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COMBINED COGNITIVE-BEHAVIORAL THERAPY (CBT) AND PSYCHOPHARMACOTHERAPY IN THE TREATMENT OF DEPRESSION

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Abstract: This study aims to investigate the combined use of cognitive behavioral therapy (CBT) and the Psychopharmacotherapy in depression treatment. A bibliographic review that was carried out, looking for original works, bibliographic reviews, meta-analysis, and specialized textbooks. The combination of both therapies has been the first choice as a depression treatment in both mild and moderate patients and hospitalized patients classified with severe depression. The isolated use of antidepressants can lead to a discontinuation because of its side effects. The combine treatment increased the adherence and decreased the discontinuation rate of the therapy. The CBT as a solo treatment or combined with medication displayed superior efficiency rate than Psychopharmacological treatment alone. This research data suggests that CBT is essential in treatments with patients with chronic depression and with childhood traumas.

Keywords: Depression. Cognitive-behavioral. Psychopharmacotherapy. Antidepressants.

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TERAPIA COMBINADA COGNITIVO-COMPORTAMENTAL (TCC) E PSICOFARMACOTERAPIA NO TRATAMENTO DA DEPRESSÃO

Resumo: Com objetivo investigar a terapia combinada, cognitivo-comportamental (TCC) e psicofarmacoterapia no tratamento da depressão, realizou-se uma revisão bibliográfica, buscando trabalhos originais, revisões e metanálises, em periódicos indexadas e livros textos especializados. A combinação destas terapias tem sido a primeira escolha no tratamento da depressão em pacientes ambulatoriais, e em pacientes internados em estado grave de depressão. Já o uso isolado de antidepressivos está sujeito ao abandono da terapia em consequência dos efeitos colaterais. A combinação de tratamento aumentou a adesão e reduziu a taxa de abandono. A TCC como tratamento único ou combinada com medicamentos, mostrou eficácia superior a psicofarmacoterapia, isoladamente. A TCC tem se mostrado essencial no tratamento de pacientes com depressão crônica e com histórico de traumas na infância.

Palavras-chave: Depressão. Cognitivo-comportamental. Psicofarmacoterapia. Antidepressivos.

Introduction

According to the revised text of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM5), depression includes: Rupt Mood Regulation Disruptive Disorder, Major Depressive Disorder (MDD), Persistent Depressive Disorder (dysthymia), Disorder Premenstrual Dysphoric, Disorder Depressive Induced by Substances/Drugs, Depressive Disorder Dueto Another Medical Condition, Other Specified Depressive Disorder and Unspecified Depressive Disorder. These disorders have in common the presence of a sad, empty or irritable mood, accompanied by somatic and

cognitive changes that significantly affect the individual's ability to function (DSM5,2014).

Botti et al, (2010), pointed out several factors related to the appearance of mental disorders, among the mare: poverty, sex (gender), age, conflicts, disasters, physical illnesses and the family and social environment. The authors also state that the Mundial World Health Organization has been warning since the 1990s, about the prominent place that depression has occupied among public health problems, being considered one of the main causes of disability in the world.

The World Health Organization reported that depression is one of the most common psychiatric disorders, affecting 350 million people worldwide (WHO, 2012), of all ages and social classes, any culture, and education level (MARTINS&AGUIAR, 2006). It has a high prevalence in adolescence and old age, and has been getting worse in the current century (FERREIRA et al. 2016).

Duailibi and da Silva, (2014) highlighted that the 2:1 relationship between women and men at MDD has been questioned and that a study presented at the XXIII Annual Meeting of the Society of Behavioral Medicine in the United States, demonstrated that men are less likely to report depressive symptoms if asked directly about depression, but if asked indirectly for example about well-being, they report a greater number of symptoms.

Depression is a long-term disorder, with a high probability of recurrence over years, being responsible for suffering and loss of quality of life, both for patients and their families, causing a decrease in school performance or at work, and aggravation can lead to suicide (GREVET and KNIJNIK, 2001).

Daskalopoulou, (2016), evidenced depression as a risk factor for cardiovascular diseases. On the other hand, depression can arise as a result of disabilities and limitations associated with chronic diseases (KATON et al, 2007).

The report of the World Health Organization (WHO) (WHO, 2001), highlights severe depression as the main cause of disability in the world, being the fourth among the main causes of pathologies worldwide. The 2009 WHO report (WHO, 2009), indicates that, until 2020, depressive disorder should occupy the second place among all disabling diseases, with cardiovascular diseases just ahead of it.

