Keratoconus and Psychosis

TO THE EDITOR: We report on a patient with a provisional diagnosis of schizophreniform disorder and keratoconus, an eye disease associated with abnormal personality characteristics (1–3). Keratoconus is a bilateral degenerative disease of the cornea beginning in adolescence, with a prevalence of 1 in 2,000 (1). Ophthalmologists have long speculated about the existence of a "keratoconic personality," described as paranoid, anxious, compulsive, and somatically oriented (1).

Several studies have documented differences in personality characteristics when keratoconic patients are compared to healthy subjects, including higher scores on the schizophrenic subscale of the MMPI (3). It is unclear, however, whether this is independent of the psychological stress caused by chronic eye disease (1).

Mr. A was a 23-year-old man admitted to our inpatient psychiatric service after a 5-month history of delusions, including the belief that his corneal transplants were radio transmitters implanted in his head. He had been diagnosed with keratoconus at age 17 and underwent bilateral corneal transplantation at age 21. He had had one previous psychiatric hospitalization in his late teens after an incident in which he lost his temper, doused his car with gasoline, and set it afire. He also had a history of cocaine, amphetamine, and LSD abuse. His last use of LSD was 2 years before admission, and his last use of amphetamines and cocaine was a month before admission.

Mr. A had illogical speech, inappropriate affect, and frequent thought derailment. He felt that his problems were due to the "audiovisual stuff" implanted in his eyes. He also complained of the sensation of being burned by cigarettes on his legs and back. Mr. A was given olanzapine, 20 mg/day. Soon after admission he became less agitated, although his thoughts easily became derailed when he discussed his delusions, which persisted throughout his 3-week hospitalization.

Although the association in our patient may have been coincidental, we believe that the co-occurrence of psychosis and other syndromes is of value and may lead to the further elucidation of genetic correlates and pathophysiological processes, as in velocardiofacial syndrome and schizophrenia (4). Keratoconus is a genetic disease with familial clustering; like schizophrenia, it is thought to be a final common pathway stemming from multiple etiologies (5). Linkage studies have identified possible genetic loci, including loci mapped to chromosome 21. Although there is no evidence of linkage between keratoconus and schizophrenia, observations of the co-occurrence of these two syndromes might prompt further investigation.

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Obstetric Complications and Schizophrenia

TO THE EDITOR: In a meta-analysis of prospective population-based studies, Mary Cannon, M.D., Ph.D., M.R.C.Psych., et al. (1) reported that three classes of complications were "significantly associated with schizophrenia: 1) complications of pregnancy (bleeding, diabetes, rhesus incompatibility, pre-eclampsia); 2) abnormal fetal growth and development: (low birth weight, congenital malformations, reduced head circumference), and 3) complications of delivery (uterine atony, asphyxia, emergency Cesarean section)" (p. 1080). Thus, there are no less than 10 factors of etiological significance for schizophrenia. But how could so diverse a list of factors all have the same effect? If any one were relevant, why would it not stand out, given proband versus healthy comparison groups of 1,923 and 527,925 births, respectively?

The authors wrote, "The findings from the population-based studies were mostly negative and surprisingly contradictory" (p. 1082) and recognized that case-control studies are not free from potential bias. One such bias in a previous study (2) that suggested eclampsia was a risk factor was detected and scrupulously corrected with negative conclusions by Kendell et al. (3). Failure to document blindness in case selection (4) was a feature of a study that suggested that asphyxia was relevant (5): for this putative risk factor, the meta-analysis detected significant heterogeneity of outcome between studies ($Q=12.56$, $df=2$, $p=0.005$). Yet in the case of each of these factors, Dr. Cannon et al. drew positive conclusions, in some cases calling on evidence, e.g., the meta-analysis of Geddes and Lawrie (6), that included studies that are clearly vulnerable to biases, e.g., maternal recall, in addition to those of case-control studies. The authors discussed pathophysiological theories (1, pp. 1083–1087) for each class of agent as though a causal relationship were established, although for any given factor, the majority of the studies included adequate and sometimes detailed records of the event in question and failed to detect an association.

The authors' inability to draw the obvious conclusion that the etiology of psychosis is simply unrelated to complications of pregnancy and birth is reflected in the complaint that "lack of statistical power to measure small and interactive effects…are major problems with current approaches" (1, p. 1080). In their relentless pursuit of a positive conclusion, Dr. Cannon et al. demonstrated that meta-analysis can be deployed as a sophisticated instrument of data torture (7).

