CHAPTER 2

REVIEW OF LITERATURE

2.1 INTRODUCTION

A review of literature has been presented on depression data mining using ANN. The section about depression highlights different groups of people affected with different types of depression. This section about ANN in data mining describes about the method of using ANN in data mining.

2.2 DEPRESSION

Depression refers to a lowered state of mind, the severity of which may be of different grades. As an effect, depression is familiar to everyone as a reaction to losses and disappointments and can be seen as a normal emotional reaction [81], [111]. Depression may also manifest itself as a symptom as part of a syndrome in different mental or somatic disorders [129]. Some patients suffer from depression-related somatic symptoms and cannot describe the lowering of their mood or want to hide it from their doctor [133].

Depressive mood lasts several weeks or months, and there are several co-occurring symptoms for a defined period of time [189]. Clinical depression may exist at different grades from a disorder. The working ability has been lost when the patient has the ability to work with a difficult illness. Patients may also suffer from delusions and have suicidal thoughts [49], [11]. Noda K and Tokosumi A [128] have analyzed the use of robots for depression study in human.
The classification of depressive disorders is based on the diagnostic criteria of International Classification of Diseases (ICD)-10 or Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV. According to DSM-IV, unipolar forms of mood disorders are divided into three groups: Major Depressive Disorder (MDD), dysthymic disorder, and depression not otherwise specified. The diagnosis of major depression requires a two-week period of depressed mood or loss of interest or pleasure together with at least four other symptoms such as fatigue or loss of energy, hopelessness, changes in appetite and weight, psychomotor retardation and agitation, inappropriate guilt, impaired concentration, insomnia or hypersomnia, and suicidal thoughts. The symptoms must not be related merely to substance use, bereavement or medical illness. In DSM-IV the severity of major depression is also categorized by the number of symptoms: mild, moderate or severe. The diagnosis of major depression is basically the same in DSM-IV and ICD-10; although, ICD-10 requires one symptom less than DSM-IV and includes fatigue or loss of energy in the core symptoms. Dysthymic disorder is a chronic disturbance of mood in which depressed mood occurs most of the day for at least two years. Depressive disorder not otherwise specified includes disorders with depressive features that do not fulfill the criteria for MDD, dysthymic disorder, adjustment disorder with depressed mood, or adjustment disorder with mixed adjustment and depressed mood. The diagnosis of adjustment disorder with depressed mood is used when clinically significant depressive symptoms occur as a psychological response to a recognizable stressor during a time period of three months after the onset of the stressor, and the disturbance does not meet the criteria for another specific Axis I disorder or is not part of a pre-existing Axis I or Axis II disorder.

The diagnosis of major depression usually requires interviewing the patient, while depressive symptoms can also be ascertained by several self-report
questionnaires such as Beck’s Depression Inventory [18], Zung self-rating Depression Scale [193] or Hopkins Symptom Checklist -25 [42].

Depression is a common public health problem that causes a remarkable amount of individual suffering, functional disability, and self-destructive behavior [43], [172]. During lifetime, approximately one fifth of the population suffers from major depression [106], [107]. According to population surveys, the prevalence of clinically significant depression varies from 2.6% to 5.5% in men and from 6.0% to 11.8% in women. The prevalence of depressive symptoms is much higher, varying from 10% to 19%, among men and from 18% to 34% among women. It is estimated that only one third of the patients suffering from major depression in Finland receive treatment [75].

In the National Comorbidity Survey (NCS) conducted in 1990-1992, the lifetime prevalence of major depression among US adults was 17.1%, and the 12-month prevalence was 10.3%. The National Comorbidity Survey Replication (NCS-R), conducted in 2001-2002, found a lifetime prevalence of major depression among US adults of 16.2%, and a 12-month prevalence of 6.6%. In a study conducted by Jacobi et al., [91] the lifetime prevalence of any unipolar depression in the German population was reported to be 17.1% and the 12-month prevalence 10.7%.

