1 (nda) has been established based on diagnostic

Life, Emotions

1 INTRODUCTION1. 1 Depression1.

1. 1 Depression as a disease entityDepression is a serious psychiatric disorder. It is characterized by a wide range of symptoms: melancholic feeling, anecdonia, loss of interest, irritability, suicide, sleep disturbances and food intake and so on. It belongs to the broader category of emotional disorders.

This disorder may show extensive variation in both symptoms and presentation. It is likely that two patients who are depressed will not share a common symptom with each other. The above symptoms and the disease as a whole often result in the development of some degree of disability. This may create the patient's inability to function and respond socially or to work, to become active and ultimately to survive (Wong and Licinio, 2001). For five decades, the diagnosis of depression and major depressive disorder (NDA) has been established based on diagnostic criteria, internationally accepted. The main and most frequently used are DSM V, 2013? Diagnostic and Statistical Manual of Psychiatric Disorders and ICD-10. These control the symptoms that occur to the sufferer and persist for more than two weeks.

Emotional disorders include bipolar disorder or otherwise manic depression, characterized by alternation of mania and depression phases. There are other, milder or shorter forms of depression that can be described as dysthymia, but the distinction between disorders remains an often difficult problem. In general, it is considered that depression is a heterogeneous syndrome consisting of a set of diseases and disorders, perhaps even with different causes and pathophysiology (Nestler et al., 2002a).

While the various biological mechanisms involved in depression may seem unrelated to each other, indicating that NDD can actually represent several biologically distinct diseases, the studies so far have shown that all of these pathways are linked and interconnected. MDS is referred to as the most frequently occurring mental illness. According to the World Health Organization, depression is the fourth cause of reduced functionality and disability in the world, and is projected to be the first in 2020. It is estimated that life expectancy is 20% of the population, that is to say, sometime in this lifetime rate is estimated to get sick. It is therefore evident that depression is a social issue with a great impact on the social fabric and its coherence, because it causes problems in interpersonal relationships, restricts the work activities of the sufferer, brings increased financial burden to society and increases mortality. 1. 1.

2 Impact of depressionDepression is a major problem for humanity. Suffice it to imagine that this disease worldwide is responsible for greater loss of function and disability, if it is calculated on the basis of years lost to disability (YLD). In particular, due to depression each year 76. 4 million years are lost worldwide due to disability, with the second and third cause being responsible for 53. 9 and 43. 6 million years (neck pain / back pain and iron anemia, respectively).

These lost years account for 10. 3% of the global burden, demonstrating how hot and important a problem this disease is. It is estimated that around 350 million people worldwide suffer from this disease. Also, if the disability is calculated and the mortality it causes, depression is ranked ninth, behind

only extremely fatal diseases and conditions such as neoplasia, cardiovascular diseases and strokes.

1. 1. 3 The hypotheses of neurotransmitters in depressionA basic hypothesis on the pathophysiology of depression, the case of monoamines, revolves around the position that depression is caused by a change in the levels of one or more of the monoamines, including serotonin (5-HT), norepinephrine (NE) dopamine (DA). Evidence for serotonergic theory includes the finding that serotonin metabolites are reduced in patients diagnosed with NSC and that antidepressants such as tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) and inhibitors serotonin-noradrenalin reuptake inhibitor have been shown to increase serotonin levels in the brain. In addition, chronic antidepressant therapy has been shown to downregulate the inhibitory presynaptic 5-HT1A somato-deficient autoreceptors.

As these presynaptic autoreceptors inhibit 5-HT release, regulation to lower concentrations increases 5-HT release, which has been associated with an antidepressant response. Similarly, the removal of tryptophan, a necessary amino acid required for 5-HT synthesis, has been shown to induce symptoms of depression in patients successfully treated for depression with an antidepressant, although tryptophan has no effect on patients with depression were not treated. These findings suggest that elevated serotonin levels are necessary for antidepressant action, although reducing serotonin alone may not be enough to cause depressive symptoms. In addition, genetic abnormalities in serotoninergic neurotransmission have been associated with depression.