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Dr. Cannon and Colleagues Reply

TO THE EDITOR: It is difficult to know how to respond to the comments of Dr. Crow. Our object was not to torture the data but to present them so that readers could see the field for what it is—contradictory—and then to dissect the evidence and expose any truth within it. We were not searching for positive findings. Indeed, we would have been pleased had there been a definitive negative result, something that the correspondent appears to see clearly, despite a lack of evidence. At no stage did we suggest that a causal relationship has been established for any one obstetric risk factor. That would have been foolhardy.

We do not understand the objection to grouping risk factors into categories that may share the same underlying mechanism. This is a well-recognized and useful practice found even in the correspondent's own research (1, 2). Neither do we understand the objection to the concept of multiple risk factors. Current understanding of causal mechanisms precludes the view that there is a single causal factor for any complex disorder. The concept of multiple risk factors for schizophrenia obviously applies to the genome (3). Why not to the "envirome" as well?

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Psychotherapy Shattered?

TO THE EDITOR: The article by Glen O. Gabbard, M.D. (1), elicited in me a momentary shattering of a little of my great regard for Glen Gabbard, who is the Gibraltar of scholarly support for the efficacy of psychotherapy. I believe while sharing with the patient his own horror of the events on September 11, that he should have withheld his testimony of having been frightened. What his fright meant to him certainly was different from what his confession of fright meant to her. He could have still been human with her by acknowledging that the event was frightening by indicating, with his calm acceptance of his patient's panic, that the feelings could be mastered, as he himself had done. Menninger was right to say, "When in doubt, be human," but another wise teacher added, "When in doubt, stop talking."

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Dr. Gabbard Replies

TO THE EDITOR: In Dr. Metcalf's letter, he suggests that I should not have disclosed to my patient that the terrorist attacks of September 11 had frightened me. He advocates that I should have offered "calm acceptance of [my] patient's panic" and that I should have demonstrated that "the feelings could be mastered," as I myself had done. This type of Monday morning quarterbacking is a major problem in discussions of difficult situations in psychotherapy. Dr. Metcalf proposes an alternative that I should have considered to maintain "proper" technique. In fact, I was only a couple of hours away from the most horrific and unprecedented attack on American soil in U.S. history. With the fate of family members in New York City uncertain, I was completely unable to offer "calm acceptance," and I certainly had not mastered the feelings I was experiencing. The notion of making a choice of the sort advocated by Dr. Metcalf would have required Oscar-caliber acting ability that I, unfortunately, do not possess. My authentic response under the circumstances ultimately proved quite productive for the psychotherapy, despite its unorthodox and most assuredly human quality.

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Primary Care and Suicide Prevention

TO THE EDITOR: On the basis of their review's finding that 58% of elderly suicide victims had visited a primary care physician in the month before their death, Jason B. Luoma, M.A., et al. (1) concluded that primary care physicians "have the potential to significantly affect suicide rates for older adults" (p. 914). However, we must investigate further how competing demands and time limitations, combined with the relative rarity of suicide, affect primary care physicians' ability to lower suicide rates.

A general practitioner loses a patient to suicide, on average, once every 6.8 years (2). Consider, too, that primary care physicians spend an average of 18 to 22 minutes with each patient

(3). MacDonald (4) calculated that if a general practitioner loses one patient to suicide in 8 years, the physician "carried out 51,199 consultations with patients who are not about to kill themselves in those eight years." To further complicate matters, studies indicate a large proportion of suicide victims who visited their primary care physician before their death presented solely with somatic complaints (5, 6) and did not disclose suicidal intent (5), even on the day of their death.

To be sure, addressing patients' emotional problems, screening for depression, being alert to the somatization of psychiatric ills, probing for potential suicide risk, and making proper referrals to mental health providers are but a few simple ways that primary care physicians can work to prevent suicide. Just how much power, however, primary care physicians do in fact have (or not have) to prevent suicide remains to be determined with further research and understanding of the use of health services before suicide.

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Neurology, Psychiatry, and Neuroscience

TO THE EDITOR: In his overview (1), Joseph B. Martin, M.D., Ph.D., suggested that the integration of neurology and psychiatry should converge within a framework of modern neuroscience. This case is made well for diseases such as Alzheimer's and Tourette's, although these conditions have long been established at the interface of the two disciplines.

The greater challenge facing the successful integration of psychiatry and neurology is not those diseases in which structural pathology is known or strongly suspected but rather the neuroses. Dr. Martin referred to Charcot and Weir Mitchell as great neurological pioneers. Both also devoted substantial parts of their lives to the treatment of the neuroses of hysteria and neurasthenia, respectively. It was hysterical neurosis that provided the impetus for Freud's abandonment of the clinicopathological model, a proposal that drove the greatest schism between the disciplines of mind and brain.