There exist several epidemiological studies in which the epidemiology of depression has been studied in Finland. In the cross-sectional mini-Finland health survey, the point prevalence of neurotic depression of individuals aged 30 or over was 4.6% being 3.9% among males and 6.0% among females [112]. In the longitudinal UKKI Study, the prevalence of depression among 31-89 year old adults was 5.3%, being 3.2% among men and 7.3% among women. Isometsa E, et al.,
reported in a study of 2293 subjects aged 25-79 years, interviewed by telephone, a 6-23 month prevalence of 4.1% for major depressive episode. The total population prevalence of major depressive episode was 9.3%, 7.2% among males and 10.9% among females.

The most recent results regarding the prevalence of depression in Finland are from the ODIN study [12] and from the health 2000 study [137]. In the ODIN study the prevalence of MDD was 4.7% among urban subjects, 2.7% among men and 6.6% among women, and 4.1% among rural subjects, 4.3% among men and 3.8% among women. In the Finnish health 2000 Study the prevalence of major depression during the past 12 months measured by the Composite International Diagnostic Interview (CIDI) among subjects 30 years or more was 3.4% among men and 6.3% among women. With regard to young adults, in the Finnish health care survey of 433 young adults the 12-month prevalence of major depression was 9.4%; 8.1% among males and 10.7% among females [71], [177]. In a study of 245 Finnish subjects aged 20-24 years the one-month prevalence of major depression was found to be 6.9%; 5.4% among males and 7.8% among females [1].

Depression is a biopsychosocial disease; there are several biological, psychological and social factors behind depressive disorders [25], [131], [104], [105]. Major depression is suggested to be a familial disorder [170], [102]. The familiarity results partly from genetic influences, although environmental factors specific to an individual are also etiologically important [136]. It is known that the risk of depression is higher among first-degree relatives of individuals suffering from unipolar depression [92]. The familiarity of depression has also been shown in twin-studies, where markedly higher rates of depression have been found among twins than in the general population, as well as significantly higher monozygotic than dizygotic concordance [121]. Major depression is suggested to
be equally heritable in men and women [32], [103]. Early adverse life experiences influence the risk of later depression and many psychosocial factors such as physical disability, social isolation, and economical problems may predict depression [10], [110], [138]. In major depression there are often generating factors which may be current negative life events or losses together with genetic and personality factors that may result in depression. It can be stated that depression is a complex disorder that does not result from either genetic or environmental influences alone, but rather from the interaction of both these factors.

Bernard Widrow and Michael L Lehr [22] have provided a detailed discussion on ANN. A machine learning method is proposed for automatically finding psychiatric diagnostic rules. It is proposed that a genetic algorithm system can find symbolic, easily readable rules that could be used by psychiatric clinicians [44]. Christopher N Chapman, et al., [34] explored that many neural network models also make use of distance functions, including RBF networks.

As the size of data warehouses increase to several hundreds of gigabytes or terabytes, the need for methods and tools that will automate the process of knowledge extraction or guide the user to subsets of the dataset that are of particular interest is becoming prominent [176]. Most clinical tasks require measurement and capture of numerous patient data, often on electronic media. Physicians who have to make diagnostic decisions based on these data may be overwhelmed by the number of data if the physician’s ability to reason with the data does not scale up to the data-storage capabilities [192]. The clinical application shows that it is possible to differentiate between patients suffering from schizophrenia, depression and normal healthy persons on the basis of Electroencephalograms (EEG) rhythms [7], [191].
Neurochemical changes play an important role in the etiology of depression [118]. The monoamine hypothesis was presented in the 1960s suggesting that an important mechanism behind depression is dysregulation in the neuronal monoamines, noradrenalin, serotonin, and dopamine [130], [165], [166]. As reviewed by Hindmarch I [82], the monoamine hypothesis is based on pharmacological observations that antidepressive medication raises the functional capacity of the biogenic amines in the brain. Although the monoamine concentrations increase in a few hours, clinical response to the antidepressive treatment comes later, usually in one to four weeks. It seems that much more complex dysregulation exists behind depression. The focus has moved away from single neurotransmitters to such areas as neurobehavioral systems, neural circuits and signal transduction [175].

Many hormonal abnormalities are related to depression. One of the most important biological factors in the pathogenesis of depression is dysregulation in the Hypothalamic Pituitary-Adrenal (HPA) axis [127], [134]. As reviewed by Barden N [14], the secretion of glucocorticoids from the adrenal glands increases in reaction to stress. The secretion of glucocorticoids is regulated by corticotrophin via stimulation of the Corticotrophin Releasing Factor (CRF), which is secreted from the hypothalamus.

