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Azam Mansourzadeh

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Ecole doctorale 139 : Connaissance, langage,
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Membre de l'université Paris Lumières

Azam Mansourzadeh

*l'efficacité du schéma thérapeutique sur l'anxiété des malades
atteints par le SEP*

Thèse présentée et soutenue publiquement le 26/11/2021
en vue de l'obtention du doctorat de Psychologie de l'Université Paris Nanterre
sous la direction de Mme Marie -Claire GAY (Université Paris Nanterre)
et de M. Vahid Shaygannejad (Université des sciences médicales, Ispahan)

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l'efficacité du schéma thérapeutique sur l'anxiété des malades atteints par le SEP.

Résumé

Sclérose en plaques (SEP) est une maladie neuro-inflammatoire chronique du système neuronal qui est la deuxième raison majeure de handicap chez la population jeune du monde occidental et cela, après « le traumatisme »(Kasper et al., 2015).

Les symptômes neuro-psychiatriques dont font l'expérience ceux qui sont atteints par SEP impliquent les différents aspects de leur vie, le cours de la maladie, ainsi que ses symptômes sont influencés par ces premiers symptômes.

La thérapie du schéma est un traitement psychologique intégratif dérivé de la (CBT), qui inclut une réflexion sur le processus émotionnel et produit les résultats positifs sur les troubles anxieux, et qui pourrait être un conseil thérapeutique efficace pour les maladies chroniques telles que le SEP dans lesquelles il y a une incertitude et une menace permanentes liées à la maladie.

La compréhension qu'acquièrent les malades à propos des schémas et des styles d'adaptation, tout aussi bien qu'à propos de leurs émotions, pourrait les aider à exercer un certain contrôle sur leurs réponses émotionnelles(Young et al., 2006).

Cette étude a pour but d'examiner l'efficacité du schéma thérapeutique sur l'anxiété des malades atteints par le SEP.

La méthodologie de la recherche :

106 patients atteints par le SEP s'étant rendus aux cliniques ambulatoires du traitement et étant éligibles pour entrer dans cette recherche, ont été choisis pour l'essai contrôlé randomisé.

Le critère de mesure principal utilisé dans cette étude était l'échelle d'anxiété de l'hôpital et de dépression d'anxiété (HADS-A) et l'IAB (inventaire d'anxiété de Beck). Les objectifs secondaires ont été mesurés par l'IDB (inventaire de dépression de Beck), l'échelle d'impact de la sclérose en plaques - 29 (MSIS), l'échelle de la gravité de la fatigue (FSS), l'indice de la qualité du sommeil de Pittsburg (IQPS) et l'EDSS.

Les résultats :

Les résultats de l'analyse à mesures répétées (ANOVA) ont mis en évidence des différences significatives dans l'anxiété et la dépression après la thérapie du schéma. De plus, il n'y avait pas de relation significative entre la thérapie du schéma et la qualité de vie, la qualité du sommeil et la fatigue. Cependant, l'absence de changement dans l'EDSS peut être considérée comme un bon résultat.

Conclusion :

Le traitement psychologique, qui modifie les schémas inadaptés précoces, peut grandement bénéficier aux patients atteints de SEP et réduire l'anxiété chez eux.

Mots-clés : l'anxiété, la thérapie du schéma, le Sclérose en plaque (SEP).

Abstract

Introduction: Multiple sclerosis (MS) is a chronic, neuroinflammatory disease and one of the leading reasons for neurological disability among young people in the Western World. MS patients commonly experience neuropsychiatric symptoms can effect on aspects of life and worsening of disease course and symptom. The aim of this study was to evaluated schema therapy on anxiety in multiple sclerosis.

Method and design: 106 MS patients who visited MS out-patients clinic and were eligible for the study recruited to the RTC. The primary outcome measure was the Hospital Anxiety and Depression Scale-Anxiety (HADS-A), and BAI (Beck Anxiety Inventory). Secondary objective measured by BDI (Beck Depression Inventory), Multiple sclerosis impact scale - 29 (MSIS), Fatigue Severity Scale(FSS), Pittsburgh Sleep Quality Index (PSQI) and EDSS.

Results: The results of repeated measure ANOVA analysis indicated there are significant difference in anxiety and depression after schema therapy. Also there was no significant association between schema therapy and quality of life, quality of sleep, fatigue.

Conclusions: psychological treatment which changes early maladaptive schemas, may significantly benefit patients with MS and reduced anxiety.

Key word: Anxiety, schema therapy, multiple sclerosis

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The effect of schema therapy on anxiety in patients with multiple sclerosis

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Chapter 1

1-1- Introduction

Multiple sclerosis (MS) is a chronic inflammatory and demyelinating disease of autoimmune origin. The most important factors responsible for MS development are exogenous, environmental, and genetic factors. MS is characterized by multifocal and temporally scattered central nervous system (CNS) damage which leads to axonal damage (Kamińska et al., 2017). Depends on lesion the patient experience symptom. But it appears many of psychological symptoms are common in these patients. The etiology of multiple sclerosis remains elusive. However, numerous animal and human studies revealed autoimmune disease have been influenced by physical and psychological stress. Having reviewed seventeen articles, (Artemiadis et al., 2011) found evidence that stress can influence MS onset. Moreover, adversely affect fatigue, medication adherence, and quality of life. (Fiest et al., 2016) Also, it makes an essential contribution to the psychosocial impact of MS. MS is associated with a psychiatric problem. Psychiatric co-morbidities are highly prevalent in patients with MS that it have a severe impact on the quality of life and interpersonal relationships (Chalah & Ayache, 2017). The chronic progressive nature of MS causes psychiatric symptoms, especially Anxiety. Some research has been conducted up to now. While the effect physiology and psychology of Anxiety is notable. Anxiety can affect disability, Cognitive performance, Bodily sensations (Hayter et al., 2016). Negative effect on QOL. and worsening of disease course and symptoms by some researches have showed, since there are not any definitive treatment for MS, patients suffer more Anxiety, because Anxiety has inevitable effects on physical and mental aspects of patients it is necessary to diagnose, and treat it at once .pharmacological and psychological treatments are available for Anxiety, but usually Anxiety is resistance and high relapse, also in illness situations, perception, and treatment of Anxiety might have been different. Due to incompatible experience with Schema, in this situation, the usual defense mechanism may not useful. Then use of more integrative psychological treatment might be beneficial. In this research, the effects of schema therapy on Anxiety in a patient with MS have been studied.

1-2-Multiple sclerosis

One chronic, neurodegenerative and autoimmune diseases is Multiple sclerosis (MS) that targets the system (CNS) with gliotic scarring, demyelination, and axonal loss. The mediating factors of the disease are autoreactive lymphocytes that extend beyond the blood-brain barrier (BBB) and enter the CNS and create local inflammation (Huang et al., 2017). Clinically, it is manifested in areas of the destruction of the brain. (Sontheimer, 2015) The nature of MS makes it an unpredictable disease with variable clinical presentation; however, the signs and symptom depend on parts of the CNS, including the brain stem, the optic nerves, cerebellum, and cervical spinal cord. (Karussis, 2017). MS has a variety of symptoms that interfere with daily activities and family, social and working life, disturb emotional well-being, and reduce the quality of life.

Chronic inflammation, demyelination, and neuronal degeneration, axonal damage (Castro-Borrero et al., 2012) lead to memory loss, depression, and cognitive problems and disability in young adults (Motl & Pilutti, 2012). Manifestations of MS vary from a being illness to a rapidly evolving and incapacitating disease requiring profound lifestyle adjustment (Pucak et al., 2007).

Among the frustrating features of the disease are symptoms including "weakness, visual loss, bowel and bladder incontinence, cognitive impairment and mood symptoms, and fatigue. Maybe these characterize of MS characteristics predispose the patients with MS to a higher prevalence of some psychiatric symptoms and disorders. Because of depression and Anxiety, patients' adherence to treatment and functional status decreases along with quality of life (Chwastiak & Ehde, 2007).

1-3-Etiology

There are ambiguities about the etiology of MS still. It is known that environmental and genetic factors are critical factors in MS (Amato et al., 2018). Some of the factors, namely vitamin D deficiency, infections, diet, lifestyle factors, stress, and co-morbidities, were introduced. Genetic predisposition to (MS) only covers a part of MS's risk; lifestyle and environmental factors have a profound effect on the risk of MS. Notably, these nongenetic factors affect pathogenetic pathways, and some can be controlled. Moreover, recognized risk factors of MS such as high latitude, female gender, smoking, vitamin D shortage due to insufficient sun exposure and, or dietary

intake, and Epstein-Barr virus (EBV) infection, and obesity during adolescence are the factors in MS (Olsson et al., 2017).

There are shreds of evidence that smoking, because of nitric oxide (NO) and carbon monoxide (CO) has played a crucial role in MS. NO is a soluble and toxic gas, and with pathological concentrations, it destroys neurons and oligodendrocytes. Lipid peroxidation and mitochondrial damages caused by NO can result in oligodendrocytes apoptosis, axonal degeneration, and demyelination (Ghasemi et al., 2017). Among the critical epidemiological characteristic is the uneven distribution of the disease between countries. The frequency of MS demonstrates a general north - south gradient in the northern hemisphere, that reverses in the southern hemisphere, so that it is rarely found in areas close to the equator. Studies have demonstrated differences in the distribution of genetically susceptible populations, is shown by racial and ethnic backgrounds and differences in environmental risk (Sahraian et al., 2012). Both genetic and environmental factors have been identified for MS. Recent genome-wide association researches have shown new susceptibility alleles for MS along with the HLA complex, which is related to the immune functions. On the other hand, little is known about a purely environmental trigger for the disease as to an infectious agent. Besides, the autoimmune hypothesis of MS is well established (Korn, 2008).

Nevertheless, Numerous animal and human studies revealed autoimmune disease has been influenced by physical and psychological stress. In a systematic review article, in seventeen articles, (Artemiadis et al., 2011) found evidence that stress can influence MS onset.

1-4-Epidemiology

The epidemiology of MS has been changing during recent decades. Generally, there has been an increase in the prevalence and incidence of MS worldwide (Maghzi et al., 2011). In 2016, there were 2221 188 prevalent cases of multiple sclerosis (95% uncertainty interval [UI] 2033866-2436858) globally, which corresponded to a 10.4% (9.1 to 11.8) increase in the age-standardized prevalence since 1990. The highest age-standardized multiple sclerosis prevalence estimates per 100000 populations were in high-income North America (164.6, 95% UI, 153.2 to 177.1), western Europe (127.0, 115.4 to 139.6), and Australasia (91.1, 81.5 to 101.7), and the lowest were in eastern sub-Saharan Africa (3.3, 2.9-3.8), central sub-Saharan African (2.8, 2.4 to 3.1),

and Oceania (2.0, 1.71 to 2.29). Approximately, 2.5 million individuals are affected worldwide, and young individuals aged between 20- and 40-years are mainly affected. The higher frequency of MS is seen in women affected twice as often as men (Huang et al., 2017).

The prevalence of MS in men and women in IRAN was estimated to be 16.5/ 100,000 (95% CI: 13.3-20.5) and 44.8/ 100,000 (95% CI: 36.2-55.4), respectively. The incidence of MS in men was estimated to be 1.2/ 100,000 (95% CI: 1.0-1.4), and the incidence of MS in women was 48.2/ 100,000 (95% CI: 39.3-59.1) (Azami et al., 2019).

Also, mortality in patients with multiple sclerosis (MS) is significantly increased compared with the general population (Scalfari et al., 2013). There were 18932 deaths due to multiple sclerosis (95% UI 16577 to 21033) and 1 151 478 DALYs (968605 to 1345776) due to multiple sclerosis in 2016. Globally, age-standardized death rates decreased significantly (change -11.5%, 95% UI -35.4 to -4.7), whereas the change in age-standardized DALYs was not significant (-4.2%, -16.4 to 0.8) (Wallin et al., 2019).

