there would be over a million abusers of steroids in the United States youth alone. Unlike professional athletes, these at-risk users will not have fame and fortune as a result of using steroids, only the side effects.

Pioneering studies in this area were done by Buckley et al in the early 1980s, when they interviewed 3403 male high school seniors nationwide (10). Their results reported in 1988 indicated that 6.6% of respondents had used steroids and more than two-thirds of the group started using steroids when they were 16 years old or younger. Twenty percent reported that health professionals were the primary source for obtaining steroids and 38% used injectable steroids. Pope et al studied 1,010 college men for use of steroids and also reported their findings in 1988 (15). The study found that only 2% of the respondents reported using steroids. The authors qualified their finding as potentially underestimating the true prevalence of steroid abuse. However, it is interesting to note that this study found that 25% of those reporting using steroids were not athletes. They abused steroids to improve personal appearance, a problem that continues today and is fueled by the media and "anti-aging" marketing. A review of published reports concluded that 3-12% of high school students used steroids, and of the group of abusers about half were adolescent females (16,17).

Contrary to popular belief and supported by Pope's early findings, steroid abuse is not exclusively related to performance enhancement. DuRant et al reported in 1993 that steroid abuse in ninth graders was associated with use of cocaine, injected drugs, alcohol, marijuana, cigarettes and smokeless tobacco (18). They then reviewed the 1991 Centers for Disease Control and Prevention Youth Risk Behavior Survey of over 12,272 male and female public and private high school students, and confirmed the earlier finding that there is an association between steroid abuse and multiple drug abuse. In a later review of the 1997 Centers for Disease Control and Prevention Youth Risk Behavior Survey of 16,262 high school students, Miller et al reported no significant correlation in male or female steroid-abusing high school students with physical activity, nor were athletic participation or strength conditioning alone associated with lifetime steroid abuse (19). Rather, they found that athletic participation was less of a factor than behavior problems such as substance abuse, fighting, binge drinking, tobacco use and high risk sexual behavior. They suggested steroid abuse may be part of a much larger syndrome of problem behaviors. In 2002, Irving et al confirmed Miller's report that physical activity was not associated with steroid abuse. This group shed light on the fact that male and female adolescent steroid abuse may also be associated with unhealthy attitudes and behaviors to lose, gain or control weight and body shape (11). Clancy and Yates reported that steroid abusers may have a unique set of clinical differences and are distinct from other drug abusers (20). Bahrke et al associated a number of personal high-risk behaviors and other factors with a partially developed profile of an adolescent anabolic steroid abuser (21).

What has become evident is that not only high school and weekend athletes are potential steroid abusers. Steroid abuse may also include a wider population of non-athletes who have behavioral problems and may experiment with these now easily available performance-enhancing drugs. Their motivation may not be athletic enhancement, but rather cosmetic and body shaping purposes. To maintain youthful appearances, weekend athletes may experiment with hormones encouraged by "anti-aging" marketing, while adolescent females desirous of the long, lean female media images of "adult women" may use steroids and hGH to reduce fat and increase muscle tone (22).

DISCUSSION

Modern sports and the media's misplaced fixation on fame, fortune and winning at all costs have unintentionally created a growing market for doping substances. These substances, once only abused by elite athletes, are clearly spreading into our schools and health clubs worldwide. They are being accepted by a whole new generation of young customers who see reports daily in the newspapers of sports icons accused of abusing drugs only to continue playing, breaking records and claiming fortunes. These same performance-enhancing drugs are also abused by adolescents and weekend athletes and non-athletes who have wider behavioral and health risk problems. In addition, these drugs are now being abused by male and female adolescents for cosmetic purposes in an attempt to achieve the "cut" and sexy look promoted by the media. Continuing educational programs developed for these at-risk populations by national olympic organizations and athletic federations are important first steps to curb these dangerous behaviors (23-25). Testing for performance-enhancing drugs in high schools as a means of early detection, intervention and prevention is now being launched in New Jersey, with other states following their lead. Medical profes-

sionals, teachers, coaches and sports organizations must all be made aware of this continuing problem in our adolescent and at-risk populations and contribute to its solution by open, honest discussion. Most importantly, professional athletes must serve as role models and spokesmen for drug-free sport and lifestyle. This position must be actively supported by the media, owners of teams and international sports federations by providing consistent leadership and advocacy of anti-doping programs in sport, regardless of costs and consequences. Accepting the magnitude of doping in at-risk populations and developing education, prevention and treatment programs is the only way we can prevent the continuing spread of the abuse of doping in sport and its spread into the most fragile groups in our society, our youth and at-risk populations.