Currently cognitive-behavioral therapy (CBT) and the psycho pharmacotherapy are very effective tools in the treatment of depression. These therapeutic forms are effective when used alone or in combination, however studies are needed that examine specifically the comparative effectiveness of psychotherapies with pharmacotherapy (KNAPP,2009).

The treatment of depression comprises managements of different orders, which have objectives: to improve the quality of life, reduce the need for hospitalization, minimize the risk of suicide and reduce the recurrences of depressive crises, that is, eliminate symptoms, recover the individual's functional and social capacity, avoiding the recurrence of the disorder. For this it is necessary to empathize and adhere to the treatment, be it psychotherapeutic, medicated or combined. In this sense, the treatment of depression usually involves the use of psychotherapies and /or medications, associated or not (BECK et al, 1979).

In recent years, several studies have been conducted on the effectiveness of treatments for depression. Such research provided

empirical support for interventional procedures that contributed to the reduction or remission of depressive symptoms (SEGAL et al, 2002). Among these practices are psychotherapies, pharmacotherapeutic treatments and combined treatments. This review will focus on studies that evaluate the use of combined CBT therapy and psychopharmacotherapy for depression, looking at the possible benefits that this practice offers to patients.

1 Development

1.1 Cognitive-behavioral model of depression

The term cognitive therapy (CT) and the generic term CBT are used as synonyms to describe psychotherapies based on the cognitive model. The term CBT is also used for a group of techniques in which there is a combination of a cognitive approach and a set of behavioral procedures. CBT is used as a broader term that includes both standard CT and theoretical combinations of cognitive and behavioral strategies (BECK, 2005).

The cognitive-behavioral model was proposed by Aaron Beck in the early 1960s and 1960s. This researcher observed that humor and negative behaviors us were usually the result of distorted thoughts and beliefs and not unconscious forces according to Freudian theory (BECK, 1963).

Thus, depression could be understood as a result of dysfunctional cognitions and cognitive schemes. Depression patients believe and act as if things are worse than they really are. This form of reasoning generated an approach emphasizing the thought called "cognitive therapy" (BECK,1963).

The cognitive model of depression highlights that the cognitive, motivational and vegetative symptoms of this disorder can be caused and maintained by distortions in the three level of cognition: automatic thoughts (ATs), intermediate beliefs and central or nuclear beliefs (schemas). ATs are part of the cognitive processing flow underlying the individual's conscious processing. They occur quickly through the assessment of the meaning of an episode in your life (NEUFELD and CAVENAGE, 2010).

Intermediate beliefs are rules, attitudes or assumptions that arise in the form of affirmations such as "if", then "or" "should", are rigid, inflexible and imperative. It is also called underlying or conditional assumptions. They form a set of beliefs, generally coherent, that support the central beliefs with which they are related (NEUFELD and CAVENAGE, 2010). According to White (2003), each person has a set of conditional beliefs that have been learned and added throughout life, with the purpose of giving meaning to the world.

Central or core beliefs, also called schemas, are acquired very early in development, and act as true "filters" where recent information and experiences are processed. These beliefs derive from identification with significant people and perception of the attitudes of others towards yourself, but they are shaped by personal experiences. In this way, a child's environment facilitates the appearance of particular types of schemes, as well as inhabiting them. The scheme of a well-adjusted person, allows realistic assessments, whereas the schemes of ill-adjusted individuals lead to distortions that generate psychological disorders (Beck,1976).

Beck et al (1997) also emphasize that the central beliefs represent the mechanisms that people develop to deal with everyday

situations, that is, the way individuals perceive themselves, others, the world, and the future.

In this sense, Beck, (1967) postulated the so-called cognitive triad in which the depressed individual is suffering from the negative view of himself, his environment and the future. Therefore, depressed individuals perceive themselves as inferior, inadequate, unwanted, incapable ("nothing that I do works"), perceive the environment in which they are inserted as hostile, as insurmountable obstacles ("people treat me bad"); the vision of the future becomes influenced by negative cognitions, as it considers having insufficient resources to modify the future ("there is no use doing anything, I will never get out of it"), and consequently develop hopelessness (KNAPP et al, 2004).