1-5-Type of MS

There are four clinical forms of MS: secondary progressive MS (SPMS), relapsing-remitting MS (RRMS), progressive relapsing MD (PRMS), and primary progressive MS (PPMS). About 87% of patients demonstrate RRMS, featured with acute attacks (relapses) and partial or full recovery (remission). Secondary Progressive Multiple Sclerosis (SPMS) is featured with early relapses, and gradual neurological deterioration, not related to acute attacks. Primary Progressive Multiple Sclerosis (PPMS) is featured with a steady functional decline since the initiation of the disease. No relapses Progressive Relapsing Multiple Sclerosis (PRMS) ever is featured with a steady functional decline since the disease's initiation followed by superimposed acute attacks. The early stages of PRMS and PPMS are not distinguishable until the relapses (Loma & Heyman, 2011).

1-6- symptoms of MS

The pattern of symptoms of MS is complex, variable, and unpredictable (Brochet & Ruet, 2019).

Loss of coordination and balance, vision impairment, severe fatigue, pain, bladder dysfunction, numbness, cognitive impairment, weakness, and mood changes are common symptoms in MS. The nature and severity of symptoms related to periods of relapse and remission (Gilmour et al., 2018). Some symptoms that not less painful recognized as secondary consequences of MS, which are spasticity, pain, bladder and bowel dysfunction, fatigue, depression, Anxiety, and side effects of medication contribute to sexual dysfunction (Cordeau & Courtois, 2014).

1-7- Sensorimotor Impairments:

Sensory disturbances (numbness, tingling, itching, burning) Walking difficulties, due to fatigue, weakness, spasticity, loss of balance and tremor, Cognitive and affective symptoms (Ghasemi et al., 2017). The researches have shown the factors' impact on impairments is variable. Hempel et al., in a meta-analysis, were studied 59 studies. Lower vitamin D levels were associated with higher Expanded Disability Status Scale (EDSS) scores ($r = -0.22$; confidence interval (CI) = $-0.32, -0.12$; 11 studies; $I^2 = 66\%$), smokers had an increased risk of MS progression (hazard ratio (HR) = 1.55; CI = 1.10, 2.19; $I^2 = 72\%$; seven studies). Also, stressful life events as a risk factor can affect disability. Maher et al. 2004 meta-analysis showed an increase in the risk of exacerbation in multiple sclerosis after stressful life events, with a weighted average effect size of $d = 0.53$ (95% confidence interval 0.40 to 0.65), $P < 0.0001$. Ackerman et al. 2002 showed an increase in the frequency of life events was associated with a greater likelihood of MS exacerbations (hazard ratio = 13.18, $p < .05$). Also, Eighty-five percent of MS exacerbations were associated with stressful life events in the preceding six weeks. Stressful life events occurred an average of 14 days before MS exacerbations. However, relapses can be connected with seasonal factors. (Harding et al., 2017; Nikolenko et al., 2019). decreased maximum walking capacity may be associated with stress, extreme temperatures, or MS-related fatigue (Çinar & Yorgun, 2018).

1-8- Special sense:

Visual disturbances are commonly reported by MS patients and include problems with the way patients see the world (afferent visual pathway symptoms) and the way the eyes move together (efferent visual pathway disorders). Efferent visual pathway lesions ocular misalignment, and nystagmus can cause diplopia and oscillopsia. (Costello, 2016). Acute vestibular symptoms with severe positional vertigo (an illusion of movement in the person's relationship with the environment), vomiting, ataxia, and headache are typically seen in acute brainstem demyelination (Carr & Shepherd, 2010). Other senses such as taste and smell may be involved.

1-9- Fatigue

Fatigue is among the most common, yet least understood, reported symptoms of MS . Among the main definitions is a sense of exhaustion, tiredness, and lack of energy (Krupp, 2006). He was observed in 75% of MS patients at least during the disease course.

Fatigue is among the most common, yet least understood, reported symptoms of MS standard definitions include a sense of exhaustion, lack of energy, or tiredness (Krupp, 2006), reported by at least 75% of MS patients at some point in the disease course.

Individuals with MS report that fatigue generally occurs daily, interferes with physical and social function and, worsens with heat. Individuals with MS, their families and, friends, can misjudge the impact of fatigue by misinterpreting it as laziness. Individuals who are work in that they have no energy for recreational activities because of needing to rest at the weekend.

Fatigue is the main debilitating symptom, that suppresses pain and physical disability (Janardhan & Bakshi, 2002). Manjaly et al. 2018 examined contemporary theories as to the four main categories of MS mechanisms that lead to: structural damage of WM/GM, inflammatory processes, maladaptive network recruitment when performing tasks, and metacognitive interpretations of brain state that hints at' helplessness. Inflammatory processes, Maladaptive network recruitment because of distributed lesions or inflammation, lesions of dopaminergic, serotonergic, or noradrenergic nuclei in the brainstem, and the consequent reduction of monoaminergic transmitter supply to the cortex and basal ganglia explains the decrease in motivation, mood, and arousal that characterize fatigue (Manjaly et al., 2019).

1-10- Autonomic involvement

MS involves the autonomic nervous system with disturbances in various parts. Frequent and common complications that decrease the quality of life and have a powerful effect on the patient are sweating abnormalities, urinary dysfunction, orthostatic dysregulation, gastrointestinal symptoms, and sexual dysfunction (Ashtari et al., 2014; Pintér et al., 2015).

1-11- Neuropsychiatric symptoms

Psychiatric symptoms in multiple sclerosis (MS) is evident since the early clinical description of sclérose en plaques by Charcot at the Hospital Pitié-Salpêtrière in the nineteenth century (Orrell, 2005). The symptoms are euphoria, pathological crying and laughing, hallucinations, and depression (Cerqueira et al., 2015).

Neuropsychiatric symptoms are also widely observed in MS patients. These are two main categories of disturbances: abnormalities of mood, abnormalities in cognition, affect, and behavior (Paparrigopoulos et al., 2010). About 65% of MS patients demonstrate neuropsychiatric abnormalities. A decrease in verbal skills, memory, and intellectual function is common in MS patients. Neuropsychological assessment of MS patients indicated a mild to moderate slow-down of a thinking process, poor recent memory, problems with word-finding problems slow information processing, and concentration difficulties (Maghzi et al., 2011). Psychiatric co-morbidities can engage 95% of MS patients in their lifetime. They are considered pathological changes of the disease. The most frequent problem is depression (50%) and Anxiety (14-41%). Besides, psychotic features can affect 2-3% of MS patients, and bipolar disorder is twice as common as those with MS as in the general population (Chalah & Ayache, 2017).

Depression is the leading psychiatric condition in MS patients (Brenner et al., 2018). Major depression is the most prevalent neuropsychiatric disorder in MS that has about a 50% lifetime prevalence rate. Through diagnosing in early stages of the disease and management of depression in MS, is it possible to control morbidity, mortality, possibly physical outcome, and disease exacerbations, quality of life, adherence to immunomodulatory treatments and risk of suicide in MS patients (Paparrigopoulos et al., 2010). Based on a meta-analysis, about 24% in population-based studies around

three-fold that of the general population. The one-year incidence was 3-10% in one clinical sample (Boeschoten et al., 2017).

Depression, anxiety, and stress are common in MS. Given the chronic and unpredictable MS course, there is a need for continuous adjustments of the patient's sense of self (Sá, 2008). The three most common emotional disturbances seen in a patient with MS include depression, pathological laughing or crying, and euphoria. These difficulties may result from the stress associated with the illness, or they may be a direct expression of the central nervous system pathology of MS itself (Minagar, 2010).

In the most extensive known study, Jones et al. 2012(Jones et al., 2012), have shown that Anxiety and depression are highly prevalent in people with MS. Also, they showed that during the early stages after an MS diagnosis, individuals experienced a notable severity of non-somatic symptoms of depression, and it causes an antagonistic and synergistic effect that results in higher anxiety (Hartoonian et al., 2015).

1-12- Anxiety

By definition, Anxiety is one's response to a threat or danger. The experience is involved with perceiving danger, thinking about harm, and a process of physiological alarm and activation (Moss, 2002). That is the same with Anxiety in patients with MS.

Anxiety disorders are usually found in MS patients during the life cycle, with a lifetime prevalence exceeding 35% (Korostil & Feinstein, 2007) and high levels of Anxiety (69%) recorded from the beginning of the disease (Janssens et al., 2006). According to (Marrie, 2017), Anxiety is recognized to affect the MS population more often than the general population. In addition to the psychological aspect of MS, Anxiety may be a consequence of neurological and physiological dysfunctions due to the disease's course. Boeschoten et al. (Boeschoten et al., 2017) explained anxiety is a natural reaction to the unpredictable course of this debilitating and chronic condition. According to marrow 2018. Anxiety is also associated with suicidal thoughts and self-harm actions in PwMS. Anxiety is also related to several common 'invisible' symptoms in PwMS. As reported by research works, Anxiety is related to more severe sleeping problems, and it is more prevalent in PwMS who deal with MS fatigue (Morrow, 2018).

There is a unique relationship between Anxiety and both high and low QOL. It is also notably related to depression (Butler et al., 2016). Anxiety is a predictor of depression in pwMS (Gay et al., 2017; Gay et al., 2010), is related to more robust somatic problems, higher social dysfunction, and more profound suicidal thoughts (Korostil & Feinstein, 2007).

Depression and Anxiety are normal responses to the unpredictable, and disabling and chronic nature of MS. Besides, the patients can be predisposed for depression or Anxiety due to many psychosocial risk factors like inadequate coping or insufficient social support, or by MS-related biological processes like changes in brain structure or immunological and inflammatory pathways (Boeschoten et al., 2017).

1-13- Depression

Depression is the most studied psychiatric condition in MS patients. Major depression is one of the most common neuropsychiatric disorders in MS with an approximate 50% lifetime prevalence rate. Early recognition and management of depression in MS is of major importance because it is a key predictor of morbidity, mortality, quality of life, possibly physical outcome and disease exacerbations, adherence to immunomodulatory treatments and suicide risk in MS patients (Paparrigopoulos et al., 2010). according to a meta-analysis around 24% in population-based studies around three-fold that of the general population. The one-year incidence in a clinical sample was 3-10% (Boeschoten et al., 2017).

Depression, anxiety, stress are common . bearing in mind chronic and unpredictable course of disease implying continuous adjustments of patient's sense of self.(Sá, 2008). the three most common emotional disturbances seen in patient with MS include depression pathological laughing or crying and euphoria .these difficulties may result from the stress associated with the illness or they may be a direct expression of the central nervous system pathology of MS itself (Minagar, 2010).

In the largest known study, Jones et al, 2012(Jones et al., 2012), have shown that anxiety and depression are highly prevalent in people with MS. Also they indicated that in the early stages after a MS diagnosis, individuals experience greater severity

of non-somatic symptoms of depression and this appears to exert a negative, synergistic effect that leads to worsening anxiety (Hartoonian et al., 2015).

1-14- Sleep disorders

Sleep disorders are widely observed in MS patients (MS) and have a significant role in health and quality of life (Veauthier, 2015).

Along with neurological morbidity, MS causes a disproportionately high prevalence of sleep problems that lower functional status (Braley & Chervin, 2010). According to (Čarnická et al., 2015), low sleep quality is expected, in MS patients with a prevalence rate from 25% to 54%. In our subjects, the rate of low sleep quality was 38%, and excessive daytime sleepiness was seen in 18%. Individuals with multiple sclerosis can have a higher co-morbidity related to sleep problems. As shown by researches, MS patients might suffer significantly more serious sleep problems compared to healthy individuals. Sleep problems in MS patients are significantly bigger than those in the general population or other chronic diseases, and this can inflict female MS patients compared to men (Bamer et al., 2008).

1-15-MS and Suicide

Patients with common neurological diseases tend to have a higher risk of suicide. In many cases, suicidal thoughts are developed during the early stages following diagnosis when the patient suffers disabling symptoms. They are also common in patients with psychiatric co-morbidities, usually associated with these neurological diseases (Alejos et al., 2020).

