Depression presents as a multi-dimensional disorder involving disruption of mood, cognition, motor function, and homeostatic/drive processes, including sleep, appetite, and libido. A striking feature of depressive disorders is that nearly all patients share at least some primary symptoms (e.g., depressed mood and anhedonia) while other symptoms can be highly variable from patient to patient. For example, some patients have severe insomnia, flattened affective response, and appetite loss while others have profound hypersomnia, increased mood reactivity, and significantly increased appetite: still other patients within each of these groups may have more or less disturbance of cognition, psychomotor function, libido, and anxiety. Beyond these symptomatic differences, patients with depression also show a highly variable response to available treatments. It is well established that up to 40% of patients will have an inadequate response to medications affecting the monoaminergic systems (serotonin, norepinephrine, and dopamine) which remain the mainstay first-line pharmacologic treatment options for depression. Similarly, certain psychotherapies (such as cognitive behavioral therapy and interpersonal psychotherapy) are clearly effective in many, but not all, depressed patients. Even electroconvulsive therapy (ECT), which remains the most effective acute treatment for depression, fails in up to 20% of patients. Research efforts over the past several decades have attempted to define how the neurobiology of depression may differ