When thoughts are associated with suicidal ideation, hopelessness makes them even more intense, with death being understood by many depressive patients as a relief from psychological suffering or as the only way out of the perception of an impossible to be supported situation (POWELL et al, 2008).

Another item of central interest in the study of depressive disorders is cognitive distortions, or systematic errors in perception and information processing. Individuals with depression have a tendency to structure experiences in an absolute and inflexible way, resulting in errors in interpretation how much to performance and judgment of external situations (BECK, 1995).

According to Powell et al, (2008) the most common cognitive distortions in depressed patients were observed by Beck et al (1979), as a typological system, and among them are: arbitrary inference (early conclusion and with little evidence), selective abstraction

(tendency to choose evidence of its poor performance), over generalization (tendency to consider that an even or negative performance will occur at other times) and personalization (personal attribution usually of a negative character) among others.

The distortions stem from rules and assumptions, which are stable patterns acquired throughout the life of the individual with depression. These rules and beliefs are sensitive to activation from primary sources such as stress and often lead to in effective interpersonal strategies (RUPKE et al, 2006).

Cognitive therapy for depression is a form of treatment that helps patients to modify beliefs and behaviors in order to change their depressed mood. For this purpose, CBT uses the following therapeutic strategies: 1) focus on automatic thoughts and depress genic schemes; 2) focus on the person's style to relate to others; and 3) change in behaviors the end in get better coping with the problem situation (LEAHY, 2017).

This therapy encourages the patient's active participation in the treatment, leading them to: a) identify their own distorted perceptions; b) recognize your negative thoughts and try to replace them with alternative thoughts that reflect reality more closely; c) find the evidence that supports negative and alternative thoughts; and d) generate more accurate and credible thoughts associated with certain situations in a process called cognitive restructuring (BECK, 1995).

1.2 Biological model of depression

Depression is currently seen as the combination of biological and psychological factors, in which the manifestations and intensities vary according to genetic, environmental and social factors.

It is also known that the biological basis of depression is based on theories that consider neurotransmitters (NT) and brain receptors as determining elements in depression. Among NT are monoamines such as catecholamines (dopamine (DA) and noradrenaline (NE)) and indolamine (5-hydroxytryptamine or serotonin (5HT)) (MÖSSNER, 2007).

Driven by a possible involvement of the NT in depression, several hypotheses have arisen over the decades. The first hypothesis, was calling Hypothesis Catecholaminergic which was based on a possible catecholamine deficiency. Then came the Serotonergic Hypothesis, which was based on the fact that selective serotonin reuptake inhibitors (SSRIs) had been used with some success in the treatment of depression (MÖSSNER, 2007).

The demonstration that the continued use of tricyclic antidepressants (TADs) increased the behavioral response to AD, and the fact that the mechanism of action of TADs and monoamine oxidase inhibitors (MAOIs), increase the concentration of monoamines in cerebral synaptic clefts, supported the Dopaminergic Hypothesis. This and other information have over the years strengthened the relevance of the monoaminergic hypothesis of Depression (MÖSSNER, 2007).

On the other hand, there is great difficulty in considering these hypotheses as definitive since, whatever the antidepressant medication used, promotes an immediate increase in monoamines in the synaptic clefts, but the clinical improvement does not come after a few weeks. And there is still evidence that some substances increase monoamine levels without improving depression (BAHLS, 1999).

Recent advances in neuroimaging studies allow a greater sense of the areas directly affected in depressed brains, having reduction volume and hypometabolism in the frontal lobes, basal ganglia and other medial and temporal structures of the brain, especially the connections between the basal nuclei, frontal lobes and the limbic system. Suggesting that brain changes in depression are located in more than a different structure and regions of the brain (ROZENTHAL, 2004).

1.3 Antidepressant medications

Since the late 1950s, antidepressant therapy has been performed in clinical practice, which has represented an advance in the treatment and understanding of possible mechanisms related to depressive disorders (PAYKEL, 1992 and STAHL, 1997). Thus, depression has become a problem that can be treated. Until the 1980s there were two classes of antidepressants, TDAs and MAOIs. These, although very effective, had side effects, potentially lethal in cases of overdose (KESSEL, 1995). Beyond of that only 70% From patients if benefit with the TDAs, others need another class of antidepressants or even electroconvulsive therapy (MORENO et al, 1993) and there is still a lack of explanation for how antidepressants work (MORENO et al, 1999; SOUZA et al, 2015).