MS patients demonstrate a high prevalence of depression and Anxiety. Also, the rate of suicidal thoughts in MS patients was higher compared to the general population. Depressive symptoms in MS patients are directly related to the risk of suicide. (Taulil et al., 2018).

In a meta-analysis, a significant association was seen between suicide and MS, with a pooled SRR 1.72 (95%CI 1.48-1.99, *I*-squared = 55.0%). Risk of suicide at diagnosis of multiple sclerosis (SRR 2.12, 95% CI 1.84-2.46; *I*-squared = 4.4%) was higher than the risk of suicide at symptom onset (SRR 1.69; 95% CI 1.43-2.00; *I*-squared = 0.0%). while ethnic and geographical differences were not included (Shen et al., 2019).

However, the higher prevalence of suicidal thoughts can be seen in individuals with minimal or no depressive symptoms. Different types of disability are related to suicidality, including: 'tremors' and 'taking longer to do things (Lewis et al., 2017). In another research by Zacharia 2016, it was demonstrated that there is a higher rate of MS relapses and suicide thoughts ($p < .05$), while there was no relationship between disability and suicide ideation.

In a systematic review higher suicide rate in patients with MS was observed in comparison with the general population, so that suicide and several risk factors were associated: Severity of depression, younger age, social isolation, progressive disease subtype, lower-income, higher levels of physical disability, earlier disease course, and not driving (Pompili et al., 2012).

Several factors may increase the risk of suicide. In the non-MS population, psychiatric disorders, genetic factors, and sociocultural factors are among these factors (Marrie, 2017).

In a meta-analysis of 170 articles published between 2011 and February 2019, the prevalence of suicidal thoughts in MS patients was estimated equal to 13% (CI 95% = 0.09-0.17). A subgroup analysis, based on the type of countries showed a higher prevalence in developed countries (15%; CI 95% = 0.1-0.2) (Kouchaki et al., 2020).

1-16-MS Treatment

The purposes of MS treatment using disease-modifying agents are to shorten the duration of acute exacerbations, decrease the frequency, and provide symptomatic relief. Currently, there is no curative, FDA-approved treatment for the disease. Furthermore, drugs are used both to decrease the severity of acute exacerbations and to shorten the term of MS attacks.

Treatments for the symptoms are designed to keep the function and to improve QOL (Goldenberg, 2012). However, there have been notable achievements in MS treatment, and the rate of progressive disability and early Mortality has remained worrying (Gholamzad et al., 2019). Bering in mind that 50% of patients need assistance for walking within 15 years following the disease's initiation. Then the nature progressive of MS causes to need other supplemental therapy for preserving

the quality of life. Patients often feel compelled to try every opportunity to heal, often stimulated or urged on by friends or relatives. 50% of patients diagnosed with multiple sclerosis search for relief in traditional and complementary medicine such as homeopathy or acupuncture (Huybregts et al., 2018). The search and try to use every way of relief showed threatening nature of MS.

CHAPTER 2

2-1-Anxiety

Anxiety has been and will be one of the main concerns of human beings. Anxiety is: "apprehensive anticipation of future danger or misfortune accompanied by a feeling of tension (Gellman & Turner, 2013). The focus of anticipated danger may be internal or external. Anxiety is a future-oriented mood state in which one is ready or prepared to attempt to cope with up coming negative event" (Barlow, 2000).

These disorders are associated with a considerable degree of impairment, high health-care utilization, and an enormous economic burden for society. Despite their high burden, anxiety disorders have the lowest proportion of professional treatment of all the classes of mental disorders (Sadock et al., 2017). However, effective psychological and pharmacological treatments exist for anxiety disorders. Not only many patients and people do not refer to health services for treatment, but some of them who use these services are not diagnosed correctly or not offered state-of-the-art treatment (Bandelow & Michaelis, 2015). Theories of Anxiety were being with psychodynamic theory by Freud with an unconscious conflict. The cognitive theory explains Anxiety as the tendency to overestimate the potential for danger, and according to the learning theory, Anxiety is a conditioned response to a specific environmental stimulus. Patients feel desperate when facing severe facts of the human state—the “givens” of existence. According to the hypothesis of the existential psychotherapy approach, Anxiety can be perceived as a subjective parameter of feeling threatened in existential structures (Längle, 1997).

Anxiety is a typical form and a survival mechanism because it alerts the organism is in danger. Anxiety allows the constant ego to be alert for signs of threat and danger. The signs of threats incite us to attempt to either flee the situation or protect ourselves against it (Fiest et al., 2016). The “fight or flight” response, as it is known, is a mechanism designed to get the body “ready.” It is this branch (sympathetic) of the human nervous system that greatly influences hormone levels in the blood to increase heart rate, blood pressure, and body temperature and with, effect on endocrine, gastrointestinal, nervous and reproductive systems, prepares the person for threats (Gordan et al., 2015).

According to Simpson 1960 Anxiety as universal emotion refers to the brain state associated with the perception of the dangerous stimulus that creates a motivation to act (Sadock et al., 2017). Anxiety vigilantes the organism to the potential threat and prepares for challenges, definitely when the threat is severe and related to our lives. Moreover, it seems Anxiety disorders are the result of activity in the emotional centers, not cognitive centers. It seems the Anxiety occurs out of the patient's awareness because it is generated non consciously in the brain. It seems the Anxiety occurs out of the patient's awareness because it is generated non consciously in the brain (Martin et al., 2009).

Then having a biological viewpoint is not enough to develop an anxiety disorder because What initiates the biological and physiological processes of anxiety is perceive Anxiety and anxious conditions, which have a psychological basis.

The two most important factors that led to Anxiety vulnerability perceived control and cognitive appraisals. Lack of perceived control over potentially adverse events represents a generalized psychological vulnerability to develop anxiety disorders (Gallagher et al., 2014). According to the theories of Lazarus and Folkman, uncontrollability, uncertainty, resource, and self-concept are factors that make an event stressful (Atkinson et al., 1996). According to Rotter 1954, locus of control, (belief to having over the outcome) depends on variables such as abilities, traits, faith, and sources (Dilmac, 2009). Also, Carol 2013 showed Low level of personal control strongly correlated with depression and Anxiety. Then an event cannot be anxious on its own. It depends on the situation and appraisal of the condition. "Cognitive appraisal is the patient's perception of an event or situation, their assessment of the degree to which the event is stressful, and their perception of the potential impact of the event on personal goals and resources" (Alhurani et al., 2018). Although Cognitive factors are considered an essential factor of anxiety (Choy et al., 2007). Nevertheless, the base of cognition is the structure, framework, as a schema or pattern imposed on reality or experience to help individuals explain it, to mediate perception. Schema can also be thought of as an abstract cognitive plan which is formed early in life. In addition to biology and psychology factors, there are some facts in a lifetime that can make Anxiety.

One of the most crucial risk factors that causes increase in Anxiety sensitivity is stressful life events (McLaughlin & Hatzenbuehler, 2009). Minor stressful life events,

even can influence healthy and make Anxiety (Bolger et al., 1989). One potential risk factor for late-life Anxiety is early life stress, such as exposure in childhood to maltreatment, separation from parents or parental divorce, death of a family member, and poverty. According to several studies and meta-analyses, ELS exposure is associated with an increased risk of adulthood Anxiety.

Accumulation of psychological factors and early life stress also increased the levels of late-adulthood anxiety symptoms and the risk of anxiety regarded as clinically significant.

2-2-Forms of anxiety

According to DSM 5 Anxiety characterized by a diffuse, unpleasant, vague sense of apprehension, commonly accompanied by physical. Anxiety disorders are classified in DSM 5 as: panic disorder (with or without agoraphobia), agoraphobia (without a history of panic disorder), specific phobia, social phobia, and generalized Anxiety disorder (GAD). Separation Anxiety disorder social Anxiety disorder (SAD). Anxiety Due to a General Medical Condition and substance induced Anxiety disorder. (Sadock et al., 2017).

Phobias (context-dependent fears), generalized anxiety (context-independent fears), and panic are three different forms of anxiety. Anxiety disorders differ from each other in the types of objects or situations that induce fear, anxiety, or avoidance behavior, and the associated cognitive ideation, as well as some characteristics. Thus, while anxiety disorders tend to be highly comorbid with each other, they can be differentiated by closely examining the types of situations that are feared or avoided and the content of the associated thoughts or beliefs. Anxiety disorders differ from normative developmental fear or anxiety in that they are excessive or persist beyond developmentally appropriate periods. They differ from transient fear or anxiety, often stress-induced, by being persistent, although the duration criterion is intended to be a general guide with a margin for certain degree of flexibility and is sometimes shorter. duration in children (as in separation anxiety disorder and selective mutism). Since people with anxiety disorders often overestimate danger in situations they fear or avoid, the primary determination of whether fear or anxiety is excessive or

disproportionate is made by the physician, taking into account cultural contextual factors. Many anxiety disorders develop in childhood and tend to persist if left untreated. Most occur more often in women than men. Each anxiety disorder is diagnosed only when the symptoms are not attributable to the physiological effects of a substance / medication or another medical condition or are not better explained by another mental disorder (Sadock & Sadock, 2000).

Trait anxiety and state anxiety are aspects of anxiety, that defined by Spielberger, 1972. State anxiety is a situation-related reaction to a particular perceived threat and refers to a transitory emotional condition; therefore, it will be present only for a limited time after the threatening event disappears (Rachman, 2004). State Anxiety is the current degree of anxiety experienced at a certain point in a specific situation and concerns the connection between trait anxiety and situational stress (Eysenck & Van Berkum, 1992). Trait anxiety is personality-related. It depends on how individuals perceive the world and react to it and a disposition to perceive a wide range of circumstances as personality threatening. The people high in trait anxiety will experience more tense situations and more intense levels of Anxiety than people that are low in trait anxiety (Bucky & Spielberger, 1971; Rachman, 2004). According to Spielberger, trait anxiety is a predisposition to respond anxiously. Fear and anxiety are universal human experiences with clear adaptive significance. Anxiety is a ordinary emotion (Ressler et al., 2015). It can also be considered from the evolutionary perspective that humans have acquired Anxiety through adaptation to ameliorate their chance of survival as it motivates them to stay away from hazardous locations. While fear and Anxiety are normal experiences, sometimes they can become maladaptive, excessive in intensity, frequency, or duration - causing the sufferer distress to the extent that their daily life is disrupted (LeDoux, 1996). Anxiety is currently classified as a psychiatric disorder since the twentieth century whose differentiation from joint adaptive stress experienced in daily life and need for treatment is ought to be assessed clinically (Crocq, 2015).

If we look at Anxiety from another aspect, Anxiety has two forms of chronic Anxiety and acute Anxiety. Acute anxiety generally occurs in response to a real treat in limited duration, and it is fed by fear of what exists. Chronic stress is likely Anxiety response to imagined threats and is experienced as having no end in sight, and it is fed by fear of what might be (Kerr, 1988).

It is likely that chronic stress is a transversal concept. To elaborate, a person exposed to severe complications in the short-term may adaptively produce a stress response, which can morph into impeding psychiatric disorders if mentioned short-term challenges are repeated in the long-term. When prompted by real or perceived menaces, the effects of chronic stress can be experienced in biological systems in several "units of analysis"—neuroendocrine, autonomic, and behavioral. Among different biological systems, the homeostatic system can be considerably affected by chronic stress as the allostatic load (i .e., the effect of stress on the human body) increases, whose mounting levels are associated with several unfavorable health conditions, including psychiatric disorders (Patriquin & Mathew, 2017).

2-3-Pathophysiology of anxiety

Anxiety disorders are characterized by a variety of neuroendocrine, neurotransmitter, and neuroanatomical disruptions. Identifying the most functionally relevant differences is complicated by the high degree of interconnectivity between neurotransmitter- and neuropeptide-containing circuits in the limbic, brain stem, and higher cortical brain areas (Martin et al., 2009).

