Dr Marcia Angell and the Illusions of Anti-Psychiatry

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[Editor's Note: American College of Neuropsychopharmacology (ACNP) president Dr John Krystal recently produced a strong rebuttal to anti-psychiatry charges made by a prominent physician and former editor of The New England Journal of Medicine. Here, with permission, is Dr Krystal's recently published piece (see link)].

In a widely read 2-part article published in the New York Review of Books ("The Epidemic of Mental Illness: Why?" and "The Illusions of Psychiatry")

Dr Marcia Angell, a former editor of The New England Journal of Medicine, used the platform of books review to criticize the field of psychiatry for issues that have long been recognized within our field and are thus targeted by current research (see, for example, my ACNP President's Letter): psychiatric diagnoses are based on symptoms rather than pathophysiology, our treatments are insufficiently effective, newer medications have provided limited (if any) benefit over older medications, the pharmaceutical industry has had inappropriate relationships with individuals and organizations within our profession, there are problems in access to psychosocial treatments for psychiatric disorders, psychiatrists prescribe medications to treat symptoms rather than correcting known biological abnormalities, our understanding of the neurobiology of psychiatric symptoms is limited, and there are not objective biomarkers to guide diagnosis or to match individual patients with particular drugs. Vigorous responses to Dr Angell's articles were offered, albeit largely rejected by her, making the points that clinical data provide empirical support for the validity of symptom-based diagnoses, psychiatry is hardly unique in prescribing medications based on symptoms rather than pathophysiology, and while psychiatric pharmacotherapies have limitations, they are not very different in relative efficacy from current treatments for many chronic medical disorders.1,2 (See also "Exchange," New York Review of Books August 18, 2011)

What was strikingly missing in the responses to Angell's article was a response to her direct and implied criticism not only of the underlying science of psychiatry, but of the reality of the distress and disability of psychiatric patients. These are critical issues because (1) the ability of psychiatry to effectively treat its patients now and in the future depends on the quality and integrity of its science, and (2) the doubt cast on the seriousness of the distress and impairments of patients seeking psychiatric treatments feeds into the residual ignorance and stigma that continue to be so harmful to patients. As president of the ACNP, I thought it was important to respond to her criticisms. Psychiatry is engaged in a challenging battle to understand the most complex aspects of human biology and behavior and to reduce the burden arising from psychiatric disorders. It is rather shocking for a former editor of a leading medical journal to fail to recognize the challenges of brain science, the progress that has been made, and the enormous and well-documented remaining unmet medical need.3 By demeaning the real-world challenges faced by psychiatrists and their patients, selectively ignoring scientific progress that challenges her assertions, and presenting tendentious and highly selected information about the status of psychiatric neuroscience, Angell misuses her standing as a former editor of The New England Journal of Medicine and the pulpit of the New York Review of Books to further stigmatize the field of psychiatry and patients with mental disorders.

1. Angell mistakenly implies that psychiatry could abandon its diagnostic system without harming patients. She begins the first part of her essay with, "Americans are in the midst of a raging epidemic of mental illness . . . are we simply expanding the criteria for mental illness so that nearly everyone has one?" She does not consider the possibility that reduction in stigmatization of people carrying psychiatric diagnoses and improved treatment may explain changing patterns of treatment seeking. While she does not draw conclusions, the review is replete with innuendo. She suggests, for example, that the medicalization of psychiatry and its
Angell seems to assume that it is a mystery to the field that the DSM system is flawed. Indeed it is widely recognized that this is a provisional diagnostic system pending progress in better understanding uniquely human disorders of our most complex organ. That said, the processes of review and revision of the DSM system involve extensive reliance on epidemiology, family studies, twin and increasingly other genetic studies, that can usefully inform a descriptive diagnostic system. It is easy to criticize a descriptive system, but given the current early state of brain science, it is not very easy to suggest a better approach. Abandoning the DSM system at present would undercut diagnosis, treatment, and communication with patients and families. In my opinion, it is a mistake to suggest, even through innuendo, that society could afford for psychiatry to abandon DSM before science is at an advanced enough stage to deliver a superior alternative.