Antidepressants, regardless of chemical structures, have in common the ability to immediately increase the availability of one or more NT in the synaptic cleft. This effect is essential for the pharmacological response, but it does not explain the delay for the initiation of the clinical response (from 2 to 4 weeks). The mismatch between treatment and clinical response may be related to adaptive processes,

such as a sub sensitization of recipients whose resolution correlates with the beginning of clinical improvement (STAHL, 1997; SOUZA et al, 2015).

2 Method

A literature review was carried out, seeking out works original, bibliographic reviews and meta-analyzes, indexed (in CAPES journals, Lilacs PubMed, Medline, SciELO) and specialized text books, in order to describe the relationship between the combined use of CBT and Psychopharmacotherapy.

The inclusion criterion was the article dealing with therapeutic processes in unipolar depression regardless of the degree or presence of comorbidity and treatment being unique (CBT or antidepressants) or CBT association with pharmacotherapy.

3 Results and discussion

According to De JONGHE et al, (2001) The psychotherapy combined with psychopharmacotherapy is the first choice for treating depression in outpatients. Since CT and CBT can be useful, not only for outpatients, but also for hospitalized patients with severe depression, even when used alone (ANTONUCCIO, 1995; POWELL, et al, 2008).

Greenberg and Fisher, (1989) carried out an extensive review verifying several clinical trials that compared active and directive psychotherapies (such as cognitive and interpersonal therapies) to psychopharmacotherapy with antidepressants. The results showed

that outpatients undergoing psychotherapy evolved as well or sometimes better than those who received medications.

When CT compared to imipramine (TDA) in depression, it was concluded that CT had significantly better results. However, this study did not have a placebo group as a control (RUSH et al, 1977).

In the 1980s, there was a considerable increase in the number of studies, which allowed a meta-analysis to be carried out including 28 studies, in which it was shown that CBT was superior to antidepressants in the treatment of depression (DOBSON, 1989). In the subsequent years, other studies came indicating that CBT was significantly effective in depression and that it guaranteed a longer duration of effect compared to psychopharmacotherapy.

In a multicenter research on depression at the National Institute of Mental Health (NIMH), CBT was compared with interpersonal therapy (IPT), pharmacotherapy with imipramine and a placebo group. CBT was as effective as IPT and imipramine in mild and moderate depressions, however, in more severe depressions, IPT and imipramine showed better outcome (ELKIN et al, 1989).

Further analysis of this study by DeRubeis et al, (1999) showed significant differences in efficacy in different centers. In Philadelphia, where therapists' loyalty to the model was more consistent, CBT, IPT and imipramine had similar results.

McPherson et al, (2005), analyzed CBT interventions in patients with depression and resistant to drug treatment. Control group studies underwent intervention with CBT and showed a reduction in depression scores after. Studies without control groups, although all reported improvement, only three showed statistical significance.

On the other hand, the evidence still does not answer a series of relevant questions from a clinical point of view, such as: definition of treatment according to the type and severity of depression, cost-effectiveness of approaches combined and specific approaches for individual patients. The studies clinical provide more comprehensive responses, related to the general effectiveness of interventions, being understood more as a basis for the indication of certain therapies (KNAPP et al, 2004).

Harrington et al, (1998) performed a meta-analysis of the effectiveness of CBT in adolescents and children with depressive disorder, with ages ranging from 6 to 19 years. Despite the small number of studies found, the rate of improvement suggests that CBT is as effective as ATCs.

Dobson, (1989) carried out a review that involved eight studies with a total of 721 depressed patients where it was compared to CT with tricyclic antidepressants. The results showed that CT was superior to psychopharmacotherapy when the Beck depression inventory (BDI score) was used, patients undergoing CT achieved an improvement of 70% above the average of patients treated with psychopharmacotherapy.

Antonuccio et al, (1995), reviewing controlled clinical studies not restricted to CT, suggest that psychotherapeutic treatments, particularly CBT, are at least as efficient as drugs in the case of severe depressive disorder.

Another clinical trial was carried out by Keller et al (2000), which involved 681 patients with non-psychotic MDD in which nefazodone was compared to CBT in a combined and isolated study. 16 to 20 sessions were performed in 12 weeks, with the group that

received combined treatment showing remission or satisfactory response in 85% of the cases while the nefazodone group alone obtained the rate of 55%.

