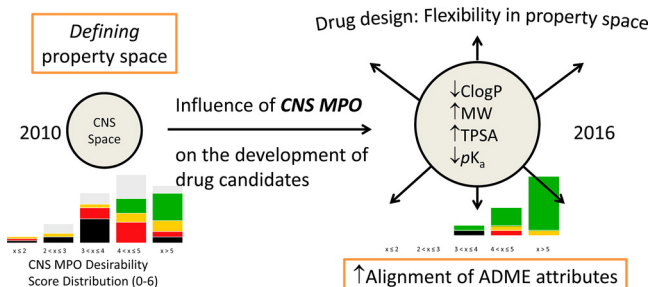


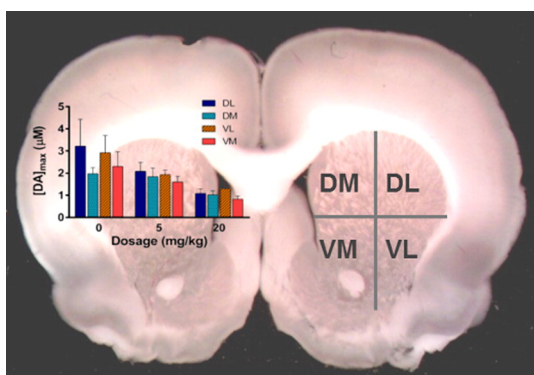
■ IMPROVING CNS DRUG DEVELOPMENT



The original description of the central nervous system multiparameter optimization (CNS MPO) scoring paradigm as a means of assessing compound quality and potential for CNS penetration based on a retrospective analysis of CNS drugs and drug candidates provided medicinal chemists with an operationally simple methodology that was easily applied. In the current issue, Wager et al. (DOI: [10.1021/acscemneuro.6b00029](https://doi.org/10.1021/acscemneuro.6b00029)) capture the impact of the prospective application of the CNS MPO scoring function by describing application to the profiling of 21 recent CNS drug candidates at Pfizer.

Descriptions of the successful application of the CNS MPO desirability tool are of importance in fostering greater use and a deeper understanding of this tool, and the authors showcase its potential. The authors provide statistics on the physicochemical properties of a cohort of contemporary CNS drug candidates that extends the range of acceptable parameters to larger, more polar, and less basic molecules.

■ INSIGHT INTO CHEMOBRAIN



It is estimated that up to one-third of cancer patients will experience cognitive decline, known as chemobrain, as a result of receiving chemotherapy treatment. Little is known about the underlying neurochemical mechanisms that contribute to the symptoms of chemobrain. In the current issue, Kaplan et al. (DOI: [10.1021/acscemneuro.5b00029](https://doi.org/10.1021/acscemneuro.5b00029)) details the impact of carboplatin, a drug commonly used in chemotherapy treatment, on dopamine release and uptake in male Wistar rats.

The authors used fast-scan cyclic voltammetry at carbon-fiber microelectrodes to measure the release and uptake of dopamine, an abundant CNS neurotransmitter involved in cognition, locomotion, and reward. Through this study, they established that carboplatin decreases dopamine release, but

that total dopamine content in the brain is unaffected. Therefore, even though dopamine is present inside neurons, it cannot efficiently get out. Behaviorally, these rats show reduced locomotor activity after carboplatin treatment, possibly due to dopamine release impairment. These studies provide the first glimpse into how dopamine release and uptake are affected by chemotherapy administration.

Published: June 15, 2016