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EDITORIAL

Psychiatrists and the pharmaceutical industry: A current topic

Los psiquiatras y la industria farmacéutica: un tema de actualidad en los Estados Unidos

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"The party has been spoiled". Those of us who attend the meetings of the American Psychiatric Association (APA) each year—among them, many Spanish colleagues—observe radical changes in the meeting held recently in San Francisco. These changes are a reflection of the decrease in the budget for the meeting, owing to the increasingly reduced participation of the pharmaceutical companies as a result of the global economy and regulations to combat conflicts of interest. For next year, the industry symposia, with their trained, authoritarian presenters, with their impeccable diction, and slides designed by publicists, will be eliminated. Moreover, an end has been put to motley commercial displays, souvenirs stamped with the brand names of medications, the "free" receptions and dinners and the *happenings* in honor of incoming and outgoing presidents, that is, the "enjoyable" elements of the annual meeting are being taken away from us.

The journals also suffer. What we observed at the annual meeting we also begin to observe in the APA publications, such as the *American Journal of Psychiatry* and *Psychiatric Services*, which have been affected by the reduction in drug advertising. You will have noticed that, in recent issues, the *American Journal of Psychiatry* has reduced the number of pages and articles drastically and *Psychiatric Services* has announced the discontinuation of its free distribution and is in search of new subscribers, a difficult goal to accomplish in this age, when we search for everything in the Internet.

What are the causes behind this situation? It is obvious that the reduction of corporate budgets, as a consequence of the world economic situation, may play a role. However, I consider that this is a knee-jerk reaction, on the part of the pharmaceutical companies, to the actions of organized groups such as the APA in their efforts to combat conflicts of interest. Although conflicts of interest also exist in the case of the other medical specialties, we psychiatrists have been the most widely affected group, at least initially, as we were the first "target" of the investigations of Senator Charles Grassley, a republican of the Senate Finance Committee, who has been "merciless" in his torment of prominent psychiatrists.

"Dignitaries" in the newspapers. The "dignitaries" involved in this scandal include Charles Nemeroff, department chairman at Emory University, accused by the senator of not reporting more than half a million dollars received from the firm GlaxoSmithKline, which apparently influenced his research and publications,¹ and Alan Schatzberg, department chair at Stanford, who, it has been claimed, controlled more than six million dollars of stock in Corcept Therapeutics, a company co-founded by him that was evaluating mifepristone, an old drug for inducing abortions, in the treatment of psychotic depression.² In the case of another department chair, Martin Keller of Brown University, there have also been reports of payments worth millions of dollars from pharmaceutical companies over the past decade, which are thought to have influenced the results of his clinical studies with drugs like Paxil.³ Then there is the case of Joseph Biederman, a Harvard professor, who received nearly two million dollars

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as a consultant and exhibitor for pharmaceutical companies between 2000 and 2007, promoting the diagnosis of bipolar disorder in childhood and justifying the use of off-label antipsychotic drugs in these young populations.¹ A recent case is that of Robert Robinson, department chair at the University of Iowa, accused by a whistleblower in the *New York Times* and the *British Medical Journal* of having a conflict of interest in relation to Lexapro, a drug that he was evaluating for the treatment of depression in patients with cerebral thrombosis.

The APA and conflict of interest. Nemeroff and Schatzberg have had to resign as chairs owing to the scandal. What is paradoxical is the fact that the members of the APA elected Schatzberg to be their new president; thus, one of the individuals most intimately related to the industry will have to head the search for the solution to the problem of conflicts of interest in psychiatry. In his presidential address of last May, Schatzberg focused on the image of psychiatry and stated that his number one plan is to "restore pride and faith in the profession". In his speech, Schatzberg attributed the erosion of the good image of psychiatry to "antipsychiatry movements", although he acknowledges that "other developments in our field" may have contributed. However, Schatzberg shows absolutely no contrition for his actions and suggests that this is all an impulsive reaction, an illusion, the result of envy and the devaluation of the psychiatrist versus other specialists on the part of the media.

Questions. Are these conflicts of interest another exaggeration on the part of the Americans? An illusion stimulated by envy, as suggested by Schatzberg? Has the pendulum swung totally to the other extreme? Will this spread to Spain and the rest of the world?

Academics and industry. In the attempt to answer these questions, I will begin with a brief historical outline. The Bayh-Dole Act of 1980 had permitted universities to maintain a more intimate relationship with pharmaceutical companies. While in 1984, private companies contributed 26 million dollars to university research budgets, this amount rose to 2.3 billion dollars in 2000, an increase of 9000%.⁵ Recent data from the University of Pennsylvania, as well as from Yale, Stanford, Columbia and New York University, indicate that they all receive significant amounts from pharmaceutical companies to support their programs of continued medical education, and that 9000 professors inform that they or a member of their family had some financial interest related to the subject they taught or their clinical area.⁶ A good number of colleagues justify the support of industry, claiming that they can maintain their neutrality, and become annoyed if questioned. However, the growing body of evidence demonstrates that financial support does influence clinical decisions and scientific publications.⁷

Literature on the subject. Over the past three to four years, a number of books have examined the subject in depth.^{5,8,9} Marcia Angell, a former editor-in-chief of *The New England Journal of Medicine*, points out that, despite the argument concerning "academic honesty", the evidence shows that studies can be designed in such a way that the results obtained are those desired or expected, and that the presentation of the data is manipulated

selectively in order to favor a certain product. Recently, in *The New York Times*,² Angell published a review of books that illustrate the principal problems: the deletion of unfavorable research findings, the way in which companies create best-selling drugs (as is the case of Neurontine), in the absence of convincing scientific evidence, and how the process of reviewing psychiatric diagnoses (DSM-IV) may have been influenced by industry to promote diagnoses such as "social anxiety disorder". In reality, the initial enthusiasm about the effectiveness of the new drugs has vanished over time. The results of studies of the National Institute of Mental Health (NIMH), such as CATIE and STAR-D, indicate that many of the advantages of the new drugs over the old were, in part, artifacts, promoted and influenced by large investments, the selective publication of "positive" data and the omission of negative studies.