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Letter to the Editor

We read with great interest the recent articles on the psychological consequences of natural disasters published in *World Psychiatry* (1,2).

Women and men may suffer from different negative health consequences following a disaster. Women are more likely to be exposed to severe threat or injuries. Their vulnerability is also increased by socially determined differences in roles and responsibilities, and inequalities in access to resources and decision-making power.

On 8 October, 2005, at 8:45 am, an earthquake of magnitude 7.6 on Richter Scale hit the northern part of Pakistan. It resulted in extensive damage to residential and other buildings. Many villages disappeared from the map of the world. There were more than 80,000 deaths and more than 90,000 got serious injuries.

We carried out a study on a group of 70 women from the mountains surrounding Balakot Valley, the epicenter of the earthquake, who had been provided shelter by a local non-governmental organization. The specific stressors identified in these women were illiteracy (82.9%), widowhood (92.0%), having lost their homes (70.0%), having lost their entire family (21.0%), caring for small children, unbearable heat in tin sheet shelters, minimal basic food, inadequate milk for children, away from relatives who themselves were struggling in the face of disastrous consequences of earthquake. The assessment was carried out eight months after the earthquake, using standardized screening instruments for traumatic stress in earthquake survivors (3).

A diagnosis of post-traumatic stress disorder (PTSD), based on a score above the cutoff point (>38) on the Traumatic Stress Symptom Checklist, was made in 94.3% of the women. Fear and avoidance were reported by 80.0% of the sample. On the Basoglu Depression Scale, 43.0% of women reported that they were extremely bothered and 38.0% reported that they were fairly bothered by depressive symptoms. Sixty-four percent of the women admitted the need for professional help.

These women not only need provision of mental health services, but also need long-term support for rehabilitation in the community. The government and other agencies need to consider the planning of long-term mental health interventions for these destitute women.

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The WPA International Congress "Treatments in Psychiatry: A New Update" (Florence, Italy, April 1-4, 2009)

Mario Maj
President of the Congress

The WPA International Congress "Treatments in Psychiatry: A New Update" will take place in Florence, Italy, from 1 to 4 April, 2009. It will be the follow-up to the 2004 WPA International Congress "Treatments in Psychiatry: An Update", which was the second most attended psychiatric congress worldwide in that year, with almost 7,000 participants. This time, more than 8,000 participants are expected. The Congress aims to provide a high-quality, comprehensive overview of all evidence-based treatments currently available for all mental disorders. Many of the most renowned experts in the various treatment areas will be among the speakers.

A first component of the Congress will be represented by the ESI[SM] Top-Cited Scientist Lectures, which will be delivered by the scientists who attracted the highest total citations to their papers in indexed journals of psychiatry and psychology over the past 10 years (according to the Essential Science Indicators[SM]). The list of these lectures is the following:

TL1. *R.C. Kessler* – The treatment gap in psychiatry
TL2. *K.S. Kendler* – Psychiatric genetics: a current perspective
TL3. *M. Rutter* – Environmentally mediated risks for psychopathology: research strategies and findings
TL4. *R.M. Murray* – The causes of schizophrenia: neurodevelopment and other risk factors
TL5. *J. Biederman* – Childhood antecedents of bipolar disorder: recognition and management
TL6. *S.V. Faraone* – Diagnosis and treatment of adult ADHD
TL7. *H.S. Akiskal* – Clinical management of bipolar disorder based on pathophysiologic understanding
TL8. *S.L. McElroy* – Management of binge eating disorder associated with obesity
TL9. *P.E. Keck* – What is a mood stabilizer?
TL10. *M.E. Thase* – Long-term management of depression: the role of pharmacotherapy and psychotherapies

A second component will consist of a series of Update Lectures, which will provide a comprehensive update on some of the most significant aspects of current treatments in psychiatry. The list of these lectures is the following:

