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Letter to the Editor

Reviving the SCNP Committee on clinical trials: the need to enhance its future mission

The paper by P. Bech and T. Ban is highly informative, aimed at reviewing the history of psychotropic drugs in the European Union, specifically, as regards the development of the Scandinavian College of Neuropsychopharmacology (SCNP). They cover its early successes, the UKU and the reasons for its later dissolution, and for determining that the UKU now needs to be revived with a somewhat broader mission. Although brief, the paper captures the early high expectations of the SCNP group when the new treatments were introduced, and the manner in which they went about dealing with the evaluation of the new drugs.

It was clear then that a mechanism was necessary that would permit objective evaluation of these agents, while at the same time, making it possible for the science to advance and for new, even more effective, drugs to be developed. To accomplish these aims they established a clinical research committee, that is, the UKU (CRC), to oversee the standardisation and select the technology to be utilised in evaluation. The Committee bent to the use of rating scales for evaluation, and to accommodate the clinicians who would use them, would select only brief rating methods. Thus, they established use of the soundly validated brief Hamilton depression and anxiety scales (1) for the affective disorders and the broader Brief Psychiatric Rating Scale (BPRS) (2) for trials of anti-psychotic agents. The authors then trace the rise and fall of enthusiasm about the drugs and the problems of conducting clinical trials during the period of 1960–2000, alluding to the reductions in government support, the dissolution of the UKU and the European Committee for Standardization of Clinical Trials, and the increase in the dominance of industry, despite some major developments in the science, led by Arvid Carlsson and Mogens Schou. Now we view a scene where industry citing the failure during the last three decades to develop any new classes of psychotropic drugs for depression or the psychoses, and highly expensive clinical trials that have produced little information of value, have severely reduced their involvement in the development of central nervous system drugs. In order to break this 'impasse', to stimulate dialogue among industry and academia, the authors recommend and the SCNP will reassemble a new UKU Committee dedicated to advancing the clinical trial.

Comment

This is a very useful document and comes at a time when a review of the current state of psychotropic drug development designed to stir it out of an inertial state is very much needed. As an investigator who has participated in research in this field, I endorse the revival of the UKU and its goal of improving clinical trials. I, however, believe that its current goal is shortsighted, that it overlooks obvious shortcomings of the established trials model, and unnecessarily narrows the aims of a new approach to these problems. The real problems lie with certain aspects of the current trials and the phasing out of the classic study of the profile of drug actions as designed in earlier clinical studies in psychopharmacology. The UKU will have to recognise that the established clinical trial model was designed more than 50 years ago and was aimed at the marketing question, 'Is this drug more efficacious than a placebo?' that allowed one to use brief scales such as the Hamilton and the BPRS, where total scores provided a valid response to the issue of efficacy. Such scales, however, are incapable of providing reliable information on any specific clinical actions of the drug in question (3). Thus, a highly expensive clinical trial results in nothing to report beyond whether the drug was or was not efficacious for this specific mental disorder. We have learned over the years, that the antidepressant drugs when effective, act clinically within the first 2 weeks, may not act directly or specifically on 'depressed mood', that different classes of drugs initiate clinical action on different aspects of the disorder [see review in (4)], that the absence of early improvement actions will almost certainly lead to non-response at treatment outcome (5), and that SSRI's are likely to be more effective in anxiety disorders than the 'anti-anxiety' benzodiazepines (6). These findings that are critical for understanding

drug actions and mechanisms have been uncovered through the use of clinical methods that go beyond total scores from the brief Hamilton and BPRS, and that provide 'profiles' of action on the major components of the disorders. This more sensitive behavioural methodology also make it possible to shorten the length of clinical trials.

It means that the goals of a new UKU should be to update the methodology, to revise the currently established clinical trial model, and to broaden their goals, that is, to not only deal with clinical trials, but to include the conduct of investigations in clinical psychopharmacology, generally.

Taking these steps will stimulate clinical investigators and the more efficient, more sensitive, and less-expensive trial should encourage the industry to get re-involved.

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