Lines of evidence coming from many branches of neuroscience indicate that anxiety disorders arise from a dysfunction in the modulation of brain circuits that regulate emotional responses to potentially threatening stimuli. These circuits involve bottom-up activity from the amygdala, indicating potentially threatening stimuli, and top-down control mechanisms originating in the prefrontal cortex, signaling the emotional salience of stimuli. The brain circuits in the amygdala are thought to comprise inhibitory networks of γ -aminobutyric *acid-ergic* (GABAergic) interneurons, and this neurotransmitter thus plays a crucial role in the modulation of anxiety responses both in the stock and pathological state (Nuss, 2015).

Various neurotransmitters are involved in Anxiety, such as serotonin, glutamate, gamma-aminobutyric acid, Cholecystokinin, Adenosine, etc. Some are inhibitory, and some are excitatory. These neurotransmitters might play a role in the upregulation or

downregulation of anxiety disorders. Individual shows different types of symptoms i.e., Cognitive, Physiological and Behavioral during Anxiety (Kaur & Singh, 2017).

Given that patients with anxiety disorders experience fear and distress in response to possible threat predictors, the amygdala has been hypothesized to be hyper-responsive in some anxiety disorders (Liberzon, 2009).

Corticotrophin Releasing Factor (CRF) systems mediate the neuroendocrine responses to psychological stressors and they are involved in the cognitive and emotional processing that accounts for many of the symptoms of depression and Anxiety. Glucocorticoids are responsible for upregulating CRH in the amygdala, frontal cortex, and bed nucleus of the stria terminalis, whereas they down regulate hypothalamic CRH. Both CRH levels and the site of activation, however, are essential to the presentation of anxiety symptoms, such that noting CRH levels alone is also insufficient to understand the response (Raglan et al., 2017). In acute Anxiety, the activation of the HPA axis is adaptive, since cortisol seems to reduce perceived fear by impairing the memory retrieval of emotionally arousing information. Conversely, in chronic Anxiety, the gradual development of a disconnection between the stressor and its behavioral consequences is the primary coping mechanism that allows the person to function normally, despite annoying events that cannot be escaped or avoided. When this mechanism fails, the HPA axis persists activated and it may become harmful, since corticoids decrease the hippocampal serotonin receptors, impairing coping mechanisms and inducing resilience and low tolerance to chronic stress. Therefore, chronic stress, such as that observed during the prolonged exposure to various stressful life events, along with the inadequacy to cope with them or the perceived loss of controllability, may lead to the persistent activation of the HPA system which exposure to stressors (i.e., early stressful life events) and sensitivity to stress have been strongly implicated in the manifestation or exacerbation of these syndromes. Accordingly, the available literature reports that adults with a history of adverse childhood experiences develop anxiety disorders more frequently than adults without early stress. childhood life events and HPA abnormalities may be specifically and transposon graphically-related to all anxiety disorders, as well as, more broadly, to all psychiatric disorders (Faravelli et al., 2012).

2-4-Epidemiology

Nearly one-fifth (17 percent) of adults report a lifetime history of one of the major anxiety disorders, and 1 in 10 suffer from a current anxiety disorder. Anxiety disorders are the most prevalent psychiatric disorders. According to epidemiological surveys, one-third of the population is affected by an anxiety disorder during their lifetime. They are more common in women. During midlife, their prevalence is highest. There is no evidence that the prevalence rates have changed in the past years. Differences in prevalence rates found in different countries and cultures may be due to differences in methodology rather than culture-specific factors. High co-morbidity is found among the Anxiety disorders and between the anxiety disorders and other mental disorders, respectively (Bandelow & Michaelis, 2015). The 12-month prevalence of anxiety disorders (not including specific phobias) was 15.6%. The prevalence of anxiety in Iran in 2018 was 12.0% in males and 19.4% in females. Anxiety disorders are common conditions with a higher prevalence among the female gender, unemployed individuals, and people with low socioeconomic conditions living in urban areas. Comorbidity of anxiety disorders with other psychological disorders aggravates the disability and significantly increases the number of days out of role (Hajebi et al., 2018).

2-5- Symptom:

symptom of anxiety includes Somatic symptoms and psychological symptom peripheral manifestations of anxiety include: palpitations, muscle tremor, sweating, Autonomic arousal, Muscle tension, Hyperventilation, Diarrhea, Dizziness, lightheadedness, hyperhidrosis, hyperreflexia, syncope, Pupillary mydriasis.

Upset stomach ("butterflies") Urinary frequency, hesitancy, urgency. An individual exposed to the emotional distress of anxiety can also suffer several physical symptoms due to the arousals of the autonomic system, including perspiration, dizziness, and dyspnea as well as insomnia, restiveness, and muscle pains (Gelenberg, 2000). Sexual dysfunction in women suffering from anxiety disorders is also reported to be highly prevalent. Also, sexual problems can be encountered in normal populations with normal to high levels of anxiety (Bradford & Meston, 2006). In 2019, Chung and her colleagues reported a correlation between the risk of anxiety and the Total aggression score; particularly, the association between oblique aggression (i.e. anger and hostility) and anxiety is more significant. Anxiety impacts the manner an individual

think, learns, and conceives his/her surroundings. It can also create bafflement and distort the perception of time and space as well as persons and events (Sadock et al., 2015). Its effect on behavior envelopes changes in both early perceptual and later, higher-order cognitive processes. Early sensory-perceptual processes in the auditory and visual system which can help the detection of threats are altered by anxiety. In addition, the capacity and performance of the working memory is reported to be considerably decreased in patients with anxiety (Lukasik et al., 2019). Furthermore, thoughts house emotional information, therefore can impede concentration. Anxiety seems to produce biases in recollecting information from long-term memory, so individuals with anxiety are more prone to biases when recollecting information regarding threats. The research conducted by(Grant & White, 2016) demonstrated that anxious individuals initially focus on threatening stimuli, misconstrue neutral ones as negative, and then, are disposed to remember them. Moreover, a majority of theoretical models have propounded that the mentioned biases can contribute to the development of clinically considerable levels of psychopathology.

2-6-Etiology

The number of studies over aetiology of anxiety have surged in the last decades. Several cognitive, biological, behavioral, and social risk factors are of importance regarding the apprehension of the development of anxiety problems, some of which are part of the developmental processes that are regarded “normal” and the others of abnormal experiences (Weems, 2008). The current aetiology of anxiety disorders points towards the exposure of an individual with genetic vulnerability to psychosocial factors (e.g., childhood misfortune or stressful experiences). Regarding generalized anxiety disorders, the serotonergic and catecholaminergic systems as well as neurotrophic signaling seem promising as potential genes, even in case of moderate genetic risk (heritability of about 30%). Besides, the causal roles of early developmental traumas and anxiety-inducing life events in interaction with molecular plasticity markers have been underscored in several genes-environment studies. It is suspected that parental behavior as a socio-environmental factor can contribute to prevent anxiety disorders (Thibaut, 2017). Several hypotheses proposed in the field of aetiology of anxiety disorders suggest the predisposition of certain individuals to anxiety disorders due to an underlying trait or temperament (Craske, 2003).

2-7- Genetic

Heritability of anxiety was shown in genetic studies disorders (30-67%), with multiple vulnerability genes such as 5-HT_{1A}, 5-HTT, MAO-A, COMT, CCK-B, ADORA2A, CRHR1, FKBP5, ACE, RGS2/7 and NPSR1 suggested by molecular genetic association studies. These genes have been shown to partially interact with each other as well as with environmental factors to shape the overall disease risk in a complex genetic model (Baldwin, Leonard 2013). Extensive genetic studies of the serotonin (5-hydroxytryptamine, 5-HT) transporter (5-HTT) gene have revealed how variation in gene expression can be correlated with anxiety phenotypes. Complete genome-wide linkage scans for panic disorder (PD) susceptibility genes have suggested a locus on chromosome arm 7p, and association studies have highlighted many candidate genes. A highly significant association between phobias, panic disorder, and a duplication at chromosomal region 15q24-26 is one of the most exciting findings to date (Morris-Rosendahl, 2002).

2-8-Comorbidity of anxiety with other psychiatric disorders

Much evidence has shown comorbidity of anxiety disorders to be the rule rather than an exception. Previous studies have also shown anxiety disorders to occur frequently in children and adolescents with other psychiatric disorders including depressive disorders, conduct disorder, oppositional defiant disorder, attention-deficit/hyperactivity disorder, and with alcohol abuse or dependence (Essau, 2003). Comorbid anxiety is common in patients with depressive disorders, Studies have shown that more than 70% of individuals with depressive disorders also have anxiety symptoms and 40 to 70% simultaneously met criteria for at least one type of anxiety disorder (Zhiguo & Yiru, 2014).

2-9-Anxiety in chronic illness

"While only a few things can be predicted with certainty, one thing that seems certain is that the future of health care will be dominated by the challenge of complex chronic disorders"(Nolte et al., 2014).

The word chronic comes from the Greek *choros* which stands for during a long period of time. The element of time is a main concept in the description of chronic illness. Illness represents a fundamental threat to survival and well-being and few life events are more capable of eliciting anxiety and fear (Cameron, 2003). Illness-relevant stimuli (bodily symptoms) elicit cognition and emotion processes for health treatment and anxiety in parallel. A chronic illness or disability can pose a threat because of the potential loss of function, independence, financial security. Threat causes anxiety. Some individuals fear the unknown or unpredictability of a condition, which provokes anxiety (Falvo & Holland, 2017). People with chronic illness are often worried and anxious about now and when their bodies fail them. Illness represents a fundamental threat to survival and well-being.

The nature of chronic illness makes it a source of anxiety: "long in duration—often with a long latency period and protracted clinical course; of multi-factorial etiology; with no definite cure; gradual changes over time, asynchronous evolution and heterogeneity in population susceptibility (Martin et al., 2009). According to construction theory, anxiety is experienced when your construction system no longer applies to the situation that confronts you. You cannot construe (make sense of) what is happening. Finding yourself in any new situation leads to some anxiety (Laster 2009, Feeist 2002). According to Kelly (1955), a person's psychological processes are directed (or in Kelly's words 'channeled') by the way they anticipate events. Thus he theorized anxiety as an awareness that one's constructions do not adequately equip one to predict the events with which one is confronted (Norton, 2010).

The prevalence rates of anxiety disorders in patients with medical illnesses are high, with percentages up to 29% in patients with epilepsy, 48.9% in patients with multiple sclerosis, 30.1% in patients with Parkinson's disease, 30% in patients with cardiovascular disease, 47.0% in patients with diabetes mellitus, and so on. After stroke, rates range between 20% to 25% and it remains a common problem several years after the stroke event (Burton et al., 2013).

Anxiety disorders co-occurring with medical illnesses have a number of clinical implications, including the greater severity of both of them and the negative impact on the treatment outcome of both medical illnesses and anxiety disorders.

Patients with chronic illnesses report that their life quality is deteriorated by physical restrictions, chronicity, symptoms, and the escalating characteristics of the illnesses.

along with their effect on everyday activities and relationships (Kristofferzon et al., 2018). The research on chronic illnesses has led to the development of a model, according to which, profuse distress can stem from the interaction of the inherent nature with several factors, such as pre-formed schema, previous life experiences, difficulty in enduring uncertainty, and meta-cognitive beliefs concerning worry. The resulting distress can initiate cognitive processes whose characteristics are alertness, worry, and introspectiveness. Activities to deal with revived control and a pattern of alertness to the signs of the illness can elevate anxiety, in the context of a spectrum of several systemic factors which can either intensify or mitigate anxiety (Curran et al., 2017). Anxiety is an invisible but integral part of the daily experiences of patients with chronic illnesses.

Anxiety is built on the ruins of fear, and the source of fear depends on the underlying condition. The fear of illness is due to the patient's expectations about the influence of pain on his/her personal and social life and how long-term pain causes disability in both. The fear of progression has been found to be the pillar of the anxiety problems of patients suffering from chronic diseases (Khatibi et al., 2020), as about 50% of these patients dread the prospect of being handicapped or crippled (Herschbach et al., 2005). Chronic diseases require a complex response, over a prolonged time period. This response should stem from a empowering system that is carefully orchestrated utilizing the inputs obtained from several health professionals, necessary medications, and, if needed, monitoring equipment.