UL1. *R.J. Baldessarini* – Disorders, syndromes, target symptoms: how do we choose medications?
UL2. *P. Fonagy* – Psychotherapies: what works for whom?
UL3. *G. Thornicroft* – Steps, challenges and mistakes to avoid in the development of community mental health care
UL4. *P.D. McGorry* – Early intervention in psychiatry
UL5. *M.F. Green* – Improving cognitive performance and real-world functioning in people with schizophrenia
UL6. *E. Vieta* – Evidence-based comprehensive management of bipolar disorder
UL7. *K. Fulford* – Evidence and values in psychiatric practice
UL8. *S.G. Resnick* – Recovery and positive psychology: an update
UL9. *R. Drake* – Management of patients with substance abuse and severe mental disorder
UL10. *M. Stone* – Comprehensive management of borderline personality disorder in ordinary clinical practice
UL11. *W.W. Fleischhacker* – Comparative efficacy, effectiveness and cost-effectiveness of antipsychotics in the treatment of schizophrenia
UL12. *P.J. Weiden* – The art and science of switching antipsychotic medications
UL13. *G.A. Fava* – Combined and sequential treatment strategies in depression and anxiety disorders
UL14. *K.A. Halmi* – Multimodal management of anorexia and bulimia nervosa

A further component will be represented by Update Symposia, focusing on specific treatment issues, with an active interaction between speakers and participants. The list of these symposia is the following:

US1. The future of psychotherapies for psychoses (*Chairperson*: *P. Bebbington*)
US2. Brain imaging in psychiatry: recent progress and clinical implications (*Chairperson*: *L. Farde*)
US3. Effectiveness and cost-effectiveness of pharmacological treatments in psychiatry: evidence from pragmatic trials (*Chairperson*: *J. Lieberman*)
US4. Endophenotypes in psychiatry (*Chairperson*: *D. Weinberger*)
US5. Advances in the management of treatment-resistant psychotic disorders (*Chairperson*: *H.-J. Möller*)
US6. Advances in the management of treatment-resistant depression (*Chairperson*: *S. Kasper*)
US7. Advances in the management of treatment-resistant bipolar disorder (*Chairperson*: *G.B. Cassano*)
US8. Patterns of collaboration between primary care and mental health services (*Chairperson*: *V. Patel*)
US9. Genomics and proteomics in psychiatry: an update (*Chairperson*: *N. Craddock*)
US10. Managing comorbidity of mental and physical illness (*Chairperson*: *N. Sartorius*)
US11. The evolving science and practice of psychosocial rehabilitation (*Chairperson: R. Warner*)
US12. ICD-11 and DSM-V: work in progress (*Chairperson*: *M. Maj*)
US13. Violence, trauma and victimization (*Chairperson*: *A. McFarlane*)
US14. Cognitive impairment: should it be part of the diagnostic criteria for

schizophrenia? (*Chairperson*: *R. Keefe*)
US15. Management of medically unexplained somatic symptoms (*Chairperson*: *O. Gureje*)
US16. Partnerships in mental health care (*Chairperson*: *B. Saraceno*)
US17. Suicide prevention: integration of public health and clinical actions (*Chairperson*: *Z. Rihmer*)
US18. Novel biological targets of pharmacological treatment in mental disorders (*Chairperson*: *G. Racagni*)
US19. Prevention and early intervention strategies in community mental health settings (*Chairperson*: *S. Saxena*)
US20. Anxiety disorders: from dimensions to targeted treatments (*Chairperson*: *J. Zohar*)
US21. Cultural issues in mental health care (*Chairperson*: *P. Ruiz*)
US22. Current management of mental disorders in old age (*Chairperson*: *C. Katona*)
US23. Prevention of substance abuse worldwide (*Chairperson*: *M.E. Medina-Mora*)
US24. Treatment advances in child psychiatry (*Chairperson*: *H. Remschmidt*)
US25. Gender-related issues in psychiatric treatments (*Chairperson*: *D. Stewart*)
US26. Mental health care in low-resource countries (*Chairperson*: *P. Deva*)

Moreover, the scientific programme will include Advanced Courses, Regular Symposia, Section and Zonal Symposia, Workshops, New Research Sessions, Poster Sessions, Satellite Symposia and other Sponsored Events.

For further information, please contact the Scientific Secretariat (secretariat@wpa2009florence.org) or visit the website of the Congress (www.wpa2009florence.org).