For example, serotonin-linked polymorphic receptor-linked polymorphic region, 5-HTTLPR is a replication in the gene encoding the serotonin transporter. The s / s genotype of this region is associated with a decrease in serotonin receptor expression associated with increased susceptibility to depression. Correspondingly, variant G (-1019) of the Htr1A promoter which controls the expression of the 5-HT1A receptor is associated with reduced 5-HT1A receptor expression. Both of these polymorphisms have been associated with emotional disturbances and depressive symptoms. NE is also involved in mood regulation, as evidenced by the fact that drugs that inhibit NE re-uptake, such as TCA, SNRI, noradrenaline-dopamine reuptake inhibitors (NDRIs), and those that increase adrenergic neurotransmission, such as mirtazapine, are effective antidepressants.

Among other things, chronic stress is thought to alter the noradrenergic system, which is linked multiplely to both the neuroendocrine and the immune system. For example, chronic stress leads to an increase in the tyrosine hydroxylase activity, the enzyme involved in the noradrenergic composition in the locus of the subterranean locus. Stress also increases the production and release of NE causing increased secretion of corticotropin releasing factor (CRF) from the hypothalamus, which in turn activates the release of adrenocorticotropin hormone (ACTH) from the pituitary gland which then stimulates the adrenal cortex in order to release NE and cortisol.

Increased levels of cortisol and NE then increase the sympathetic autonomic nervous system (ACS) activity and the release of cytokines, which have been shown to have an effect on the hypothalamus – pituitary – adrenals (HPA)

axis as well as neurotoxic effects . The intramedullary pathway, consisting of dopaminergic neurons coming from the ventral tegmental area (VTA) and projected into the inclined nucleus, mediates the reward path and other functions, such as the treatment of motives. There are several indications that involve the pathological dopaminergic neurotransmission in the pathophysiology of depression. These are based on the fact that some symptoms of depression, including anodynia and reduced mobilization, are related to a malfunction of the reward system. It is also suggested that neurological disorders of dopamine production, such as Parkinson’s disease, can cause depression. Finally, the fact that antidepressants such as bupropion increase dopamine levels in the brain provides indirect evidence of the role of dopamine in mood regulation.

In a concept of depression, Watt and Panksepp have suggested a disorder of the inter-median system in which a person who has undergone significant psychological pressure / stress or loss develops a disturbance of the reward path, appearing as anxonia and despair. Advocating this theory, studies have shown that chronic stress causes neuropathic alterations in the dopaminergic midterm tract and that these changes are implicated in the change in brain-derived neurotrophic factor (BDNF) and neuroplasticity. Serotonin, noradrenaline and dopamine interact and interfere with their brain concentrations. For example, dopamine has been shown to have an inhibitory effect on the release of noradrenaline from the subterranean locus, while noradrenaline has a stimulatory and inhibitory effect on the release of dopamine in the abdominal capillary region through the stimulation of ?-1 and ?-2 receptors, respectively. Both noradrenaline and dopamine increase

the release of serotonin from the dorsal core of the seam through the ?-1 and D-2 receptors, respectively. These findings show that the moles do not exert their neurotransmitter function alone, but rather that these neurotransmitter systems are interconnected. A change to one of these neurotransmitters may affect the functioning of the other two. Another neurotransmitter, glutamate or glutamate, has also been implicated in mood regulation.

The fact that ketamine, a NMDA receptor antagonist, acts as a potent and rapid-acting antidepressant has been of great interest in the involvement of the glutamatergic system but has identified it as a potential target for antidepressant treatment. Clinical studies have shown that ketamine leads to rapid antidepressant action, occurring in hours rather than weeks, as with traditional antidepressants. Its action has been hypothesised to occur through the antagonism of NMDA receptors in GABAergic endonucleases, which reduces inhibition of glutamate release in glutamatergic neurons. This decrease in inhibition leads to glutamate elevation and then selective binding to AMPA receptors. Increased stimulation of AMPA receptors leads to several sequences of second messengers, including inhibition of eEF2k, inhibition of GSK-3 and mTOR activation, all leading to increased neuroplasticity. Ketamine has also been shown to increase the release of BDNF in hippocampal pyramidal neurons, which also increases neuroplasticity. These findings suggest that glutamate may be involved in mood regulation, presumably through the maintenance of neuroplasticity. 1.