A chronic organic disease usually necessitates a change in the patient's lifestyle, makes life more complicated and often less pleasant, and thus forces the patient to indulge in less activities and interests compared to his/her former life (Armstrong, 2014). These changes are inconsistent with patient's imaging and schema and can cause anxiety. Chronic illnesses not only affect all aspects of the patient's life; it also reduces the life quality of the family members of the patient (Golics et al., 2013). conducted several semi-structured interviews with 133 family members of the patients with chronic illnesses from 26 medical fields and identified the major ways in which family lives can be affected by disease and the commonality of issues across all diseases. The results were classified in the following categories: emotional impact (mentioned by 92% of subjects), daily activities (91%), family relationships (69%), sleep and health (67%), holidays (62%), involvement in medical care and support

given to family members (61%), work and study (52%), financial impact (51%), social life (37%), and time planning (14%).

2-10-Co-morbidity of Anxiety with other psychiatric disorders

Much evidence has shown the co-morbidity of anxiety disorders to be the rule rather than an exception. Previous studies have also shown anxiety disorders to occur frequently in children and adolescents with other psychiatric disorders, including depressive disorders, conduct disorder, oppositional defiant disorder, attention-deficit/hyperactivity disorder, and alcohol abuse or dependence (Essau, 2003). Comorbid Anxiety is common in patients with depressive disorders. Studies have shown that more than 70% of individuals with depressive disorders also have anxiety symptoms, and 40 to 70% simultaneously met the criteria for at least one type of anxiety disorder (Zhiguo & Yiru, 2014).

2-11-Anxiety is chronic illness

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underlying condition. The fear of illness is due to the patient's expectations about the influence of pain on his/her personal and social life and how long-term pain causes disability in both. The fear of progression is the pillar of the anxiety problems of patients suffering from chronic diseases (Khatibi et al., 2020), as about 50% of these patients dread the prospect of being handicapped or crippled (Herschbach et al., 2005). Chronic diseases require a complex response, over a prolonged period. This response should stem from an empowering system that is carefully orchestrated utilizing the inputs obtained from several health professionals, necessary medications and, if needed, monitoring equipment.

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2-12-Anxiety in MS

Multiple sclerosis is one of the causes of disability and the second after trauma. It has an extensive the scope of symptoms and effects on every part of the body. Living with MS was described by The philosopher Toombs (1955) that suffered from MS as "a global disorder. A disorder that incorporates a changed relationship with self and other, a transformation in the surrounding world, a threat to the self, and a change in one's relation to others (Van Reenen et al., 2019). One of the most important sequences of this change is Anxiety, approximately three times that of the general population

(Gascoyne et al., 2020). In the most extensive study till 2012, Jones et al. have shown Anxiety rates were notably high, with over half (54.1%). Other research has shown the high rate of Anxiety in MS (Boeschoten et al., 2017; Janssens et al., 2006; Korostil & Feinstein, 2007).

There is a reciprocal relationship between Anxiety disorder and inflammation (Rossi et al., 2017). Moreover, studies have suggested that "damage of frontal and temporal cortices, lack of functional connectivity between two prefrontal areas and the amygdala plays an important role in the genesis of emotional disorders in multiple sclerosis." (Passamonti et al., 2009). Also, biological events, that no less important than the traditional psychosocial factors. The researchers identified the factors affecting Anxiety in the patients in MS. Depression, low levels of self-efficacy, disability, and stress (Garfield & Lincoln, 2012), cognitive and social factors (Butler et al., 2016), social support (Hanna & Strober, 2020). Then Anxiety and MS have a reciprocal relationship, MS can develop Anxiety, and Anxiety influence relapses (Hartoonian et al., 2015; Potagas et al., 2008).

One risk factor for Anxiety in MS is uncertainty. Uncertainty is the common factor in anxiety disorder (Boswell et al., 2013). Also, uncertainty is an inevitable part of the MS experience. They never know if there will be an exacerbation, how severe the symptoms will be, or how fast the symptoms will progress. All patients with MS face uncertainty (Alschuler & Beier, 2015).

Uncertainty according to Merle Mishel's theory, is a mental state characteristic for a human being, meaning the sense of loss of control, lack of knowledge about the changes that may occur in the future, and the feeling of doubt. Previous studies identified the following correlates of uncertainty: stress and anxiety, loss of control, lack of information, and waiting (Kurta-Nowicka & Jaracz, 2019). The unpredictable nature of MS can be a source of Anxiety.

Patients diagnosed with MS do not know when they might have their next relapse and do not estimate the severity of the relapse and its consequences. Generally, it is well-accepted that a new relapse is a sign of disease progression and has its complications. It has also been suggested that fear of progression (in its general term and as an emotional response) is related to the depression observed in patients with MS. At the same time, it is not correlated with gender, age, disease duration, and the stage of the disease (Nielsen et al., 2018).

MS has sweeping effects on the aspects of life, that each of them increases Anxiety alone. Anxiety has been linked to many other common 'invisible' symptoms in PwMS. Studies have found that Anxiety is associated with more significant sleeping problems, and there is a higher prevalence of anxiety in PwMS who suffer from MS fatigue. (Morrow, 2018). Strong negative emotions concerning their illness and interpersonal relation, negative impact on sexual functioning (McCabe et al., 1996). Unfortunately, MS not only has an effect on the patient, but also causes the source of Anxiety in family members. In the study by Janssens et al. 2003, 2006 showed partners of PwMS have high levels of Anxiety in the early period after the diagnosis. Also results have shown 40% of the partners and 24% of the partners had levels of high levels of Anxiety.

In the additional effect of psychological and biological of MS, the patient with MS experiences stress of life events more, because MS is associated with a substantial burden on society owing to the high cost of the available treatments and lower employment prospects and job retention for patients and their caregivers (Piehl, 2018). Evidence supporting the concept that stressful life events may play an essential role in triggering MS relapses (Mitsonis et al., 2009; Mohr et al., 2004). Anxiety can interfere with a person's ability to manage diseases and other aspects of daily life (Kennedy 2012). Furthermore, this situation can exacerbate Anxiety.

2-13-Treatment

According to Paul Tillich," therapy can put anxiety in the proper place because of the structure of finitude." when the patient lives with a chronic and disabling disease, every moment likely they always confront with nonbeing anxiety, as well as disabling anxiety , that the source of anxiety is not removable. Then we must focus on the management of anxiety in chronic illness.

2-14-Medical treatment

The first-line pharmacologic treatment for anxiety disorders is a selective serotonin uptake inhibitor(SSRI), with serotonin-norepinephrine uptake inhibitors (SNRIs) also playing a prominent role (Murrough et al., 2015)

Calcium channel modulator pregabalin: calcium channel blockers have been used successfully for anxiety (Zamponi et al., 2015). Tricyclic antidepressants (TCAs) Tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs), Reversible inhibitor of monoamine oxidase A (RIMA) Moclobemide , and Benzodiazepines are drugs that use in anxiety. Because of side effects, patient cannot tolerate, and therefore may stop taking the drug. Some of side effects are: addiction and drug interaction (Stewart et al., 2015) Sexual dysfunction, Gastrointestinal effects, Central nervous system side effects, Discontinuation syndrome (Predictable et al., 2006). The majority of patients with an anxiety disorder experience at least three side effects, no matter which medication they take (Murrough et al., 2015). The studies have shown efficacy in reducing anxiety with drugs, they ameliorate symptoms but have numerous side effects, like Insomnia, nausea, hyperhidrosis, fatigue, somnolence, headache, decreased libido, anorgasmia, and ejaculation disorders. They also often do not achieve lasting relief from anxiety and do nothing to resolve the life situation or internal relationships that caused the anxiety (Sadock, 2007). Pincus & Duberstein, 2007 conducted a comparative meta-analysis on 32 studies of treatments focused on anxiety disorders in older adults (N = 2,484) receiving behavioral interventions or pharmacotherapy.

In separate analyses of the effects of interventions, greater improvements of anxiety symptoms are found in pharmacotherapy than in behavioral interventions ($d = 1.76$ versus $d = 0.81$ SD units). This difference disappears when computing effect sizes that control for nonspecific change in the control group ($d = 0.80$ and $d = 0.83$ SD units) because effect sizes are greater in pill-placebo controls of pharmacological studies than in control groups (e.g., waitlist) of behavioral interventions ($d = 1.06$ versus $d = 0.10$ SD units). Both interventions also yield moderate reductions in depressive symptoms ($d = 0.59$ versus $d = 0.61$ SD units), and dropout rates were comparable.

Several meta-analyses have found contradictory results regarding the efficacy of the psychological and pharmacological treatment of anxiety disorders. The main reasons for these inconsistent results seem to be the inclusion of heterogeneous studies and influences of selection biases. Sixteen studies on panic disorder, six studies on social anxiety disorder, and two studies on generalized anxiety disorder have been analyzed in a meta-analysis. Effect sizes for differences between the different treatment modalities were calculated there was no evidence for a difference between drugs and

CBT. A combination of CBT and drug was superior to pure drug treatment on both the clinician and the self-ratings. For both ratings, a combination of CBT and drug was more effective than CBT alone. However, the effect sizes were small and not statistically different (this was based on only two studies). A combination of CBT and drug was significantly more effective than CBT plus placebo both on the investigators' and the patients' rating. The effect sizes were small (Bandelow et al., 2007).

2-15-Psychological treatments on anxiety

The empirically supported treatments developed to treat anxiety have consistently demonstrated better results than medications without the side effects and treatment dropout that often accompany medications. Basic and clinical studies have led to advances in our understanding of the neural circuitry of anxiety and related disorders. Research shows that the neural circuitry in the processing and regulation of emotions (frontal cortex and limbic system) seems to be more sensitive to changes following psychotherapy of anxiety and related disorders (Brooks & Stein, 2015) .

Cognitive-emotional neuroscience Anxiety and related disorders show the role of discrete types of "false alarms" that can be effectively targeted with psychotherapy. There are types of psychological treatment that effect on anxiety. Psychoanalytic Therapy, Gestalt Therapy, Emotional Freedom Technique (EFT), Short-Term Dynamic Therapy (STDT), Art Therapy/Music Therapy/Play Therapy, exposure in vivo, Self-help treatment are treatment that use for anxiety. some research has shown the efficacy of the psychological intervention in the treatment of anxiety.

Bruce, et al. 2005 in USA in the longitudinal, prospective, short-interval follow-up study of adults with a current or past history of anxiety disorders, In 1989-1991. Data were drawn from the Harvard/Brown Anxiety Disorders Research Program (Bruce et al., 2005).The samples were 473 patient with age from 18 to 86 years (mean=40.5 years) base on DSM-III-R criteria .357 subjects (50%) were experiencing an episode of panic disorder with agoraphobia, 82 (12%) panic disorder without agoraphobia, 179 (25%) generalized anxiety disorder, and 176 (24%) social phobia. Some subjects had more than one disorder. A total of 473 subjects remained enrolled in the study at the 12-year follow-up in June 2003. No significant demographic or diagnostic differences were found between the subjects included in the 12-year follow-up and those who dropped

out of the study, nor were there significant differences in treatment received between those two groups. 12-Year Longitudinal Course subjects with panic disorder without agoraphobia were more likely to have a recovery at all-time points and had a 0.82 probability of achieving recovery of their intake episode of panic disorder without agoraphobia by year 12. In comparison, patients with generalized anxiety disorder, panic disorder with agoraphobia, and social phobia had much lower probabilities of achieving recovery over 12 years of follow-up (probabilities of 0.58, 0.48, and 0.37, respectively). Subjects who had a prospectively observed recovery from their intake anxiety disorder had a high probability of subsequently having a recurrence over the follow up period. Although subjects with panic disorder without agoraphobia were found to have a higher likelihood of recovery, compared to those with panic disorder with agoraphobia, the probability of recurrence of the two disorders was quite similar (0.56 and 0.58, respectively). Individuals with generalized anxiety disorder or social phobia who recovered were somewhat less likely to have a recurrence over the 12-year follow-up period. The probability of having a recurrence of social phobia was 0.39 over 12 years, and the probability of recurrence in patients who had recovered from generalized anxiety disorder was 0.45 at the end of the 12 years.