WPA Scientific Meetings as a vehicle for psychiatry leadership growth and development

PEDRO RUIZ
WPA Secretary for Meetings

When I became WPA Secretary for Meetings, in August 2002, I already had some experience in planning, developing, operating and evaluating WPA Scientific Meetings. I already had served for three years (1999-2002) in the WPA Operational Committee on Scientific Meetings. Based on these experiences, as well as the experiences acquired while I chaired the Scientific Committee of the American Psychiatric Association for two years in a row, I began my term with the knowledge of planning, designing, operating and evaluating scientific meetings following a traditional or classical approach. My main objective was to maximize the use of new knowledge resulting from research efforts, with the hope that this knowledge would be translated in better patient care throughout the world. I described this approach in a previous article written in this journal (1).

While this objective is a very important one and should continue to be used within the scope of WPA Scientific Meetings, I additionally realized that there were some additional problems in the field that could be addressed via the planning and implementation of classical or traditional WPA Scientific Meetings. I began to realize this situation during my first year (2002-2003) as WPA Secretary for Meetings. While talking with many of the delegates or participants, I observed that some of them had major constraints in using the knowledge acquired during their attendance to WPA Scientific Meetings. In general, these delegates or participants came from WPA Regions that had very limited psychiatrist manpower, such as Sub-Saharan Africa, South-East Asia, Eastern Europe, some countries from Latin America and also some countries from the Middle East. Additionally, many of these delegates or participants came from countries where the systems of mental health care were almost non-existent. Also, from countries where the socioeconomic situation was so bad that mental health services were quite fragmented, inefficient or of poor quality. When these situations were present, usually the socioeconomic capacity of the mental health patients from these countries was such that they could not afford paying for their psychiatric medications or services. Besides, if the psychiatric services were of such low quality, the mental health patients were inclined to reject or refuse seeking these services.

Upon reflecting for a while on an issue of such a high importance for many WPA Regions, I realized that what was needed was to design, implement and evaluate scientific meetings organized for the purposes of achieving leadership development and growth among the mental health specialists, primarily psychiatrists, in certain regions of the world where this type of activity was both needed and welcomed. Once this decision was made in my mind, I proceeded to find and/or select the appropriate venue for such a scientific meeting approach. Shortly after I made the decision, an opportunity aroused: I was talking with the WPA Zone Representative from Western and Central Asia (Zone 15), H. Chaudhry, who was very concerned with the lack of a network system among the WPA Member Societies from his Zone, as well as with the fragmentation of mental health services which existed in that Zone. Soon thereafter, he introduced me to a Pakistani psychiatrist, A. Javed, who was practicing in Birmingham, UK, and who also shared his views in this regard. After several weeks of planning and negotiating, I submitted a proposal to the WPA Executive Committee to hold a WPA Regional Meeting in Lahore, Pakistan on September 2004. Some resistance

evolved on the part of the Pakistan Psychiatric Society and also on the part of the WPA Executive Committee. I persisted with the plan and we held that WPA Scientific Meeting as planned. This WPA Regional Meeting was an outstanding success. Not only did the leadership of the WPA attend this meeting, but also the leadership of the UK Royal College of Psychiatrists. Also, about 20 psychiatric societies from the WPA Zone 15 and nearby WPA Zones were represented.

Concomitantly, I planned and negotiated with T. Udristoiu from Romania another WPA Regional Meeting for the purpose of leadership development in the area of Eastern Europe and the Balkans. After two or three months of hard work, we mastered all obstacles and resistance, and in December 2005 we held such a WPA Regional Meeting in Craiova, Romania, under the auspices of the Romanian Psychiatric Association. About 15-20 leaders from Eastern Europe and the Balkans attended this very successful scientific event. The outcome of this meeting was the Craiova Declaration and the organization of a WPA Affiliated Society, the Psychiatric Association for Eastern Europe and the Balkans.

Following these two successful WPA Regional Meetings focusing on leadership purposes, the field became wide open. Without difficulties, we conducted in March 2006 a WPA Regional Meeting in Havana, Cuba, in collaboration with the Cuban Psychiatric Society, and under the auspices of the WPA. C. Martinez Gomez from the Cuban Psychiatric Society was instrumental in making this scientific event a very successful one.

In January 2007, we also conducted another WPA Regional Meeting for leadership development purposes in Budapest, Hungary, in full partnership with the Hungarian Psychiatric Association and in full collaboration with its leaders A. Nemeth and F. Tury. This scientific meeting was also well attended and very successful.