The randomized clinical trial carried out by Nemeroff et al, (2003) included 681 patients, from a multicenter study, with the aim of comparing monotherapy (nefazodone or CBT) with the combination of interventions, in individuals aged 18 to 75 years diagnosed with chronic MDD. Among the sample participants, 65% were victims of abuse during childhood or were subjected to stressful events of great importance, such as: sexual or physical abuse, loss of a parent before the age of 15, or parental neglect. The results made it clear that patients who suffered early childhood trauma responded better to psychotherapy compared to patients treated with antidepressants alone, and even combination therapy (nefazodone and CBT) was only weakly superior to psychotherapeutic monotherapy.

Even when variables such as age, gender, race and severity of depression at the baseline are controlled, psychotherapy with or without the association of nefazodone remained superior to treatment with only the ingestion of the drug. Individuals with chronic depression and child trauma showed 48.3% remission of symptoms with psychotherapy, compared with 32.9% treated with nefazodone, whereas combined treatment led to remission of symptoms in 53.9% of patients. The data suggest that psychotherapy is essential in the treatment of patients with chronic depression and with a history of childhood trauma (NEMEROFF et al, 2003).

De Oliveira, (1998) concluded that, although the drugs are effective in improving sleep-related symptoms, psychotherapy was

more effective in helping patients with depression and apathy. In addition, unlike psychotherapy, medications proved to be incapable of helping out patients to adjust socially, in relation to professional performance and interpersonal relationships.

Systematic reviews and meta-analyzes have found controversial results, although in clinical practice there is a common sense that combined approaches are always preferable. Some reviews do not find superiority in relation to isolated treatments (KNAPP et al, 2004).

Most of the reviews presented included studies comparing psychotherapy with ATCs, drugs that have been used more and more strictly, due to the low tolerability on the part of many patients, which allows a high rate of interruption treatment, due to adverse effects and end up compromising the effectiveness of the medication. Wexler and Cicchetti, (1992) state that when the rate of treatment abandonment is taken into account in the analysis along with the rate of clinical improvement, psychopharmacotherapy mac becomes much lower than isolated psychotherapy or combined treatment. Other studies that included nefazodone a non-tricyclic antidepressant, the results indicated that psychotherapy and combination therapy have greater therapeutic efficacy in depression greater.

Most recent findings, point what the combination in psychotherapy and psychopharmacotherapy have been more accepted by patients than exclusive pharmacotherapy, with a lower proportion of treatment abandonment (De Jonghe et al, 2001). On the other hand, the new antidepressants are more selective and have a profile of greater tolerability on the part of patients.

Conclusions

Currently, depressive disorder has been identified as one of the biggest problems for health services worldwide, and several studies have emphasized the therapeutic efficacy of CBT in depression, making this form of therapy, considered a major instrument. Valuable in the treatment of this disorder. The combination of psychotherapy and psychopharmacotherapy, has been the first choice for treating depression in outpatients and CBT has been useful even in isolation for patients hospitalized in a severe state of depression.

It was shown in this review that CBT, combined or not with antidepressants, causes a reduction in the symptoms of MDD and that psychotherapeutic interventions are important tools in the management of depression regardless of age, sex (gender), social class or degree of depression. Some studies have shown that CBT is superior as a single treatment or combined with antidepressants, in relationship monotherapy pharmacological. Other studies have indicated that CBT is equivalent in effectiveness to TDAs in adolescents and children with mild and moderate depressive disorder.

Clinical trials have observed remission of depression in 85% of patients who received combined CBT treatment with antidepressants, against 55% of patients who received medication as the only form of therapy. Another controlled clinical study, showed that CBT and other psychotherapies, are at least as efficient as drugs in the case of severe depressive disorder. CBT was of great relevance for depressed patients who presented early trauma, they responded better to psychotherapy than to psychopharmacotherapy, and the

combined therapy with antidepressants showed slight superiority to monotherapy with CBT.

The study suggests that psychotherapy is essential in treating patients with chronic depression especially those with a history of childhood trauma.

Bibliographic references

AMERICAN PSYCHIATRIC ASSOCIATION et al. **Diagnostic and statistical manual of mental disorders: revised text (DSM 5).** Artmed, 2014.

ANTONUCCIO, D. Psychotherapy for depression: No stronger medicine. 1995. **American Psychologist**, v. 50, p.450-452, 1995.