In depression, there is hyperactivity of the HPA axis caused by hypersecretion of CRF [8]. Increased plasma corticotrophin release factor concentrations have been found among depressed individuals [31], [63]. Elevated CRF concentrations have also been found in the locus ceruleus of depressed subjects [23]. High cortisol concentrations may cause cortical atrophy in the brain.
and thus damage the negative feedback to the hypothalamus. Hyperactivity of the HPA axis is normalized by sufficient pharmacological treatment of depression.

As reviewed by Brunner EJ, et al., [27] depression may be associated with many medical conditions influenced by dysregulation of the HPA axis. One of the disorders is metabolic syndrome in which HPA axis abnormalities have been reported concurrently with other etiological factors [47], [80]. Hypersensitivity of the HPA axis seems to associate especially with abdominal obesity [16], [24], [30] and an association also exists between intra-abdominal fat and depression [36], [148], [174], [168], [169]. The HPA axis is involved in the associations between depression and cardiovascular diseases and depression and diabetes mellitus [125].

There are several hormonal and other biological factors that are suggested to be related to the pathophysiology of depression. As the prevalence of depression worldwide is greater among women than among men, it has been suggested that gonadal hormones, especially estrogen, may play an important role in the pathophysiology of depression among women [74], [135]. As reviewed by Rubinow DR, et al., [153], estradiol may regulate serotonergic activity by regulating the number and function of serotonin receptors in the brain. As reviewed by Epperson, et al., [52], estrogen may increase serotonin biosynthesis and affect dopaminergic function by increasing dopamine neuro transmission in the pituitary gland, hypothalamus and nigrostriatal system and mesolimbic brain regions. Estrogen treatment has been beneficial in treating depression especially in perimenopausal and postpartum depression [4], [142]. Lowered follicular phase plasma estradiol levels have been found in women with depression. The prevalence of depression among women is also high in reproductive age when estrogen levels are high. The role of estrogen in depression is not clear and needs much more research. With regard to progesterone, as per the earlier review there is
no evidence on the effect of progesterone in the treatment of depression. It is suggested that progesterone may also have a role in the pathogenesis of depression.

Thyroid dysfunction has been found to be associated with depression. As per the earlier study, alterations in thyroid-stimulating hormone response to Thyreotropin-Releasing Hormone (TRH), an abnormally high rate of antithyroid antibodies and elevated Cerebro Spinal Fluid (CSF) TRH concentrations have been documented in depressed individuals [160]. Chronobiological disturbances are common in depression, and sleeping problems are one of the most common symptoms of depression. In addition, abnormalities in sleep EEG have been found among depressed individuals. The Rapid Eye Movement (REM) sleep latency has been shown to be shortened and the first REM sleep period lengthened [20]. A higher consumption of fish has been shown to be associated with a reduced risk of depression suggesting that omega-3 fatty acids may also play a role in the pathophysiology of depression [173], [179].

Depression occurs together with many chronic somatic diseases [53], [54]. As per research a medical illness may be a risk factor for depression, and depression itself may be a causal factor in many somatic diseases such as ischemic heart disease and stroke [41], [93], [119]. Depression may hamper recovering from a somatic disease and many patients do not receive appropriate treatment for depression. Depression may be difficult to recognize in patients with somatic symptoms or patients may be ashamed of depressive symptoms and unwilling to share them with a physician.

Depression has been shown to be a risk factor for cardiovascular diseases [68], [29], [113]. Depression increases the mortality in patients with Coronary Heart disease. As per the earlier study, the associations between depression and
cardiovascular diseases are given in the Nationally Representative Mini-Finland health survey. The study was based on 5355 individuals diagnosed at baseline with chronic somatic diseases and mental disorders and followed for 6.6 years. Depression was associated with cardiovascular diseases at the baseline. In the follow-up, the risk of developing and dying of cardiovascular diseases was significantly elevated among depressed individuals, both with and without cardiovascular diseases [126]. In a study conducted by Barefoot JC and Schroll M [15], 730 individuals born in Glostrup, Denmark, were examined physically and psychologically in 1964 and 1974 and were followed for about 27 years. In the follow-up, subjects with elevated depressive symptoms had a significantly higher risk of developing ischaemic heart disease. As reviewed by Rudisch B and Nemeroff CB [154], 17% to 27% of patients with coronary artery disease have major depression, and a much larger proportion have depressive symptoms.