Subsequently, we organized another WPA Regional Meeting in Nairobi, Kenya, in March 2007, in partnership with another WPA Affiliated Association, the African Association of Psychiatrists and Allied Professions, and with the full collaboration of F. Njenga, O. Gureje (Zone 13 WPA Zone Representative) and F. Kigozi (Zone 14 WPA Zone Representative).

As I look at the future of WPA Scientific Meetings, it is obvious to me that this new model of meetings is here to stay. As I also reflect back on my five years tenure as WPA Secretary for Meetings, I see this new model of WPA Scientific Meetings as my major contribution to world psychiatry, with focus where the needs are most acute and relevant. I hope that future WPA Secretaries for Meetings will not only retain this model of WPA Scientific Meetings, but will double their efforts in making them more successful, unique and effective.

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The new WPA Educational Program on Personality Disorders

Allan Tasman
WPA Secretary for Education

Few problems in the field of psychiatry are more complex to address than personality disorders. The dilemma starts, in fact, with trying to decide what is personality, and how we understand the influences that determine the mature personality. Contemporary views assume a complex interaction between genetic factors, with a present emphasis on temperament, and life experiences. While most believe that what will become the mature personality is, for most people, essentially determined by late adolescence, we know that a variety of factors can exert modifying effects throughout the life cycle. Thus, the conceptualization that personality reflects a matrix of qualities of character and patterns of reactivity has become generally accepted, though still difficult to quantify.

Moving from a general framework of understanding to a definition of specific aspects of personality has, therefore, been difficult. This leads to one of the most complex issues in our field, which is the differentiation of normal from abnormal personality. It is within this area of inquiry that the definition of personality disorders lies. Complicating this definition is the fact that not only genetic heritage and life experiences exert influences on personality development, but a wide range of cultural and ethnic variables also play a substantial, though thus far not quantifiable, role.

If, given all of the dilemmas enumerated above, we can arrive at a consensus about what is a personality disorder, this leads to the next dilemma of how we can best assess personality disorders. There is little agreement in this area, best conceptualized through the ongoing debate about whether the diagnosis of personality disorders should occur within a dimensional or categorical approach. A further complication arises due to the fact that advocates for either categorical or dimensional approaches have thus far not reached a consensus on the optimal approach even within their own domain of study.

Finally, how to treat something defined as a disorder, but which is embedded in the person of the individual seeking treatment, and thus not easily amenable to modification, remains one of the most complex clinical problems in the field of psychiatry. The conceptual and diagnostic dilemmas have made research in the area of treatment of personality disorders quite difficult, and comparisons across studies are difficult

to make. An additional level of complexity occurs because we well know that personality disorders and other psychiatric disorders often co-exist, but unfortunately not in ways which lead us to easy construction of frameworks for treatment planning. Molecular genetics holds out the promise that, if we identify genetic predispositions for a variety of psychiatric illnesses, we can use this knowledge to develop more effective treatments for them. Few would suggest a similar likely outcome in the area of personality disorders.

Our task, then, is to provide state-of-the-art information which can be used by clinicians at any stage of training in understanding personality disorders and developing a treatment plan. This monumental task has been handled with aplomb by the workgroup responsible for the preparation of the new WPA Educational Program on Personality Disorders, which is now available on the WPA website (www.wpanet.org).

Calling upon an outstanding group of experts in all aspects of personality studies around the globe, Eric Simonsen and colleagues have produced a work that is comprehensive, yet organized in a way that makes access to the material easy for individuals at any stage of their professional career. Their work is an excellent illustration of ways in which the WPA can productively collaborate with other international organizations, in this case the International Society on the Study of Personality Disorders (ISSPD).

The work is designed in three modules. Module 1 reviews the scholarly contributions to our understanding of personality and how we might classify personality and personality disorders, and summarizes a variety of therapeutic management approaches. Module 2 addresses each personality disorder and reviews diagnostic criteria, etiology, epidemiology, comorbidity, and treatment. Module 3 presents a "casebook" to illustrate the range of personality disorders. The vignettes are concise, yet illustrative, and accompanied by expert commentaries. Recommended readings and curricular recommendations also are included for all three modules.

While no one work can possibly encompass the entire field of personality disorders, and whether the reader is interested in a specific topic or an in-depth review, there is little question that time spent with this material will be universally felt to be very useful.

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