ANTONUCCIO, et al., Psychotherapy versus medication for depression: challenging the conventional wisdom with data. **Professional Psychology: Research and Practice**, v. 26, n. 6, p. 574, 1995.

BAHLS, S. C. Depression: a brief review of the biological and cognitive foundations. **Interaction in Psychology**, v. 3, n. 1, 1999.

BECK, A. T. Thinking and depression: I. Idiosyncratic content and cognitive distortions. **Archives of general psychiatry**, v. 9, n. 4, p. 324-333, 1963.

BECK, A. T. Cognitive therapy and the emotional disorders. New York: International Universities Press; 1976.

BECK, A. T. et al. Cognitive therapy of depression. **New York: Guilford Press Google Scholar**, 1979.

BECK, A. T. Cognitive Therapy: Past, Present and Future. **Journal of Consulting and Clinical Psychology**, v. 61, n. 2, p. 194-198, 1993

BECK, A. T. **Cognitive Depression Therapy**. 1ª ed., Porto Alegre, Medical Arts, 316 p. 1997.

BECK, A. T. The current state of cognitive therapy: a 40-year retrospective. **Archives of General Psychiatry**, v. 62, n. 9, p. 953-959, 2005.
BECK, J. S. **Cognitive therapy: Basics and beyond**. New York: Guilford Press; 1995.

BECK, J. S. Introduction to cognitive-behavioral therapy. **BECK, J. Cognitive-Behavioral Therapy: Theory and Practice**, p. 21-23, 2013.

BOTTI, N. C. L. et al. Prevalence of depression among adult men living on the streets in Belo Horizonte. **J Bras Psiquiatr**, v. 59, n. 1, p. 10-16, 2010.

CAMARGO, J.; ANDRETTA, I. Cognitive-behavioral therapy for depression: a clinical case. **Clinical Contexts**, v. 6, n. 1, p. 25-32, 2013.

DASKALOPOULOU, M. et al. Depression as a risk factor for the initial presentation of twelve cardiac, cerebrovascular, and peripheral arterial diseases: data linkage study of 1.9 million women and men. **PLoS One**, v. 11, n. 4, p. e0153838, 2016.

De JONGHE, F. et al. Combining psychotherapy and antidepressants in the treatment of depression. **Journal of Affective disorders**, v. 64, n. 2, p. 217-229, 2001.

De OLIVEIRA, I. R. The treatment of unipolar major depression: pharmacotherapy, cognitive behaviour therapy or both? **Journal of clinical pharmacy and therapeutics**, v. 23, n. 6, p. 467-475, 1998.

DOBSON, K. S. A meta-analysis of the efficacy of cognitive therapy for depression. **Journal of Consulting and Clinical Psychology**, v.57*, n.3,* p. 414-419, 1989.

DUAILIBI, K., SILVA, A. S. M. D. Depression: DSM-5 criteria and treatment. **Brazilian Journal of Clinic and Therapeutics**, v. 40, n. 1, p. 27-32, 2014.
ELKIN, I. et al. National Institute of Mental Health treatment of depression collaborative research program: General effectiveness of treatments. **Archives of general psychiatry**, v. 46, n. 11, p. 971-982, 1989.

FERREIRA, R. A. et al. Depression: Viewpoint and knowledge of nurses from the Family Health Program of São Sebastião do Paraíso. **Libertas Scientific Initiation Journal**, v. 5, n. 2, 2016.

GREVET, E. H.; KNIJNIK, L. Diagnosis of major depression and dysthymia. **Rev. AMRIGS**, v. 45, n. 3-4, p. 108-110, 2001.

HARRINGTON, R. et al. Systematic review of efficacy of cognitive behaviour therapies in childhood and adolescent depressive disorder. **Bmj**, v. 316, n. 7144, p. 1559-1563, 1998.

KATON, W.; LIN, E. H. B; KROENKE, K. The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. **General hospital psychiatry**, v. 29, n. 2, p. 147-155, 2007.

KESSEL, J.B; SIMPSON, G. M. Tryciclic and Tetracyclic Drugs. In: Kaplan HI, Sadock B.J, editors. Comprehensive Textbook of Psychiatry. 6th ed. Baltimore: Williams e Wilkins; 1995. p. 2096-112

KNAPP, P. et al. **Cognitive-behavioral therapy in psychiatric practice.** Artmed Publisher, 2004.