The mechanism behind the association between depression and cardiovascular diseases is complex and unclear, although several interaction mechanisms have been proposed. Joynt KE, et al., [97] introduced seven possible mechanisms for the relationship between depression and cardiovascular diseases such as non-compliance with cardiac rehabilitation programmes and medical regimens, clustering of risk factors (e.g. obesity, hypertension, smoking, diabetes, hypercholesterolemia), HPA axis hyperactivity and increased cortisol secretion, heart rhythm disturbances, elevated plasma levels of cytokines leading to atherosclerosis, platelet reactivity and psychological stress. As per the study activation of the HPA axis may speed up the development of cardiovascular diseases by elevated cortisol and catecholamines which have also been found in depression. Recognizing and treating depression is important among patients with cardiovascular diseases. Selective Serotonin reuptake inhibitors appear to be a
relatively safe and effective treatment for depression in patients with comorbid coronary heart disease [152].

According to World Health Organisation (WHO), diabetes mellitus is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both [56]. Type 1 diabetes mellitus comprises the majority of cases that are deficient and in which pancreatic islet beta-cell destruction is present while type 2 includes the common major form of diabetes resulting from defect(s) in insulin secretion, almost always with a major contribution from insulin resistance [73], [143], [144]. Depression has been shown to be associated with an increased risk of onset of diabetes mellitus [46], [190]. In the Epidemiologic Catchment Area (ECA) Program survey with 3481 adults it was found that MDD predicted the onset of diabetes mellitus. Diabetes is also a risk factor for depression and according to a meta-analysis by Anderson I and Rossner S [6] the presence of diabetes doubles the risk of comorbid depression. As per the earlier review, depression is associated with biological modifications that may lead to increased sensitivity of depressed individuals to type 2 diabetes. The mechanisms behind the association between depression and diabetes are still unclear. Depression is associated with such metabolic abnormalities as increased release of catecholamines, glucocorticoids and growth hormone, alterations in glucose transport and increased secretion of cytokines. These can lead to insulin resistance and eventually to diabetes. Insulin resistance has been suggested to be associated with depression [182], [183].

Most malignant cancers are experienced as life-threatening, and are thus significant stressors for individuals [66]. As reviewed by Spiegel D and Giese-Davis J [164], the prevalence of depression among cancer patients is high. It
has been suggested that chronic and severe depression may also increase the risk of cancer, speed cancer progression and increase mortality. In a recent Finnish cohort study of 10,892 women depression did not increase breast cancer risk during a follow-up of 6 to 9 years.

Patients with chronic pain often have comorbid depression [28], [48]. The prevalence rates of depression among patients with chronic pain have been found to be as high as from 30% to 54% [13]. Depression may be a consequence of pain, but depression may also be manifested as a pain symptom. As per the study, long-lasting pain may produce several maladjusted coping responses that may in turn have an effect on how the pain is experienced. The same neurochemical transmitters may be involved in depression and pain.

Depression is common among post-stroke patients: the prevalence of major depression among hospitalized subjects has been found to be as high as 19% [149]. Depression may also increase the risk of stroke. Treatment of depression among post stroke patients is important, as it also enhances recovery from stroke and improves function and cognition. As reviewed by Kanner AM [99], epilepsy is the most frequent psychiatric disorder. Lifetime prevalence of depression among epilepsy patients is 6% to 30%, and the risk of dying from suicide has been reported as much as 10 times higher compared to general population. Depression may be hard to recognize among epileptics as the symptoms are often atypical, which is why it is untreated and causes much suffering. In Parkinson disease, about 50% of the patients have depressive symptoms [120].

