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Development of a cross-pharmaceutical database: a paradigm change for accelerating the drug-development process

Larry Alphs*

"Continued successful development of innovative new treatments for neuropsychiatric disorders requires a paradigm shift in the drug development process."

In recent years, advances in brain biology, neuroimaging technology and genetics have greatly expanded our understanding of neuroscience [1–5]. Among these advances, the advent of noninvasive neuroimaging techniques such as diffusion imaging and resting-state functional magnetic resonance imaging (fMRI) has led to the development of the new field of connectomics, where neuronal connectivity is comprehensively mapped at the macroscopic level (studying long-distance pathways for the whole brain) and at the microscopic level (studying axons, dendrites and synapses in a small region of the brain) [3,6]. Similarly, recent advances in virtual computer-modeling techniques now allow for assessment of abnormalities at the cellular level and exploration into ways that they contribute to neuropsychiatric disease symptoms, thus providing vast new insights into how more effective treatments can be developed [7]. Taken together, such advances have enormously expanded our potential to understand and address the etiological basis of brain dysfunction.

Despite these advances, our expanding knowledge of neurobiology has not been matched by major treatment breakthroughs. CNS disorders remain poorly understood and continue to represent a significant and, indeed, increasing global disease burden [101]. Many of our major psychiatric disorders have seen only incremental improvements in treatment in recent decades. Diseases such as Alzheimer's, dementia and autism remain poorly treated [8,9] and represent a looming public health calamity with the growth of all segments of the global population.

Expanding challenges to the development of neuropsychiatric treatments

The pharmaceutical industry remains the source of novel neuropsychiatric treatments, yet, despite vastly increased levels of investment to successfully develop novel CNS compounds, the rate at which new products are coming to market has declined. Ironically, these increased development costs are driven in part by our expanding knowledge of neurobiology. Greater understanding of neuropsychiatric diseases raises expectations for expanding exploration of treatment effects, and increasing insight into potential safety risks leads to demands that they be explored. Limitations in healthcare resources further require that new neuropsychiatric treatments provide value beyond that of existing products. This has increasingly necessitated the inclusion of outcomes data and patient-rated outcomes at the time of market launch.

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*Therapeutic Team Leader, Psychiatry, Janssen Scientific Affairs, LLC, 1125 Trenton-Harbourton Road, A32404, Titusville, NJ 08560, USA
Tel.: +1 609 730 3693
Fax: +1 609 730 3125
E-mail: lalphs@its.jnj.com

Pressure from clinicians and from payers for precision (or personalized) medicine and for comparative effectiveness research is driving the need for still more complex trials.

This demand for information is nearly impossible to meet with traditional approaches to drug development. Scientifically valid work would require enormous study samples and expanded expenditure of resources that would go well beyond those currently available.

As a result of these challenges, many companies within the pharmaceutical industry have abandoned the development of treatments for neuropsychiatric disease, and venture capital support for CNS drug development has dwindled [4]. Taken together, this confluence of drug development trends demands significant changes in the way neuropsychiatric drugs are developed.

Precompetitive data sharing among pharmaceutical companies as a solution

One approach to improving the drug development process would be for pharmaceutical companies to share data from completed clinical trials already available in antipsychotic drug databases. Over recent decades, enormous quantities of clinical data have been gathered on an array of neuropsychiatric disorders during the development of new treatments. I would contend that much of the value of these data remains untapped.

These clinical trial data are generally cross-sectional in nature and represent selected samples of disease populations as a whole. However, combining data from many trials would permit deeper insights into these diseases and into patient responses to pharmacological treatments. In addition, agglomerating these databases into a single large unit could promote better clinical trial designs, could help researchers identify and standardize better end points and might support the validation of biological markers. Models for such collaboration are already emerging with growing success. Specific examples include the International Serious Adverse Event Consortium, the Coalition Against Major Diseases, the Innovative Medicines Initiative: NEWMEDS, TransCelerate BioPharma Inc. and the Neuroscience Peer Review Consortium. Each of these initiatives aims to reduce time, cost and duplicative effort in setting up clinical trials by establishing a repository where mutually agreed upon data from clinical trials can be stored and analyzed [102]. These initiatives already show how industry collaboration can meet drug development challenges, but their value is only starting to be realized.

Sharing such databases among stakeholders may facilitate drug development by increasing the pool of informative data points. Pooling of phenotypic, response, safety, outcomes and biomarker (e.g., genetic or imaging) data can be useful for identifying important treatment subgroups, optimizing end points and modeling clinical trial results, so as to improve the design, conduct, efficiency and overall informative value of clinical trials. Opportunities to use these databases for modeling of pharmacological and clinical trial responses are particularly intriguing.

Opportunities that might accompany the formation of a cross-industry, noncompetitive database are accompanied by various hurdles to success. Optimal implementation requires identifying a clear purpose and mission, establishing both an effective governance plan and a sound financial basis and solving intellectual property and other legal issues. As has been noted, similar consortia are already in existence, and it is valuable to set up alliances with sister organizations so that experience reflected in their work can be incorporated, pitfalls avoided and, perhaps, mutually interesting questions explored.

Another critical consideration in the formation of such precompetitive databases is determining membership. Most questions that might be explored by such a consortium are of interest to numerous stakeholders. When a clear focus on mission and goals is established, inclusion in or relationship to these different groups must be considered. In particular, relationships with clinicians, patients, caregivers, advocacy groups, academics, payers and regulatory and other governmental agencies, as well as with selected industry partners, must be contemplated. Inclusion of academic and governmental members would help avoid antitrust concerns. Given the global implications of most of this work and the global nature of the databases that have been generated by potential industry partners, a consortium developed to bring these databases together should be international in scope.

To be successful, this consortium should start with a more constrained focus, but the foundation should be built so as to allow for expansion of the vision as the consortium matures. Success will require a balance of competing considerations. The organization must be small enough to be efficient and effective, yet large enough to address the broad needs of a wide variety of interested parties.

Conclusion

Continued successful development of innovative new treatments for neuropsychiatric disorders requires a paradigm shift in the drug development process. I believe that the formation of a cross-company, precompetitive database that uses existing data as a foundation on which to develop better standards and models for future work represents a viable and desirable mechanism to achieve this shift through expansion of models that are already emerging. Numerous challenges to its formation would need to be overcome, but if society wants better treatments in the future, the pharmaceutical industry must rise to the challenge.

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