2-16 Psychology interventions on anxiety

Cognitive therapy as a first-line treatment in disorders is an effective treatment for problems as diverse as depression, anxiety disorders with emphasis on formal operational thinking. Many studies show that Cognitive Behavioral Therapy (CBT) is an effective therapeutic strategy for a wide variety of mental disorders. However, due to methodological issues, the magnitude of the effect is currently difficult to estimate.

Wootton et al., 2015 In a prospective analysis of long-term outcomes of 98 individuals with anxiety and related disorders treated in an outpatient, by using CBT approach during 2007-2011. All participants were diagnosed at pre-treatment with the MINI International Neuropsychiatric Interview (MINI), and follow-up interviews were conducted by clinic staff or clinic volunteers, commencing approximately 12-months after treatment termination. The follow-up interviews included the self-report CGI-S and Sheehan Disability Scale (SDS).

They were completed over the telephone. Both measures were performed at pre-treatment, post-treatment, and each of the follow-up time points. Participants were followed up each year after their discharge, for 3 years. The results of the MLM analysis indicated a statistically significant effect of time for both of the outcome measures, (CGI-S, $F(4, 158) = 32.85, p < 0.001$) SDS, $F(4, 152) = 27.08, p < 0.001$). Scores also remained significantly lower than pre-treatment at each of the follow-up time-points on both measures (p 's = < 0.001). Also patients maintained their treatment gains, with large effect sizes obtained from pre-treatment to each follow-up time point ($d = 1.11-1.60$). Limitations are: the high attrition rate, lack of use of diagnosis-specific measures (Wootton et al., 2015).

Hoffman et al. 2008 were investigated researches of MEDLINE, PsycINFO, PubMed, Scopus, the Institute of Scientific Information, and Dissertation Abstracts International till 2007. the criteria included studies that randomly assigned adult patients between ages 18 and 65 years meeting DSM-III-R or DSM-IV criteria for an anxiety disorder to either CBT or placebo 27 studies .

There were no significant differences in attrition rates between CBT and placebo. Random-effects models of completer samples yielded a pooled effect size (Hedges' g) of 0.73 (95% CI = 0.88 to 1.65) for continuous anxiety severity measures and 0.45 (95% CI = 0.25 to 0.65) for depressive symptom severity measures. The pooled odds ratio for completer treatment response rates was 4.06 (95% CI = 2.78 to 5.92). The strongest effect sizes were observed in obsessive-compulsive disorder and acute stress disorder, and the weakest effect size was found in panic disorder. The advantage of CBT over placebo did not depend on placebo modality, number of sessions, or study year. The result of this review of randomized placebo-controlled trials indicates that CBT is efficacious for adult anxiety disorders. Limitations in this research were: high-quality randomized placebo-controlled CBT trials (6 N): One of the limitations are the presence of differences between the specific treatment techniques and the treatment components from one disorder to another. These differences might have accounted for some of the differences in the treatment efficacy. Also, there is variations in the placebo conditions, and some placebo conditions is possible to be more efficacious than others. Another shortcomings is the impossibility of estimating the effect sizes of panic disorder with agoraphobia separate from panic

disorder without agoraphobia, and this is due to the limitations in diagnoses in the criteria of DSM-III-R and DSM-IV (Hofmann & Smits, 2008).

Carpenter et al. (2018) examined the efficacy of cognitive-behavioral therapy (CBT) for anxiety-related disorders based on randomized placebo-controlled trials. 41 studies that randomly assigned patients ($N = 2,843$) with acute stress disorder, generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), panic disorder (PD), posttraumatic stress disorder (PTSD), or social anxiety disorder (SAD) to CBT or a psychological or pill placebo condition were studied. The average study sample had a mean age of 36.0 years ($SD = 6.53$), was 58.9% female ($SD = 21.21$) and was 73.0% white ($SD = 21.87$). Examination of dropout rates showed a significantly greater likelihood of dropout in CBT compared to placebo (OR = 1.35, 95% CI = 1.05 to 1.77, $p < .05$). The weighted mean dropout rate across all studies was 24.0% in CBT and 17.2% in placebo. This difference in dropout rates was largely due to a greater attrition rate in the 14 studies. Findings demonstrated moderate placebo-controlled effects of CBT on target disorder symptoms (Hedges' $g = 0.56$), and small to moderate effects on other anxiety symptoms (Hedges' $g = 0.38$), depression (Hedges' $g = 0.31$), and quality of life (Hedges' $g = 0.30$). Response rates in CBT compared to placebo were associated with an odds ratio of 2.97 (Carpenter et al., 2018).

Importance Cognitive behavioral therapy is recommended for anxiety-related disorders, but evidence for its long-term outcome is limited. The risk of bias assessment showed that missing data were not considered properly by many studies or these studies did not provide adequate information on why and how data were missing. Criteria for treatment response were different between studies, and this has potentially contributed to increased heterogeneity in the effect sizes for the categorical outcomes.

The low diversity of the samples leads to lesser generalization. Also, it should be considered that there was some degree of heterogeneity in the types of placebo conditions used across the studies. Although no difference was found for either controlled or pre-post placebo effect sizes between studies using psychological vs. pill placebo, the lack of complete uniformity in control conditions limits the precision of the comparison. Studies using pill placebo typically do not control for the time spent with a clinician, and it may attract a unique sample that is open to both pharmacological

and psychotherapy treatments. In studies using psychological placebos, on the other hand, researchers and even patients may know that they are attributed to a control condition.

Loerinc et al. 2015 investigated the CBT response rate on treatment outcome studies for anxiety disorders. cognitive-behavioral therapy (CBT) studies in English language publications, from 2000 to 2014 on PubMed, MEDLINE, and PsycINFO were selected. 87 studies have met the following criteria: participants met DSM-IV criteria for an anxiety disorder; randomized controlled or open studies for a specific anxiety disorder with at least one treatment condition being CBT in the absence of medication, reported response rates.

The overall response rate across all anxiety disorders was lower than expected, with post-treatment rates averaging 49.5% and long-term rates averaging 53.6%. Post-treatment rates for specific anxiety disorders were 0%-86% for OCD, 10%-97% for PD, 3%-86% for GAD, 4%-80% for SAD, 8%-100% for SP, and 28%-88% for PTSD. Long-term rates were 0%-64% for OCD, 1%-100% for PD, 3%-86% for GAD, 19%-89% for SAD, and 13%-93% for PTSD (none of the SP studies reported long-term response rates). The response rates varied substantially from study to study. This research explained almost 55% of the post-treatment variability, and about 69% of the variability at follow-up in reported response rate. This review identified Eighty-four of the studies (96.5%) reported response rates at post-treatment (providing 194 response rates); 53 studies (60.9%) reported response rates at follow-up (173 response rates). The number of response rates (data points) per study ranged from 1 (in 30 out of the 87 studies) to 14 (in 1 study; Mean = 2.05, Median = 2.0). Number of treatment sessions ranged from 1 to 28 (Mean = 11.3, Median = 12), and attrition ranged from 0 to 53% (Mean = 15.6%, Median = 14.0%). Most response rates were based on intent-to-treat samples (63.0%). The most common form of treatment was individual CBT (38.9%). The limitations of this research were: First, the number of studies, with power especially for follow-up analyses, were limited. Second, no established best practices for determination of response rate, third no established guideline for objectively determining the overall response rate (Loerinc et al., 2015).

Van Dis et al.2019 conducted a systematic review and meta-analysis aimed to assess the long-term outcomes after cognitive behavioral therapy (compared with care as usual, relaxation, psychoeducation, pill placebo, supportive therapy, or waiting list for

anxiety disorder. Data were gathered from English-language publications were identified from PubMed, PsycINFO, Embase, Cochrane, Open Grey (1980 to January 2019), and recent reviews. Of 69 randomized clinical trials (4118 outpatients) that were mainly of low quality, cognitive behavioral therapy compared with control conditions was associated with improved outcomes after treatment completion and at 1 to 6 months and at 6 to 12 months of follow-up for a generalized anxiety disorder (Hedges g , 0.07-0.40), panic disorder with or without agoraphobia (Hedges g , 0.22-0.35), social anxiety disorder (Hedges g , 0.34-0.60), specific phobia (Hedges g , 0.49-0.72), PTSD (Hedges g , 0.59-0.72), and OCD (Hedges g , 0.70-0.85). At a follow-up of 12 months or more, these associations were still significant for generalized anxiety disorder (Hedges g , 0.22; number of studies [k] = 10), social anxiety disorder (Hedges g , 0.42; k = 3), and PTSD (Hedges g , 0.84; k = 5), but not for panic disorder with or without agoraphobia (k = 5) and could not be calculated for specific phobia (k = 1) and OCD (k = 0). Relapse rates after 3 to 12 months were 0% to 14% , but it were reported in only 6 randomized Experimental control is limited during follow-up periods, and this leads to the confounding factors may threaten the validity of the long-term effect estimates. Also, symptom outcome measures were averaged to handle dependent outcomes, that may have resulted in overestimated SEs. Most studies had suboptimal designs and a high risk of researcher allegiance bias, that may have affected the reliability of the effect estimates (Van Dis et al., 2020).

Springer et al.2018 studied in a meta-analyze the remission in CBT for adult anxiety disorders Journal articles by using searches of the PsycINFO, and Medline electronic databases from January 2000 through February 2018. Researches were limited to English-language articles and adult populations. Studies were also identified through the reference lists of originally obtained articles, review papers, and meta-analyses. Inclusion criteria: participants were adults (age 18 years and older) who met DSM-IV criteria for an anxiety disorder; that it was a treatment study (randomized controlled trial or open trial) for a specific DSM-IV anxiety disorder, in which at least one treatment condition was CBT monotherapy; and a number or percentage of participants remitted was reported. Excluded samples were: combined CBT with other treatments (e.g., medications), web-based and self-help interventions, concurrent treatment (e.g., concurrent CBT for co-occurring anxiety and substance use), previously failed treatment (e.g., participants received CBT after failing to respond to

pharmacotherapy), and studies that did not require medication stabilization prior to treatment. Articles reporting secondary analyses of a data set already included in the meta-analysis were excluded. From the initial 228 abstracts, 100 full-text articles were retained for analyses and overall participant were 7407. Across all analyses, the mean remission rate was 51.0% (95% CI = 47.8%-54.2%) at post-treatment and 55.1% (95% CI = 51.0%-59.1%) at follow-up. Although CBT is an empirically supported treatment for anxiety disorders and often outperforms other treatments the present results suggest that there is significant room for improvement as only half of patients achieve remission status. First, there is no definition for “remission,” which, in case of any, would yield more accurate estimates of the efficacy of CBT on its own and in comparison to control treatments. Second, there is a lack of more specific questions about remission for specific patients and disorders, such as whether certain definitions, measures, or evaluation criteria yield more accurate estimates of remission rates for certain individuals and problems. Ultimately, a more nuanced understanding of remission and how it may differ between individuals and, to this end, presenting problems may lead to more effective and tailored treatments (Springer et al., 2018) .

Hunsley et al. in 2014 studied the efficacy of CBT on anxiety. They searched the related publication from the beginning of 2000 until the end of 2012 on PsycINFO and MEDLINE. Concerning to GAD, forms of CBT are efficacious across the life span. of 11 study Results suggested that pre-test to post-test effect sizes for self-reported GAD symptom measures were substantial (g 0.92, 95% CI [0.77, 1.07]).