If hysteria was the battlefield in which neurology and psychiatry became estranged, it can also provide the backdrop for their reconciliation. It remains the case that as many as one-third of the patients seen by clinical neurologists have symptoms that are better explained by neurosis than by neurological disease (2). Little attention is paid to these patients in textbooks of neurology or training programs. Although neuroscience is providing some understanding of these symptoms (3), they are illnesses with important psychological and social dimensions. The great psychiatrist Adolf Meyer, when shown the brain of a patient who had committed suicide at a postmortem examination, is reported to have challenged the pathologist to tell him by looking at the brain what was in his mind when he died. Important aspects of neurosis are likely to remain out of the reach of the scanner.

Dr. Martin called for "a seamless interconnection in training and in clinical practice" (1, p. 702). Will a greater shared understanding of neuroscience mean that psychiatry will simply follow neurology in abandoning the patients who fail to fit into a reductionist paradigm? A true convergence of the disciplines will also require neurology to regain its 19th century interest in the psychological and social factors that contribute to the neuroses. Like Adolf Meyer, we suspect that a focus on neuroscience alone will be inadequate for that task.

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TO THE EDITOR: I read with great interest the article by Dr. Martin concerning the future of psychiatry in relation to neurology and neuroscience. In the main, I agree with his analysis and with his predictions about the growing rapprochement among these three fields.

But the small differences are important, too, and I welcome this opportunity to make my own position clearer. The question comes down to this: if psychiatry and neurology have a strong common ground in brain science, then what distinguishes them? Why maintain any degree of separation between these two fields? What is the unique value of psychiatry? What does psychiatry bring to the table that neurology cannot be expected to provide?

The answer to all of these questions is psychiatry's concern with subjectivity: how do people think, how do people feel, and how can we relate their cognitive and affective experiences to brain activity? Great progress has been made in this brain/mind domain in the past decade, almost all of it by psychiatrists using neuroscience as a source of data and/or models.

My own field, sleep and dream research, affords abundant examples. One of the most striking and relevant recent discoveries is that the localization of stroke lesions can be correlated with changes in dreaming. Mark Solms (1), a psychoanalytically oriented neuropsychologist, studied 300 cases of stroke and found that dreaming is suppressed and/or permanently eliminated by stroke damage to the parietal operculum or to frontal white matter. Now, these findings could have

been made at any time, by any neurologist (including Sigmund Freud), but they were not. Why not? The reason is clear. Sleep and especially dreaming were not taken into account by neurology, but they were of great interest to psychiatry.

At exactly the same time that Solms was doing this work on brain-damage effects on dreaming, positron emission tomography (PET) imaging studies were revealing the intense activation of these same regions in REM sleep. The PET studies were performed by a neuroscientist (2), a neurologist (3), and a psychiatrist (4). This concatenation of expertise is exactly what Dr. Martin and I acknowledge and applaud. But who will carry this work forward by quantifying the subjective experience of dreaming so that its distinctive formal features can be linked to regional activation and inactivation of the brain?

My answer is that, because of their overriding interest in the mind, psychiatrists are likely to take the initiative in this effort. They may also, as Dr. Martin suggested, concern themselves more than neurologists with "functional" problems. I do not accept Dr. Martin's distinction between functional and structural. For me, all conditions of the mind are based upon both structural and functional properties of the brain. That is why I coined the term "dynamic neurology" in reformulating the important aspects of theory regarding sleep and dream dissociation and disorders of thought and mood.

To ignore the important and mainstream contributions of psychiatry to resolution of the mind/brain question is to seriously underrate psychiatry. When Jonathan Leonard and I decided to title our book *Out of Its Mind* (5), we meant to chastise psychiatry, as much as neurology, for failing to create a psychology that could match progress in neuroscience. That task must remain at the top of the scientific agenda until it is successfully undertaken.

Now more than ever we need a scientific psychiatry as well as a closer tie to neuroscience and neurology. Dr. Martin is in a position to help build such a psychiatry, and I am eager to know how he plans to do so.

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Neuropsychiatry

TO THE EDITOR: The editorial by Stuart C. Yudofsky, M.D., and Robert E. Hales, M.D. (1), was thoughtful and addressed a large conceptual issue in psychiatry. However, I am less sanguine about the rapprochement between neurology and psychiatry and their subsequent unification in neuropsychiatry. Psychiatry is the only medical specialty that concerns itself with the patient's subjective world and labors at the uncomfortable interface between mind and brain, attempting to straddle both. As frustrating as the results of the effort sometimes become, it is at the core of our professional identity.

