

Potential Neurotrophic and Neuroprotective Effects of Bipolar Illness, Lithium, Valproate, and Antidepressants

	<u>Stress</u>	<u>Glucocorticoids</u>	<u>Bipolar Illness</u>	<u>Lithium</u>	<u>Valproate</u>	<u>Antidepressants</u>
<u>Neurotrophic Factors</u>						
BDNF	↓	↓		↑		↑ (and block stress effects)
Bcl-2				↑	↑	
<u>Cell Death Factors</u>						
Bax, p53	↑	↑		↓		
<u>Stroke Model</u>						
Severity	↑	↑	(↑, ?)	↓	↓?	
<u>Calcium Signaling</u>						
Ca _i	↑		↑ Ca _i , WBCs			
CaMK-II			↓ PFC CaMK-II			↑
Mineralocorticoid receptors (MR)			↓ MR			↑
<u>New Neurons/Glia</u>						
Neurogenesis	↓	↓	(↓ neurons)	↑		↑
Gliogenesis			(↓ glia)	↑		
<u>Neuronal Integrity</u>						
NAA (PFC > Hippo)	----	----	↓	↑		
Gray matter on MRI			↓	↑		
<u>Clinical Suicide</u>	↑	↑	↑↑ incidence	↓	?	↓?
<u>Excess Medical Mortality if Depressed</u>		(↑)	↑ incidence	↓	?	?

Abbreviations: ↑, increase; ↓, decrease; ?, unknown or not definite; BDNF, brain-derived neurotrophic factor; Ca_i, intracellular calcium; CaMK-II, calcium calmodulin kinase-II; NAA, N-acetyl-aspartate; PFC, prefrontal cortex; Hippo, hippocampus; MRI, magnetic resonance imaging; WBCs, white blood cells;