

## From a Clinician's Perspective

TO THE EDITOR: When I read the "2010 in Review" editorial in the December 2010 issue of the *Journal* (1), I noticed that in contrast to other years there was neither an imaging study among the selections, nor any article primarily focusing on genetic and molecular mechanisms. To someone regularly reading the *Journal*, this may seem interesting. Over the past decade, nearly 20% of the *Journal's* articles and brief reports were neuroimaging related. Although there are always changes reflecting major trends, such as fewer PET studies published in recent years compared with the early 2000s, the overall number of imaging studies published per year remains largely constant. Reports that specifically investigate genetic topics in psychiatry are on the rise, and they now account for about another 10% of the *Journal's* articles. Although these articles provide new insights into the mechanisms of behavior, disease, or treatment response, we may tend to perceive all these studies in a certain way when we shift our view from one month's issue of the *Journal* to the larger time frame of an entire year. Do these articles simply address a smaller percentage of the *Journal's* readers? Are they too focused, not reflecting the "big picture"? It could be something else.

I was reminded of a recent conversation with a colleague about whether or not we should obtain cerebrospinal fluid or imaging data for a study participant group with mild cognitive impairment. He was arguing that without these data we would not be able to ensure that all participants would have prodromal Alzheimer's disease. We would certainly better characterize the sample, but is there really a biomarker composition that would allow us to draw a precise conclusion about whether someone at risk would already be in a disease stage that implies future development of dementia? There is, however, a tendency to use many biomarkers in that way, as if they would always enable us to prove whether someone would truly have a condition or not. Our desire for causality could make a clinical evaluation based on accepted diagnostic criteria that these markers were aimed to complement look less scientifically valid. With that discussion in mind, I was relieved to find the article by Terry E. Goldberg and colleagues (2) among the articles selected as being most influential in 2010. Using a clinically defined participant group, the authors raise awareness for symptoms beyond memory deficits that will help clinicians better understand mild cognitive impairment as a clinical syndrome. This also "characterizes" the condition rather than providing a new prognostic tool. However, it makes clinicians interact with patients and lets us detect dysfunctional behavior patterns that they themselves might not be aware of. It could influence how we treat these patients or advise their loved ones. Clearly, cerebrospinal fluid or imaging markers could also influence therapeutic decisions. But is something we can measure in a body fluid sample or something we can see in an image more valuable than a clinical/neuropsychological assessment, when there currently is no answer to what causes a disease or determines its progress?

To be honest, I am deeply in love with technology and every time I work with colleagues at a nearby 7-Tesla MRI scanner I feel in touch with the future, and I always wonder what such amazing machines will help us achieve in the days ahead.

However, back in the memory clinic I see one of my patients, a calm and soft-spoken man in his early sixties. His memory problems are progressive, and now they severely interfere with his profession as a photographer. He has difficulty organizing exhibitions and remembering locations, and most importantly, he is aware of his decline and it sometimes makes him cry and worry about the future. In the end, there is no treatment that would make him feel confident again. There is also no biomarker I can use to change this. When we conduct imaging or genetics studies, we always try to push today's limits forward to better understand pathology and behavior. But we have a responsibility not to lose the individual patient on that journey and not to let technology define clinical practice. There is an opportunity to educate students and residents to allow them to envision themselves as future clinician-scientists. I therefore applaud the *Journal* editors for their insightful selection of articles for the "2010 in Review." It illustrates the importance and sensitivity of such a decision as it contributes to how we ourselves perceive psychiatry.

## References

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2. Goldberg TE, Koppel J, Keehlisen L, Christen E, Dreses-Werringer U, Conejero-Goldberg C, Gordon ML, Davies P: Performance-based measures of everyday function in mild cognitive impairment. *Am J Psychiatry* 2010; 167:845–853

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## Limitations of Retrospective Research

TO THE EDITOR: There are several issues with the article by Tami L. Mark and colleagues (1) published in the October 2010 issue of the *Journal* that deserve attention. The first issue is that of validity. The statistical analyses performed do not solve the concerns with the validity of the fundamental question in this paper: Does it make clinical sense that the branded antidepressant medications available between 2003 and 2006 would outperform the generic antidepressants in effectiveness? Or, even if that argument was valid for that period of time, does it make clinical sense that the currently available branded medications would be able to outperform the currently available generic antidepressants in effectiveness, to the point of affecting outcomes?

The article has other limitations. The most concerning is the significant difference in baseline characteristics between the two groups. The group who received step therapy had a lower average income, higher levels of comorbidity, and a higher burden of chronic illness, indicating that the group that received step therapy might have been at higher risk for worse outcomes and higher utilization. Although the study used statistical models to adjust for the differences between the two groups, it is likely that baseline differences in the two groups explain the difference in outcomes. The currently