KNAPP, P. et al. Cognitive-behavioral therapy of addictive behaviors. *In:* A.V. CORDIOLI (ed.), **Psychotherapies: Current Approaches**. Porto Alegre, Artmed, p. 616-640, 2008

LEAHY, R. L. **Cognitive therapy techniques: A practitioner's guide**. Guilford Publications, 2017.

MARTINS, S. B.; AGUIAR, J. E. Depression in old age: depression is more common in the elderly, why? How to get out of it? **Revista Cesumar – Applied Human and Social Sciences**, v. 11, n. 1, p. 101-113, 2007.

MCPHERSON, S. et al. The effectiveness of psychological treatments for treatment□resistant depression: a systematic review. **Acta Psychiatrica Scandinavica**, v. 111, n. 5, p. 331-340, 2005.

MORENO, D. H.; MORENO, R. A. Treatment-resistant depressions: proposed approach. **J. bras. psiquiatr**, v. 42, n. supl. 1, p. 41-5s, 1993.

MORENO, R. A.; MORENO, D. H.; SOARES, M. B. M. Psychopharmacology of antidepressants. **Brazilian Journal of Psychiatry**, v. 21, p. 24-40, 1999.

MÖSSNER, R. et al. Consensus paper of the WFSBP Task Force on Biological Markers: biological markers in depression. The world **journal of biological psychiatry**, v. 8, n. 3, p. 141-174, 2007.

NEMEROFF, C. B. et al. Differential responses to psychotherapy versus pharmacotherapy in patients with chronic forms of major depression and childhood trauma. **Proceedings of the National Academy of Sciences**, v. 100, n. 24, p. 14293-14296, 2003.

NEUFELD, C. B.; CAVENAGE, C. C. cognitive conceptualization of case: a proposal for systematization from clinical practice and training of cognitive-behavioral therapists. **Brazilian journal of cognitive therapies**, v. 6, n. 2, p. 3-36, 2010.

PAYKEL, E. S. **Handbook of affective disorders**. 2nd ed. New York: Guilford Press, 1992.

POWELL, V. B. et al. Cognitive-behavioral therapy of depression. **Brazilian Journal of Psychiatry**. v. 30, n. 2, p. 73-80, 2008.

ROZENTHAL, M.; LAKS, J.; ENGELHARDT, E. Neuropsychological aspects of depression. **Journal of Psychiatry**, v. 26, n. 2, p. 204-12, 2004.

RUPKE, S. J.; BLECKE, D; RENFROW, M. Cognitive therapy for depression. **Am Fam Physician**, v. 73, n. 1, p. 83-86, 2006.

RUSH, A. J. et al. Comparative efficacy of cognitive therapy and pharmacotherapy in the treatment of depressed outpatients. **Cognitive therapy and research**, v. 1, n. 1, p. 17-37, 1977.

SEGAL, Z.; VINCENT, P.; LEVITT, A. Efficacy of combined, sequential and crossover psychotherapy and pharmacotherapy in improving outcomes in depression. **Journal of Psychiatry and Neuroscience**, v. 27, n. 4, p. 281, 2002.

SOUZA, A. E. C., et al. The effects of antidepressants on the body. **UNILUS Teaching and Research**, v. 12, n. 28, p. 146, 2015.

STAHL, S. M. **Psychopharmacology of antidepressants**. Taylor & Francis, 1997.

WEXLER, B. E.; CICCHETTI, D. V. The outpatient treatment of depression: Implications of outcome research for clinical prac-

tice. **The Journal of nervous and mental disease**, v. 180, n. 5, p. 277-286, 1992.

WORLD HEALTH ORGANIZATION (WHO). **The World Health Report 2001: Mental health: new understanding, new hope**. World Health Organization, 2001.

WORLD HEALTH ORGANIZATION (WHO) et al. **Mental health: new understanding, new hope**. Genova, WHO, 2009. Available in: http://www.who.int/whr/2001/en/whr01_po.pdf. Access in: 26/01/2018.

WORLD HEALTH ORGANIZATION (WHO) et al. Depression: A global public health concern. **Last modified October**, v. 5, p. 2012, 2012.

WHITE, J. R.; FREEMAN, A, S. **Group cognitive-behavioral therapy for specific populations and problems**. Roca, 2003.