2. **Angell uses a biased argument in the attempt to label antidepressants as both ineffective and harmful, without consideration of the impact of these assertions on patients who currently benefit from these medications or who might need these medications in the future.** It is widely known that antidepressant medications are variably effective in people with depression. The studies by Turner et al.⁴ and Kirsch et al.⁵ raise important questions about who benefits from antidepressant treatment and to what degree they benefit. But these studies also have limitations, critiqued elsewhere⁶ (See also "Exchange," New York Review of Books August 18, 2011). Other studies provide evidence of antidepressant efficacy in the majority of patients,⁷ even those patients with relatively mild depression.⁸ In one of these studies,⁷ non-responders to antidepressant medication improved less than patients treated with placebo, suggesting that ongoing monitoring of treatment response may be a critical step for improving outcomes and limiting negative effects of treatment. Additional signals of antidepressant effectiveness also emerge from health services research. For example, one randomized clinical trial suggests that antidepressant treatment is more cost-effective than either an evidence-based psychotherapy or placebo.⁹ The cost-effectiveness of antidepressant treatment, generally embedded within psychosocial treatment,¹⁰ is further supported by evidence that optimal antidepressant treatment is more costly but more cost-effective than antidepressant treatment marred by suboptimal dosing, non-adherence to prescribed medication, or medication discontinuation.¹¹-¹³ Also, although the newer antidepressant medications offer little if any evidence of enhanced efficacy over older medications, improved medication adherence with the new medications may make them more cost-effective.¹⁴ Clinicians face enormous challenges in weighing the risks and benefits of pharmacotherapy with each patient, educating patients about these risks and benefits, and monitoring these risks and benefits on an ongoing basis during treatment. Faced with a conflicting literature and the responsibility to mobilize all available resources in the effort to alleviate suffering, physicians do not have the luxury of abandoning current antidepressants while waiting for more effective alternatives. As with DSM, in my opinion it is a mistake, even through innuendo, to suggest that this might be possible. To quote Dr Peter Kramer on this issue, "It is dangerous for the press to hammer away at the theme that antidepressants are placebos. They're not. To give the impression that they are is to cause needless suffering" (See: New York Times, July 9, 2011).

Similarly, Angell writes about medication effects on the brain in a pejorative and misleading manner: "After several weeks on psychoactive drugs, the brain's compensatory efforts begin to fail, and side effects emerge that reflect the mechanism of action of the drugs. For example, the SSRIs may cause episodes of mania, because of the excess of serotonin. Antipsychotics cause side effects that resemble Parkinson's disease, because of the depletion of dopamine (which is also depleted in Parkinson's disease)" (See: The Epidemic of Mental Illness: Why?). She fails to be clear that antidepressant medications do not cause bipolar disorder and it is not at all clear that antidepressants have a causal effect in most "switches" in mood among bipolar patients. Moreover, parkinsonian side effects of antipsychotic medications are avoidable in most patients, even when treated with older antipsychotic medications.¹⁵-¹⁷

3. **Angell employs information selectively and inappropriately to attack the lack of credibility of psychiatric diagnoses and psychiatric treatments.** Dr Angell highlights widely acknowledged limitations in our symptom-based diagnostic system, but she fails to celebrate the substantial efforts led by Dr Thomas Insel and NIMH to advance psychiatry toward pathophysiology-based diagnoses, the Research Domain Criteria.¹⁸ She cites neuroimaging evidence to support her hypothesis that psychiatric medications are harmful to the brain. However, she does not cite evidence that antidepressants and lithium protect against or reverse the ill effect of stress¹⁹-²⁶ and other neurotoxic insults²⁷-²⁹ in animal studies. She quotes Dr Steven Hyman as saying that long-term treatment with psychoactive substances produce "substantial and long-lasting alterations in neural function . . . the brain . . . begins to function in a manner 'qualitatively as well as quantitatively different from the normal state'" (See: The Epidemic of Mental Illness: Why?). But she fails to note that this partial quotation, taken out of context, omits the critical aspect of Dr Hyman's message. In a personal communication to me, Dr Hyman noted that the lasting alterations of which he frequently speaks, i.e., brain alterations and neurotoxic insults, are not the significant clinical findings. Instead,
Rather, antidepressant psychotherapies, pharmacotherapies, and brain stimulation treatments have converging effects on brain circuit function, and generally work more effectively in combination, something that is recognized in most modern treatment guidelines.