There is also extensive efficacy evidence for CBT in the treatment of SAD with youth and adults. In 14 comparison study, the psychological treatment results confirmed the findings of earlier meta-analyses, the findings were shown the effect of psychological treatment on self-report measures of social anxiety (d 0.77, 95% CI [0.60, 0.94]). Efficacy evidence supports CBT for the treatment of specific phobias, but almost all of the evidence is for the treatment of adults For the treatment of the panic disorder, 17 studies focused on the treatment of PD. Results suggested that pretest to posttest effect sizes were substantial for self-reports of panic attacks (d 1.01, 95% CI [0.77, 1.25]) and avoidance (d 0.83, 95% CI [0.60, 1.06]), The review of 38 studies indicated that TFCBT showed clinical benefit over waitlist and usual care controls on both clinician-rated measures of PTSD symptoms (SMD 1.40, 95% CI [0.91, 1.89]) and self-rated measures of PTSD symptoms (SMD 1.70, 95% CI [1.24, 2.17]). CBT appears

to be efficacious for adults and older adults, with effectiveness evidence supporting its use with adults. This research limits to the generalizability (Hunsley et al., 2014) .

2-17 Treatment anxiety in chronic diseases

Clarke&Currie2009 reviewed the evidence for an association between depression and anxiety in heart disease, stroke, diabetes mellitus, asthma, cancer, arthritis and osteoporosis also the effectiveness of treatments for depression and anxiety in these settings. They conducted a Systematic literature search of systematic reviews, meta-analyses and evidence-based clinical practice guidelines published between 1995 and 2007, inclusive. A total of 159 reviews were identified (32 on heart disease, 23 on stroke, 19 on diabetes mellitus, 12 on asthma, 36 on cancer, 24 on arthritis and osteoporosis, and 13 general reviews. The results shown that Depression is more common in all disease groups than in the general population; anxiety is more common in people with heart disease, stroke, and cancer than in the general population. Heterogeneity of studies makes the determination of risk and the direction of causal relationships difficult to determines, but there is consistent evidence that depression is a risk factor for heart disease, stroke and diabetes mellitus. Antidepressants appear to be effective for treating depression and anxiety in patients with heart disease, stroke, cancer and arthritis, although the number of studies in this area is small. A range of psychological and behavioral treatments are also effective in improving mood in patients with cancer and arthritis but, again, the number of studies is small. Cognitive behavior therapy (CBT) was a modestly effective treatment for depression and anxiety in patients with heart disease, adult patients with diabetes, children with asthma, and people with various cancers.

To assess the effects of psychological therapies for the treatment of anxiety disorders in people with the chronic obstructive pulmonary disease were searched the specialized registers of two Cochrane Review Groups: Cochrane Common Mental Disorders (CCMD) and Cochrane Airways (CAG) (to 14 August 2015). The specialized registers include reports of relevant randomized controlled trials from The Cochrane Library, MEDLINE, Embase, and PsycINFO . Inclusion criteria were: all randomized controlled trials (RCTs), cluster-randomized trials, and cross-over trials of psychological therapies for people (aged over 40 years) with COPD and coexisting

anxiety disorders that this was compared with neither intervention nor education. Psychological therapies were observed to be more effective for the treatment of anxiety compared with co-interventions or usual care (mean difference (MD) -4.41, 95% confidence interval (CI) -8.28 to -0.53; participants = 319; $I^2 = 62\%$; $P = 0.03$); However, there was substantial heterogeneity ($I^2 = 62\%$), which limits the reliability of the findings.

Two studies with 289 participants reported quality of life through the use of three different tools, SGRQ, SF36 and CRQ. Psychological interventions were observed to be more effective compared to the control population for the combination of SGRQ and the physical composite of SF36 (standardised mean difference (SMD) -0.40, 95% CI -0.88 to -0.08; participants = 289; studies = 2; $I^2 = 61\%$; $P = 0.10$). No evidence of any effect was observed for SGRQ and the emotional composite of SF36 (SMD -0.30, 95% CI -1.03 to 0.44; participants = 289; studies = 2; $I^2 = 82\%$).

2-18 Psychological interventions in multiple sclerosis

To determine the overall effect of psychological and pharmacological treatments for depression or anxiety in persons with MS. Fiest et al. 2016 searched the Medline, EMBASE, PsycINFO, Psyc ARTICLES Full Text, Cochrane Central Register of Controlled Trials, CINAHL, Web of Science, and Scopus databases using systematic review methodology from database inception until March 25, 2015.

Of 1753 abstracts screened, 21 articles reporting on 13 unique clinical trials met the inclusion criteria. : (1) randomized controlled trial conducted in any setting; (2) published in any language; and (3) conducted in a depressed or anxious population of adults with MS. Depression severity improved in nine psychological trials of depression treatment ($N=307$; SMD: -0.45 (95%CI: -0.74, -0.16)). The severity of depression also improved in three pharmacological trials of depression treatment (SMD: -0.63 ($N=165$; 95%CI: -1.07, -0.20)). For anxiety, only a single trial examined psychological therapy for injection phobia and reported no statistically significant improvement.

The data are insufficient to determine the effectiveness of treatments for anxiety. limitation: While some of the depression trials also measured symptoms of anxiety, none explicitly reported comorbidity in the proportions of people with anxiety disorder

or elevated anxiety symptoms. The trials also did not assess whether the presence of symptoms of anxiety influenced the likelihood of responding to treatment for depression. Since these analyzes did not find a reduction in anxiety symptoms with interventions for depression, different interventions may be needed to reduce symptoms of anxiety in people with depression and Psychological trials were ranked lower on the risk of bias and quality of evidence scales due to a lack of blindness inherent in their design.

Ghodsipour et al. 2018 in Iran conducted a quasi-experimental research with pretest-posttest and control group. It was designed on 30 members of the MS Society of Semnan City, by purposive sampling. They examined the effect of Mindfulness-based cognitive therapy on a patient with MS on two, experimental group and the control group. The measurements were the Lovibond psychological distress scale and the multiple sclerosis Quality of Life questionnaire. The collected data were analyzed using multivariate analysis of covariance.

The results showed a significant difference between the experimental and control groups in health distress, mental well-being, cognitive function, and role limitations, but no significant difference was found between the two groups in overall Quality of Life. Also there is not any significant difference between the experimental and control group in term of depression, anxiety and stress. Mindfulness-based cognitive therapy has a significant effect on psychological aspects of Quality of Life, including health distress, mental well-being, role limitations due to emotional problems, and cognitive performance ($P < 0.05$). However, this effect was not statistically significant on one of the psychological aspects of Quality of Life (overall Quality of Life), depression, anxiety, and stress in patients with multiple sclerosis ($P > 0.05$). Small sample size, the presence of measurement error and generalizability can be considered as limitation of this study.

Sesel et al. in 2018 published the result of meta-analysis about the efficacy of Psychosocial Interventions for People with Multiple Sclerosis: A Meta-Analysis of Specific Treatment Effects :data gathered from the six electronic databases (Medline, Embase, PsycINFO, Cochrane Central Register of Controlled Trials, CINAHL, and Clinicaltrials.gov) until April 21, 2016, for randomized controlled trials reporting the

effect of psychological interventions for depressive symptoms, anxiety, pain, fatigue, or health-related quality of life (HRQoL) in PwMS. The search yielded 356 articles with 13 included studies (n = 1,617). Benefits of psychological interventions were found for depressive symptoms (Cohen's $d = 0.281$), anxiety ($d = 0.285$), fatigue ($d = 0.228$), and mental ($d = 0.398$) and total HRQoL ($d = 0.444$), but not physical HRQoL. There were insufficient studies to meta-analyze post treatment outcomes for pain. Interventions were more effective for HRQoL for patients with relapsing-remitting MS and when treatment doses were larger. Cognitive behavioral therapy (CBT) was not efficacious for PwMS when considered alone.

There was some indication that CBT was less efficacious than other interventions. However, this may be due to smaller treatment doses in CBT studies. Limitations of this research were: Studies were performed with different interventions in heterogeneous groups of patients; however, these moderators were not necessarily independent (e.g., CBT and dose). This makes it difficult to determine which of these factors accounted for differences in the outcomes between studies. Additionally, multiple moderator analyses were conducted, which may have inflated the possibility of a type I error. Although we completed a protocol (available from the authors) in advance of conducting the meta-analysis, this was not published or registered. Nonetheless, it should be noted that when moderators were significant, the pattern of results was similar across different outcomes, reducing the likelihood that these moderation analyses were subject to type I errors. Given that there were only 13 studies, many of the moderator analyses were underpowered, and there may be other patient or treatment characteristics that affect treatment efficacy (Sesel et al., 2018).

2-19-Conclusion

Standard cognitive models have proven to be effective and sufficient for many patients with anxiety disorder. However, a large subgroup may suffer from chronic anxiety, and pharmacological treatment. These patients may fail to progress during cognitive therapy due to schema-related issues. While cognitive behavior therapy (CBT) is useful for anxiety disorders (Bandelow & Michaelis, 2015; Olatunji et al., 2010), it has modest efficacy, and half of the sufferers of anxiety respond successfully to CBT (Carpenter et al., 2018). relapses and residual symptoms are also common

(Martin et al., 2009). Thinking can affect our emotions. But Changes in cognitions can be affected by emotional impulses.

As well as the cognitive appraisal of an event generates an emotional response. So changing cognitions may not necessarily cause a shift in emotion working because feelings are aroused by nonconsciousness neural processes, and it effect on thoughts. Cognitive interventions teach the consciously control anxiety and manage emotions without attention to the cause and emotion with focus on willpower and repeated practice technique, but, it seems the unconscious feelings and core emotions trigger anxiety, based on conditioned responses.

While anxiety can be regulated through sharp focus and self-soothing, it will continue to be triggered when feelings arise. Unless the patient is helped to bear those previously warded-off feelings, the patient will not help cope with the Anxiety. According to Gross's process model, any emotion can become dysregulated when the patient lacks or fails to use an appropriate regulatory strategy (Grecucci et al., 2016).

A shortcoming of CBT as a power treatment maybe does not typically address universal needs (Rafaeli et al., 2010). Also the tendency to "intellectualize" the emotional experience by adopting a more instructional, as opposed to an explorative approach (Baker et al., 2012). Schemas as profound cognitive structures containing the basic rules for selecting, filtering, and coding information (Restrepo, 2007) can be considered as one of the underlying sources of anxiety in CBT that is ignored. The fact that the emotional and cognitive aspects of traumatic experience located in different brain systems, may explain why schemas are not changeable by simple cognitive methods (Young et al., 2014). The research on the efficacy and effectiveness of cognitive techniques alone for anxiety disorders has shown variable results. (Kaczurkin & Foa, 2015). if we review the nature of anxiety as, emotional responses with survival value can occur without the participation of the higher processing systems of the brain—those involved in thinking, reasoning, and consciousness, also, the trait and state anxiety are mapped differently in the human brain, then treatment anxiety that is evoked to protect the human organism against predatory threat must be multi-disciplinary.

In the case of a chronic disease like MS, where the sources of anxiety are multiple and linked to the course of the disease, CBT maybe not the best indication for the treatment of anxiety since it focuses on acute anxiety and on specific targets that elicit

anxiety. However, in some cases like the main problem is a chronic illness and with the illness that threat their future, and the gap between here and now till vague future fill suffer from side effects of the drug, method of administration, no definitive cure, stigma (Cook et al., 2016) and problem co- occurred anxiety of disability and nonbeing. Unfortunately, there is little anxiety-focused treatment literatures in MS (Turner & Alschuler, 2018). Therapeutic efforts can be more effective if aimed at mechanisms underlying anxiety disorders. in this research, the effect of schema therapy on anxiety in a patient with MS as an integrated model of treatment was studied. Given that the theory's and the treatment arise of them, have made in the ordinary world, it must be considered that patient with MS has a new special world related to illness with challenges, anxieties, fears, and hopes, Therefore, no specific treatment can be considered with confidence for everyone, especially patients with the chronic illness. Furthermore, it needs further research to find a more efficient treatment for everyone. According to Yalom, I. D., & Crouch, E. (1990). as work on emotion is not sufficient, intellectualization and logic in treatment is not enough. then, maybe the patient profit of schema therapy due to notice to emotion and cognition simultaneously.

