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# Pharmacology of mood stabilizers

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## Abstract

Neuropharmacology as a part of Neuroscience has a cardinal role to develop of neuroscience area. We can describe many neurological pathways after recognition of detailed mechanisms of neuropharmacology. This is will explain the scientific basis of mood stabilizers that is not only human brain's function saving but also, life saving for so many patients with bipolar disorders. Cyclothymia today is a common and more growing problem among young individuals and we as physicians can save their life by science. Mood stabilizers represent a class of drugs that are efficacious in the treatment of bipolar disorder. The most established medications in this class are lithium, valproic acid, and carbamazepine. In addition to their therapeutic effects for treatment of acute manic episodes, these medications often are useful as prophylaxis against future episodes and as adjunctive antidepressant medications. While important extracellular effects have not been excluded, most available evidence suggests that the therapeutically relevant targets of this class of medications are in the interior of cells. Herein we give a prospective of a rapidly evolving field, discussing common effects of mood stabilizers as well as effects that are unique to individual medications. Mood stabilizers have been shown to modulate the activity of enzymes, ion channels, arachidonic acid turnover, G protein coupled receptors and intracellular pathways involved in synaptic plasticity and neuroprotection. Understanding the therapeutic targets of mood stabilizers will undoubtedly lead to a better understanding of the pathophysiology of bipolar disorder and to the development of improved therapeutics for the treatment of this disease. Furthermore, the involvement of mood stabilizers in pathways operative in neuroprotection suggests that they may have utility in the treatment of classical neurodegenerative disorders. The intent of this review is to describe research in this dynamic field, and to present the leading hypotheses regarding the mechanisms of action of mood stabilizers. Although it is not known for certain how any mood stabilizer exerts its therapeutic effects, there is suggestive evidence for various mechanisms. It appears likely that lithium exerts its initial effects by targeting the activity of an enzyme, or perhaps multiple enzymes, inside cells. Lithium has a hydrated ionic radius which is very similar to that of magnesium, and it inhibits some enzymes through competition for this required cofactor. A primary mechanism by which cell surface receptors transduce their signals to secondary signals within cells is via G proteins. G proteins are molecules in cells composed of three subunits (α, β, and γ, which are thereafter subdefined further) that interact to transfer a signal from extracellular membrane receptors to the interior of the cell. Thus, G proteins couple neurotransmitters – via their receptors – to intracellular signaling cascades that are involved in many cellular processes including growth, differentiation, metabolism, and synaptic plasticity. The development of mood stabilizers in the past was mostly due to many serendipitous discoveries. Without knowledge of how these drugs exert their therapeutic effects, it is impossible to develop new agents in a hypothesis driven manner. Based on the intracellular targets described in this review, current research is aiming to investigate modulators of these pathways in animal models and the clinical treatment of mania. Modeling drugs after the putative mechanisms of mood stabilizing agents represents a viable option of both developing more specific therapies and as 'proof of concept' of the pathways implicated in the pathophysiology and treatment of bipolar disorder. In this regard, drugs mimicking the effects of some of the available anticonvulsants (e.g. attenuation of glutamatergic function, enhancement of GABAergic functioning, blockade of sodium channels) are not currently being developed for bipolar disorder per se, but new agents with this profile (likely developed for epilepsy) will undoubtedly be investigated (albeit possibly only in initial open studies) in bipolar disorder. While there does not currently exist any predictive value when comparing antimanic efficacy to the anti-epileptic function of drugs, future studies may provide some valuable information about which systems and pathways in the brain are most responsible for mania and consequently valuable to target.Nevertheless, several parameters rule the final in vivo application of such contrast agents, making their translation to routine use in clinic application a demanding process. Such parameters include: the thermodynamic stability and kinetic inertness of the Gd3+ complex; its conjugation to a targeting unit (which should insure the maintenance of a good affinity and selectivity towards the desired target/biomarker); maximal relaxivity; optimal pharmacokinetic properties and good clearance, while guarantying an adequate imaging window; no in vivo toxicity and good solubility. Understanding how changes in the structure of the ligands can influence the main relaxometric parameters, together with the choice of a good target, enables the rational design of optimal contrast agents. The clinical translation of targeted contrast agents is indeed still scarce, with only few contrast agents reaching clinical trials phase.

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