

Executive Summary

Central nervous system (CNS) diseases are a major focus of the pharmaceutical industry, with CNS drugs representing some of its most successful products. However, drug discovery and development researchers experience difficulty in developing CNS drugs that complete clinical trials and win regulatory approval—especially drugs which meet major unmet needs in the CNS area, such as Alzheimer’s disease. A major bottleneck in successful development of CNS drugs is the discovery or design of drugs that can cross the blood-brain barrier (BBB).

This report reviews the discovery and design of small- and large-molecule drugs that can efficiently cross the BBB. This includes more traditional, medicinal chemistry-based methods for design of small-molecule drugs as well as methods that exploit receptor-mediated transport (which the body uses to get essential nutrients, hormones, and other substances into the brain) of small and large molecules. Also covered is use of nanoparticle technology to enable BBB penetration, and in vitro and in vivo assays as well as imaging methods to determine a drug’s ability to cross the BBB and reach its target.

This report also includes the results of a survey of researchers and executives—from corporate and academic organizations—who are active in the CNS drug development area, which explores their involvement in BBB-related technologies and programs. The survey results are discussed in terms of what they reveal about the current state of BBB research and the future potential for developing drugs that are able to cross it.