1. 4 Reducing the HPA axis and responding to stressStress and depression are often related. Anxiety and life experiences can cause depressive episodes in vulnerable individuals and childhood anxiety in the form of abuse or neglect increases the risk of depression later in life. In recent decades, they have been found in patients with depressed HPA disorders associated with a hyperactive response to stress.

Some of these changes include CRF hypersecretion from the hypothalamic subcortical nucleus, impaired negative feedback of the HPA axis, adrenal swelling, hypercortisolaemia, and decreased cortisol suppression in response to dexamethasone. In a subset of patients with depression, a hypersensitive HFA axis results in the release of high cortisol concentrations in response to lower stress levels as well as chronically elevated cortisol levels. The neurobiological consequences of elevated levels of cortisol in the brain include some mechanisms that can explain the depression-related effects of hypercholesterolaemia. In the next paragraph, we will look closely at the relationship between the HPA, stress and depression axis, linking these systems and diseases to the sex factor (see 1.

5. 1). Three brain regions that have been shown to be affected by elevated glucocorticoid levels are prefrontal cortex, PFC, hippocampus and amygdala. If we want to look at the functions of these areas, PFC deals with the executive function and the processing of emotion, the hippocampus deals with memory and learning, and the tonsil is involved in the treatment of emotions, among others. Chronic stress has been shown to reduce the

complexity of dendritic pyramidal neurons and increase GABAergic neuronal transcriptional activity in PFCs, reducing activity in this area.

As PFC is involved in cognitive processing of emotions created by subcortical structures such as amygdala, reduced activity in this area leads to inadequate treatment of negative emotions. In addition, elevated cortisol levels reduce the ability of the hippocampus to adapt to a changing environment. Animals exposed to chronic stress exhibit reduced plasticity and long-term potentiation (LTP) in hippocampal CA1 neurons, a glucocorticoid receptor mediated effect, leading to reduced adaptation and learning. In addition to the above cellular changes, high levels of cortisol also alter functional connections in the brain that deal with emotional and adaptation processing. Chronic stress reduces the LTP of the projections from the amygdala to the PFC and increases the stimulation of the tonsil in response to stress, resulting in increased resistance to stress and reduced cognitive treatment. Chronic stress also shifts hippocampus learning to striatal-based learning, as glucocorticoids cause the tonsil detachment from the hippocampus and increased connectivity to the striatum.

Another concept of depression, the Diathesis-Stress model, provides a neurological basis for a link between chronic psychological stress / depression and depression. This model counteracts depression and many other psychiatric disorders as developmental deviations that evolve over time. Mood is defined as a predisposition, which can be either biological or psychological. Depression therefore according to this view is not caused by an isolated biological or psychological factor. On the contrary, in a vulnerable

patient predisposed to a negative response to stress, recurrent stressors can cause the occurrence of the pre-existing vulnerability. An example of this view could be the genetic polymorphisms in the serotonin transporter gene mentioned above.

Individuals with the s / s genotype of this polymorphism have been shown to react more strongly to stressful conditions and have increased rates of depression. This mood or genetic predisposition is not enough to cause depression itself until it is exploited by environmental pressure factors. It is the combination of stressors and a pre-existing vulnerability and predisposition, nature and upbringing that causes the disorder. The HPA axis can be a biological basis for this process, in which initial early stress leads to a functional hyperactivity of the HPA axis and a predisposition towards a maladaptation reaction to anxiety instead of directly leading to depressive symptoms. When the concept of stress is expanded by objective external factors and internal psychological pressure, chronic stress-inducing depression is offered in many psychological theories.