Angell condemns psychiatric neuroscience for espousing a theory that it never fully accepted and certainly abandoned more than 2 decades ago. The monoamine hypotheses of depression were introduced in the 1960s and 1970s in the context of the first biological studies in patients, conducted largely by founding members of the ACNP. It was doubted almost from its origin, based on the temporal dissociation between the rise in monoamine levels produced by antidepressants and the emergence of their therapeutic effects. It was fully abandoned by the 1990s, when it was evident that depression had a complex biology that went beyond global monoamine deficits. She does not refer to the past 30 years of research on the neurobiology of depression that introduced fundamentally new mechanistic hypotheses.

While it is fair to criticize simplistic phrases like "low serotonin" and "chemical imbalance" used in advertising or by some physician communications to patients, all fields of medicine strive to find ways of communicating complex biology to lay audiences. The "chemical imbalance" location is not one that I endorse, but it hardly reflects the state of psychiatric neuroscience.

4. Angell presents without seriously questioning the hypothesis that neurobiological findings in psychiatry reflect toxic effects of psychopharmacologic treatment rather than the underlying neurobiology of psychiatric disorders. Dr Angell fails to acknowledge that there are now replicable genetic risk variants for a growing list of psychiatric disorders, including autism, schizophrenia, and mood disorders. Similarly, she did not acknowledge growing evidence that risk genotypes for psychiatric disorders also contribute to neuropsychological and clinical phenotypes associated with these psychiatric disorders. In addition, she criticizes psychiatry for its lack of understanding of the neurobiology of psychiatric symptoms, but she ignores progress toward explanatory cognitive neuroscience models of psychiatric symptoms, including hallucinations, delusions, depression, and fear/anxiety.

5. Perhaps most seriously, Angell seems to belittle the plight of people suffering with psychiatric disorders. According to the World Health Organization, neuropsychiatric disorders are the largest cause of disability (DALYs) in the world and depression, a major focus of Dr Angell's essay, is the leading cause of disability. Yet she denigrates the diagnostic system that enables depressed people to obtain care, she denies the efficacy and safety of the most common treatment for major depressive disorder, and she repudiates the notion that psychiatry research has the capacity to identify brain mechanisms underlying depression that could lead to new treatments. Dr Angell never gets beyond her criticisms to assert a positive agenda that might help to alleviate the suffering of patients. Depression is under-funded by NIH relative to its burden of disease. As a result, she might have called for more research to better understand the neurobiology of depression and to improve treatment. Also, she notes, correctly, that there are important barriers to access to psychotherapies. But, she fails to call for better funding for these treatments by third party payers. She stigmatizes psychiatry, but fails to address the consequences of stigma for psychiatrists and patients, including discouraging medical students from entering psychiatry or dissuading suffering people from seeking needed treatment. The absence of a positive agenda in Angell's essay was unfortunate. After all, what value is there in critiquing psychiatry, if not to call for actions that address the needs of psychiatric patients and society? Angell's article was an example of bad journalism. It is shocking that it was written by a former editor of The New England Journal of Medicine, a journal renowned for impartiality and rigor.

Angell has written an article filled with half-truths that would seem to call for society to abandon psychiatric diagnoses, antidepressant medications, and psychiatric neuroscience. Angell shows utter disregard for the negative impact of each of these actions on individuals with psychiatric disorders and society. She provides no alternatives to the status quo or a constructive agenda that might ultimately speed the alleviation of human suffering. Instead, she attacks the one clear path to better diagnoses and more effective pharmacotherapies, translational neuroscience. By stigmatizing a field progressing toward a scientific foundation and by disparaging treatments that show signs of efficacy, Dr Angell's facile criticism of psychiatry could do harm. Perhaps, in this case, doing harm in the name of ethics is, to borrow a phrase from Angell, a form of illusion.