The economic incentive. The psychiatric drug market, especially that of antidepressive and antipsychotic agents, has increased drastically in recent decades. In the case of antipsychotic medications, while in the seventies, the market barely reached annual sales of 200 million dollars, in the nineties, it increased nearly six-fold (600%) to 1.1 billion dollars a year and has continued to grow, with estimated yearly sales of 4.6 billion dollars for 2004-2005.¹⁰ Meanwhile, the use of antipsychotic medications increased by only 0.4% between 1996 and 2005 (0.8% to 1.2% of the noninstitutionalized population in 2004). The use of second generation or atypical antipsychotic agents increased much more drastically (from 0.15% in 1996-1997 to 1.1% in 2004-2005), whereas that of typical antipsychotic drugs decreased from 0.6% to 0.15% respectively, during those same years.¹¹ It is interesting to observe that the average dose of antipsychotic medications has remained very constant over time and that the use of these agents has not increased in the case of schizophrenia and psychoses, but in other disorders, such as mood disorders, a fact that reflects their off-label use. In short, the arrival of blockbuster drugs produced fundamental changes in the relationship with industry, converting it into a marketing paradigm.¹² All these commercial factors have stimulated aggressive competition among pharmaceutical companies and the recruitment of "opinion leaders" who mostly have been academicians belonging to the vanguard, like those mentioned above.

Why the emphasis on psychiatry? It's deplorable that the emphasis of this scrutiny has focused nearly exclusively on psychiatry and the psychiatrists since similar abuses abound on other fronts. We could recall, for example, the case of the COX-2 inhibitors and the delay in reporting adverse or negative effects of the medication on the part of researchers "paid" by the manufacturer of the drug. The case of the questionable efficacy of new drugs as compared to old ones (statins and others) in the reduction of cholesterol concentrations or gastroesophageal reflux, which, despite their high cost, are aggressively promoted by academic authorities, who receive funds from the maker. It is interesting to observe that a large part of the debate over "aspirin resistance" has been influenced by corporative funds and instigated by physicians who receive money from the companies that compete with aspirin.¹³

Recommendations and regulations. The influential Institute of Medicine of the United States recently published a 300-page report on the subject, entitled "Conflicts of interest in medical research, education and practice", that contains 16 specific recommendations for avoiding conflicts of interest in relationships with industry.¹⁴ Moreover, universities in the United States are constantly issuing new institutional regulations for interaction with industry. They hold that ethics courses stressing conflicts of interest should be taken as requirements in the universities. For example, my university (the University of Medicine and Dentistry of New Jersey) has created strict ethical structures that encourage whistleblowers and apply strong penalties, including job loss. This could lead to financial benefits, as in the recent case of a whistleblower at our university who received millions following civil proceedings.¹⁵ A good model for these regulations is that of Johns Hopkins University in Baltimore. The document, entitled "Interactions with industry", prohibits, among other things, free medical samples and gifts from industry.

Disclosure. Although virtually all publications require prior disclosure concerning possible conflicts of interest, a simple declaration does not solve the scientific dilemmas or justify the publication of many studies. It seems to me that editors will have to exert a greater degree of editorial control.

Bills and bills. A new law introduced in congress last January, the "Sunshine" bill, proposes that the names of colleagues involved with industry and the amount of money they receive by this means be aired. In accordance with this requirement, doctors who receive more than 100 dollars from pharmaceutical companies or other commercial interests will have their names posted on the Internet. In my opinion, this will be a minor inconvenience for many and will not have a major impact on the abuses.

New relationships between academicians and industry. It will be essential to conceive a new relationship between the academic world and industry that encourages new developments and protects science. Should the present confrontation persist, we will all lose in the end. The new relationship with industry should change the marketing paradigm and become a symbiotic relationship for industry and the profession. This relationship should respect the professional integrity of physicians, ensure that they receive complete, objective information about the products, and openly disclose the scientific or commercial relationships existing between physicians and industry. Studies comparing two or more drugs should be coordinated by researchers or institutions with no profit motive in mind. Researchers and practitioners should have access to the results of negative studies, which should be taken into account in the evaluation of the efficacy of the medication.

Will this spread to other countries? In this globalized world, it would be absurd to think that other countries would fail to confront this problem openly, especially developed countries like Spain, whose contributions to universal science are gradually increasing. Prophetically, nearly two decades ago, Professor Jerónimo Saiz and coworkers, in an excellent article the contents of which are still applicable, warned that "owing to the influence of

private funding, we can not overlook the ethical and legal issues that this circumstance entails, without excluding the valuable contribution of said companies to the progress in basic and clinical research".¹⁶ We should hope that, in the case of Spain, the reaction will be less drastic, more rational, although it is necessary to introduce procedures and regulations that protect integrity in science. Will the Mediterranean community manage to discover the way to conserve the "enjoyable" aspects without losing sight of scientific objectivity? The Anglo-Saxons have clearly gone to the other extreme, perhaps reflecting cultural attitudes that Luis Racionero had traced with precision in his book entitled *El Mediterráneo y los Bárbaros del Norte*.¹⁷

Finally, in the case of the developing countries, like those of Latin America, I assume that the changes will be much less drastic since the subsidies provided by industry are vital for the limited number of academicians living there. In fact, the pharmaceutical industry finances the travels of many colleagues to international meetings, such as that of the APA, since, otherwise, they would not have access to the new information concerning the specialty.

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