Huurre TM and Aro HM [88] investigated long-term psychosocial effects of persistent chronic illness in a follow-up study of subjects aged 16-32 years. Adults with persistent chronic illness limiting daily life reported more depression
and lower self-esteem than those with non-limiting chronic illness or healthy controls. No significant differences in psychosocial well-being were found between adults with any chronic illness and healthy controls. The associations between major depression and characteristics of chronic illness were studied in a general population study of 509 Finnish adolescents and 433 young adults. As a result, chronic illness, respiratory allergies, poor self-rated health and frequent sick-days were associated with depression. The associations were stronger in the younger age group [72].

Within the northern Finland 1966 Birth Cohort, atopic disorders have been found to increase the risk of depression about two to three-fold when compared with subjects without atopic disorders [180], [181]. With regard to risk factors of cardiovascular diseases, depressive symptoms measured by Beck’s Depression Inventory during early adulthood have been found to be associated with higher levels of carotid intima-media thickness in men, but not in women [50]. In a study conducted by Elovainio M, et al., [51] higher levels of depressive symptoms were associated with higher levels of C-Reactive Protein (CRP) among young adults. A similar finding was found in the northern Finland 1966 Birth Cohort among men [117], suggesting that an inflammatory process may contribute to the pathophysiology of depression.

Some previous studies have suggested an association between low birth weight and later depression or psychological distress [187], but contradictory findings have also been presented [132]. In a study conducted by Gale CR and Martyn CN [64], birth weight and risk of psychological distress and depression at the ages of 16 and 26 years were examined. The results showed that women whose birth weight was ≤ 3 kg had an increased risk of depression at the age of 26 years compared with those who weighed >3.5 kg and men who weighed < 2.5 kg
at birth were more likely to report a history of depression at the age of 26 years compared with men of normal birth weight.

Thompson C, et al., [178] investigated the association between birth weight and depression in late life in the Hertfordshire birth cohort study of 882 subjects at the age of 68 years. As per study among men there was an association between low birth weight and risk of depression measured by the Geriatric Depression Scale while no association was found among women. In a Danish study of 12270 men, no relation between birth dimensions and later hospital-treated depression was found. In another recent study of the Aberdeen children of the 1950s low birth weight for gestational age was associated with adult psychological distress measured by four items from the 12-items specified. The authors suggested that children born at full term but having low birth weight are at higher risk of psychological distress in adulthood.

The first menstrual period in girls is called menarche. The mean age of menarche is around 13 years [186], and it is controlled by genetic, environmental and psychosocial factors [2], [151]. Growth in utero and childhood is associated with the age at menarche [45]. The hormonal mechanism behind menarche consists of the development of positive estrogen feedback on the pituitary and hypothalamus.

2.3 ANN IN DATA MINING

ANN represents a useful technique for data mining applications [40], [114]. It can be trained to properly represent various categories occurring in a data set. In large databases and data warehousing techniques, the size of data sets can be huge.
which may result in inefficient ANNs learning. It is useful to find an efficient and practical training set size without compromising the results. Two important issues play a major role in the learning process of an ANN. The first one is the proper selection of the data set size and the second is the sampling distribution of the data set. Samples represent positive and negative examples in supervised learning [87]. Many researchers have highlighted the importance of having adequate data to train, test and validate ANNs [76]. Data mining applications have traditionally used inductive logic to extract rules describing various interesting conditions that occur in the data set. ANNs have been demonstrated to be an effective tool for mining large data sets and to extract relevant knowledge. Although many researchers do not associate the use of ANNs with rule extraction, successful results in extracting logic-oriented rules from the weights of a trained ANN have been demonstrated for a specific type of domains [101].

ANNs are used for data mining [86], [19] with the perspective of training and testing using a limited data set. A trained ANN is then used in conjunction with additional or unseen data sets for classification based upon its previous training phase. The ability of an ANN to generalize its learning is dependent upon the proper selection of its training and testing data sets. Generalization features of ANNs are not trivial since in some conditions neural network gaps can occur [100]. In other cases, ANNs can be over trained and it can reach a saturation level that increases its memorization ability rather than its generalization ability.
2.4 SUMMARY

This Chapter presents the review of literature related to depression diagnosis using ANN and data mining. Chapter 3 discusses the functional update neural network model compared with conventional back propagation algorithm to prove its performance in data mining.