A Review on animal models of depression

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Animal models in psychopharmacology are difficult to develop because of the convolution of the human mind and the inherent difficulty in stimulating a similar condition in laboratory animals. However, animal models in the psychopharmacology have contributed a lot to drug research. Depression is one among the most rampant forms of psychiatric disorders and a leading cause for morbidity and mortality. Since, the unexpected breakthrough of the first antidepressants the progress in developing more efficient medications has marked time, emphasizing the need to establish novel classes of antidepressants. Various animal models have been developed and are instrumental in detecting the antidepressant-like potential of novel compounds in preclinical settings. The models commonly used are diverse and were developed originally based on the behavioral consequences of stress, drug, lesion or genetic manipulations. The present review is an attempt to compile together various animal models employed for the screening of antidepressants.

Key words : Depression, Model, Animal, Antidepressants

Depression is a common, chronic, and potentially debilitating form of psychiatric disorders with a lifetime prevalence of about 15-20% (Kessler *et al*., 2005). According to World Health Organization, unipolar depression is projected to reach second place as leading contributor to the global burden of disease by the year 2020 (Murray and Lopez, 1997). As defined by the American Psychiatric Association (American Psychiatric Association, 1994), depression is a heterogeneous disorder often manifested with symptoms at the psychological, behavioral and physiological levels (Box 1).These symptoms are often recurrent and prone to become chronic, substantially interfering with an individual's ability to cope with everyday life. Depression is considered as a stress-related disorder underscoring the role of stress as a key determinant in disease etiology (Fava and Kendler, 2000). An estimated 40–50% of the risks for depression are genetically determined (Levinson, 2006). However; no single vulnerability gene has been identified yet, indicating a far more complex interplay of genetic and environmental factors underlying the causative etiology of this disorder (Nestler *et al*., 2002). It is exceedingly difficult to predict an animal model that perfectly recapitulates the symptoms of depression in human patients. Animals not only lack consciousness of self, self reflection and consideration of others but also hallmarks of the disorder such as depressed mood, low self-esteem or suicidality are hardly accessible in non-humans. However, depression, as other mental disorders, constitutes of intermediate or so-called endophenotypes that can be reproduced independently and evaluated in animals, including physiological, endocrinological and neuroanatomical alterations as well as behavioral traits (Box 2).

Requirements for an animal depression model :

Nonetheless, numerous attempts have been made to create animal models of depression, or at least of the symptoms of depression, and criteria for their evaluation have been established. Some of the most widely cited criteria were developed by McKinney and Bunney around 40 years ago (McKinney and Bunney, 1969). They proposed that the minimal requirements for a valid animal

Box 1 : Symptoms of major depression (American Psychiatric Association, 1994)
• Depressed mood most of the day (in children and adolescents, irritability might signify a depressed mood)
• Markedly diminished interest or pleasure in all or most activities most of the day
• Large increase or decrease in appetite
• Insomnia or excessive sleeping
• Psychomotor agitation (evident by, for example, hand wringing) or slowness of movement
• Fatigue or loss of energy
• Indecisiveness or diminished ability to think or concentrate
• Feelings of worthlessness or excessive or inappropriate guilt
• Recurrent thoughts of death or suicide