Jaspers put it well when he outlined the coexisting scientific and subjective roles of the psychiatrist (2). I am concerned that our interest in the emotional lives of our patients and the meaning that they assign to their existence may be lost with a neuropsychiatric perspective, which in my experience tends to focus on more narrow data. Of course, if a new neuropsychiatry enlarges its purview, then we may be able to preserve the uniqueness of psychiatry and the unfolding of neuroscience. I am actually of the opinion that psychotherapy may be susceptible to reconceptualization in neurobiological terms, which would move toward synthesis and congruence with the scientific zeitgeist of the day.

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TO THE EDITOR: A perusal of any issue of the *Journal* can only lead to the conclusion that psychiatry and neuroscience are now well integrated. A recent overview by Joseph B. Martin, M.D., Ph.D. (1), and an editorial by Stuart C. Yudofsky, M.D., and Robert E. Hales, M.D., serve to remind us that this integration has not gone far enough, and, more important, clinical psychiatry and neurology have not breached the barriers between the two disciplines. In Australia, as in many other countries around the world, the teaching of the two disciplines remains frozen in tradition, with only weak attempts at integration. This is partly due to the comfort offered by continuity. It is also because clinicians are pragmatic by nature and will change their teaching and management practices only if they are convinced that real difference to the patient is in the offing.

Most clinicians would accept that there have been remarkable changes in neuroscientific understanding in recent decades. The change in psychiatric practice has, however, been brought about more by developments in diagnostic practice and psychopharmacology and a greater empiricism in clinical care. Specialist neurological training is still not necessary for good psychiatric practice. A considerable proportion of neurological practice does not require psychiatric knowledge. While integrated teaching of the neurosciences is laudable at the undergraduate level, specialists continue to usefully train in one discipline or the other. Given the increasing complexity of diagnostic and treatment practices, there appears to be no alternative but to continue with such a division so as not to dilute expertise.

There is, of course, a middle path, which Drs. Yudofsky and Hales suggested: that of clinical neuropsychiatry. This emerging discipline defines itself as "the application of neuroscientific principles to psychiatric practice," thereby claiming all of psychiatry (2). In reality, its practice relates to the disorders that require comfortable expertise in both psychiatry and neurology. The basic training can be in either discipline, with

advanced training in neuropsychiatry itself. The field defines itself by what it does—treats disorders such as dementia, epilepsy, traumatic brain injury, substance-related neuropsychiatric problems, movement disorders, secondary psychoses, etc. It obviates the need to indulge in boundary disputes. It recognizes the need for both psychiatry and neurology and the place for a hybrid discipline for neurological diseases that have psychiatric manifestations. The integration of neurology and psychiatry is thereby seeing the emergence of a new discipline rather than the disappearance of old ones. The leaders of this discipline must ensure that its training is robust and that its boundaries remain permeable in both directions.

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Drs. Yudofsky and Hales Reply

TO THE EDITOR: We appreciate the thoughtful responses by our colleagues, Drs. Chaitin and Sachdev, to our editorial. We believe that the "new neuropsychiatry," with the enlarged purview that "preserve[s] the uniqueness of psychiatry and the unfolding of neuroscience," welcomed by Dr. Chaitin has already emerged and has been gaining momentum over the past decade. In our opinion, the new neuropsychiatry currently is best manifested by the members and scientific programs of the vibrant and growing American Neuropsychiatric Association. Increasingly, the younger members of the American Neuropsychiatric Association are psychiatrists and neurologists who have had 2 years of subspecialty training in neuropsychiatry or behavioral neurology after completing their respective residencies. The clinical and research foci of most members of the American Neuropsychiatric Association coincide closely with the middle path of clinical neuropsychiatry advocated by Dr. Sachdev.

Although we are both active members and supporters of the American Neuropsychiatric Association, we do not believe that subspecialties of the disciplines of psychiatry and neurology best solve the pervasive problems of the two specialties that we raised in our editorial. Among the most serious of these deficiencies are 1) the continuing stigmatization of people conceptualized to have psychiatric disorders, 2) the failure of many psychiatrists to understand, diagnose, and treat the neurobiological aspects of patients with behavioral and emotional disorders, 3) the failure of many neurologists to understand and treat the psychosocial aspects of patients with sensory-motor disorders, and 4) the arbitrary and confusing cleavage of brain-based disorders into two disparate specialties.

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