2-20- Theoretical Conceptualization of Schema

2-20-1- Brief history of schema

the schema is an old concept. Kant, Bergson, Bartlett (1932), Piaget (1923), Ellis (1962), Vaihinger (1911), Adler(1925) used this concept in different way .the term schema in psychology is most commonly associated with Piaget, who wrote in detail about schemas in different stages of childhood cognition development and Bartlett (1932)who originated the use of this term and demonstrated the roles of schema in learning new information, as well as in recalling memories, Schemas which were also referred to as 'core beliefs' were initially proposed by Beck (1967), who suggested that "negative self-schemas set of negative and pessimistic beliefs and expectations about oneself were acquired through early childhood experiences," and can be held responsible for depression and unhelpful coping styles (Rawlinson, 2018). Beck's cognitive theory suggests that early childhood experiences lead to early maladaptive schemas and related assumptions about ourselves, the world, and the future .Following a critical incident, typically a stressor or life event, early maladaptive schemas, and dysfunctional assumptions are activated, which results in negative

automatic thoughts and the behavioral, motivational, affective, cognitive, and somatic symptoms of depression. Three classes of negative core beliefs about the self-identified by Beck (2005): helplessness, unlovability, and worthlessness. (Osimo et al., 2018). Young, et al. 1990 developed Schema Therapy as an extension of CBT with a focus on characterological disorders and “treatment failures” and make out 18 schemas (Young et al., 2003).

2-20-2-Schema therapy

Over 20 years ago the schema therapy approach was born as a rich treatment model with a combination of cognitive-behavioral therapy, attachment, Gestalt, object relations, constructivist, and psychoanalytic schools (Young et al., 2014).

According to Young 2003, schemas result from five unmet core emotional needs in childhood. The central concept in ST are: Needs, Early maladaptive schemas, coping styles', and schema modes, also Young explained that schemas are internalized, and they are manifested in a specific situation out of consciousness. According to Yang, each treatment model has strengths, but the difference between ST is in integrating these strengths. Another critical component of ST is therapeutic alliance, which plays a role in the treatment and is less emphasized in other approaches. According to existentialism, awareness cannot make a change by itself, because an individual is confronted with the fact that an individual could have made changes before but did not take responsibility for life, and change requires a sense of guilt. In ST, through empathy with the patient, this guilt is placed on their childhood conditions. This awareness without a sense of guilt makes changes and a feeling of more control over life.

2-20-3-Needs

The concept of need in ST is one of the leading and primary concepts. The concept of need in other theory is by Karen Horney (ten need in three categories), Sullivan (general need and zone need), Skinner (previous experiment and reinforcement), Cattell (ergs), Maslow (hierarchy of needs) (Feist & Feist, 2006). In ST, five, universal needs were identified, which unmet needs led to schema formation.

Emotional needs targeted by ST: Secure attachments, Autonomy, competence, and sense of identity, Freedom to express valid needs and emotions, Spontaneity, and play, Realistic limits and self-control (Young et al., 2003).

2-20-4-EMS

EMS is the central concept in ST. It has defined as “a broad, pervasive theme or pattern, comprised of memories, emotions, cognitions, and bodily sensations, regarding oneself and one’s relationships with others, developed during childhood or adolescence, elaborated throughout one’s lifetime and dysfunctional to a significant degree” (Thimm,2010). According to Young, there are five domain and 18 schemas, including: Rejection and Disconnection including: Abuse/Mistrust, Instability/ Abandonment, Shame/Defectiveness, Deprivation Emotional Alienation/ Social Isolation), Impaired Autonomy and Performance dependence/ incompetence, Vulnerability to harm or illness, Enmeshment/underdeveloped self, Failure, Impaired limits: Entitlement/grandiosity, Insufficient self-control/self-discipline Other-directedness: Subjugation, Self-sacrifice, Approval-seeking/recognition-seeking. Overvigilance and inhibition: Negativity/pessimism, Overcontrol/emotional inhibition, Unrelenting standards/hyper criticalness, Punitiveness (Young et al., 2014).

2-21-Coping style and maladaptive coping style

The Concept of coping indicates composition of behavioral and mental strategies chosen by an individual so that they can endure, minimize, or overcome conflict and stress (Folkman, 2013). Coping abilities reflect the adoption of both mental and behavioral strategies when confronting stress or distressing experiences. It has been suggested that coping styles involving avoidance can render the individual more vulnerable to several psychiatric disorders, including PTSD, Anxiety, and major depression (Santarnecchi et al., 2018).

In fact, EMSs mediate maladaptive or adaptive coping (Dozois et al., 2009). Adler 1992 states, "Anxiety can be revealed in the dragging of one’s feet over a problem, approaching a situation

hesitantly, or looking for an excuse to avoid it." They involve the typical fight, flight, and freeze responses and allow them to survive in a specific family environment.

Unlike behaviors, defined as a way individuals cope with stress or conflict, a schema reflects feelings, memories, cognitions, and bodily sensations. Coping styles are usually some healthy and adaptive mechanisms a child adopts to survive the environment and faces; however, it is possible for these styles can become maladaptive in case of their contribution to the perpetuation of an EMS, even when the individual finds him/herself in different conditions and provided with more adaptive coping strategies and, or schemas.

Commonly, that most patients adopt a mixture of coping styles and responses. It is noteworthy that some specific schemas do not always produce the same coping behaviors as, despite the immutable nature of schemas, coping styles can change in various conditions and at different stages of life.

Regarding schemas, individuals can adapt to behave in different ways. One can accept that a schema is valid and give in to it; thus, schema surrender; one can practice schema avoidance by finding ways to block or escape from a schema on a conscious or unconscious level; and finally, one can gravitate towards schema overcompensation, which is behaving in opposite ways one's Schema makes feel (Dobson & Giovannoni, 2013).

Freeze, flight, and fight the three coping styles before explained by Lazarus and Folkman Moreover, Young and colleagues are expressed surrender, avoidance, and overcompensation as the coping style in ST. While schema surrender occurs when an individual accepts that a Schema is dedicated, Schema avoidance occurs when an individual tries not to activate Schemas on either a conscious or unconscious level and Schema overcompensation is when an individual attempts to fight the schema by thinking, feeling, and behaving as though the opposite of the Schema were true (Mairet et al., 2014; van Wijk-Herbrink et al., 2018; Young et al., 2003).

2-22-Modes

Modes are the most difficult concepts in ST. It defined: "Schemas or schema operations—adaptive or maladaptive—that are currently active for an individual." made

chose to cope responses, or it activates maladaptive schema in distressing emotions (Young et al., 2006). An individual may shift from one dysfunctional schema mode into another; as that shift occurs, different Schemas or coping responses, previously dormant, become active. Schema modes can be clustered into four categories: (1) child modes, (2) maladaptive coping modes, (3) maladaptive parent modes, and (4) adaptive modes (Talbot et al., 2015).

The general mode model defines four-mode categories that organize more than 20 modes. Maladaptive child modes are characterized by intense negative emotions that ensue when patients' needs are not met. They can be subdivided into inwardly directed vulnerable modes and outwardly directed modes. In the maladaptive parent modes, patients put too much pressure on themselves to meet unrelenting standards, take too much responsibility for others, or act overly critical, impatient, and aggressive toward themselves. Maladaptive coping modes reflect rigidly used coping responses. They can be divided into the compliant surrender mode, avoidant modes, and over compensator modes. In the adaptive happy child mode, patients feel loved, validated, and secure, and they behave playfully and spontaneously. The adaptive, healthy adult mode includes functional cognitions and behaviors that promote healthy relationships and adequate self-regulation (Jacobs et al., 2020).

2-23-Psychological aspects of schema

Schemas are the emotional and cognitive patterns that form at the beginning of growth and development. According to Young et al. 2003, Schemas are experiences related to childhood, and they contain emotions, cognitions, and bodily sensations. They're the results of unmet emotional needs. They rep is reinforced, accentuating information that confirms the schema and minimizing or denying information that contradicts the schema" (Calvete et al., 2013). Because of avoidance of schema pains, individuals may block the emotions related to a schema. When the effect is blocked, the Schema does not reach the extent of conscious awareness. Individuals try to preserve them. (Young et al., 2003).

2-24-Neurological aspects of schema

With a traumatic learning situation, a system that affects the hippocampus and pertinent cortical areas lays down conscious memories. Besides, the unconscious memories created by the fear conditioning mechanism function via an amygdala-based system. These systems' function is similar and different types of information pertinent to the experience are stored by them. After encountering the stimuli during the initial trauma, each system potentially retrieves its dedicated memories. With the amygdala system, the retrieval leads to an expression of bodily responses for facing the imminent risk, while with the hippocampal system, conscious remembering happens (LeDoux, 2015). Therefore, the amygdala can represent embodied attention, which is the essential link that connects central (mental) and peripheral (bodily) resources. Based on neuroanatomical data, the amygdala has a more substantial effect on the cortex and triggers or stops cortical activity; afterward, the cortex exerts on the amygdala. The pathways that come from the sensory thalamic relay station carry sensory data independently to the amygdala and the cortex; still, the subsequent effect of the amygdala on the cortex is more potent than the two reciprocal connections. Amygdala's role is to sub-serve the fear response with no reference to conscious memory and substantiate (Sadock et al., 2017). Therefore, treatment can regulate the expression.

2-25- Conclusion

All humans experience Anxiety, and it seems Anxiety is a multi-factorial issue that has aspects of Evaluatory and also survival value. According to information theory, a chronic illness have an information value, and then base on the Innate Idea of Kant, phylogenetic endowment Freud, collective unconscious Yung and genetics theory, the patient feels Anxiety because illness has targeted their existence.

Le Deux believed The modern-day individual encounters lesser significant dangers, but the brain's ability to anticipate threats, including those that may never happen, makes up for it. It is emphasized that fear results from brain structures that, even though they produce no feelings by themselves, can still detect danger, and generate defensive responses that ensure survival. The type of threats has changed, also thank

the development of science, increase awareness and ability to anticipate disability has increased, so these two things make somebody anxious, and somebody motivated.

The central core of MS is a disability. Most patients have a relapsing-remitting course, many of residual impairment after each relapse. Furthermore, loss of ability and restriction can have a black shadow on their lives. The anticipation of disability and pain in a lifetime makes them more anxious. According to studies coping with a disability rather than end-of-life was a significant concern for patients and their careers. (Borreani et al., 2014). All theories have been trying to explain Anxiety, and according to those theories, a series of the solution have been put forward that's useful for some of patient. But many of patient cannot benefit because of their schemas.

2-26The role of SCHEMA in anxiety

According to beck et al. 1985, In anxiety disorder, the disturbance in information processing which underlies anxiety vulnerability and anxiety maintenance, can be viewed as a preoccupation with or 'fixation' on the concept of danger, and an associated underestimation of personal ability to cope. The theme of danger in anxiety is evident in the content of anxious schemas (i.e. assumptions and beliefs) and the content of negative automatic thoughts. The overestimation of danger and underestimation of ability to cope with situations in anxiety disorder reflects the activation of underlying maladaptive schemas(Wells & Leahy, 1998). The literature indicates that people with mood disorders and anxiety disorders show high levels of early maladaptive schemas, some of which tend to represent the features of individual disorders. Preliminary evidence shows that schema therapy can be successfully applied to mood and anxiety disorders. The nature and developmental causes of EMSs in personality disorders and mood disorders have been supported by a reasonably large body of literature. Various studies have been reviewed the EMSs related to anxiety disorders among patients . Most EMSs are elevated in anxiety disorders. As EMSs play a relevant role of activation in the onset of anxiety disorders, they have been hypothesized to play a similar role in trait anxiety, (Wilt et al., 2011).

Hawke and Provencher 2011, in a review in PsycINFO and Medline databases in August 2010, explored the relationship between EMSs and psychiatric symptoms among day-treatment patients with a wide range of disorders and comorbidities.

Results showed EMSs also accounted for 52% of the variance of anxiety symptoms, significant contributors being Abandonment, Vulnerability to Harm or Illness, Failure, Self-Sacrifice, and Emotional Inhibition. In all, 13 of the 15 assessed EMSs were significantly correlated with the symptoms of anxiety. Results were not presented by primary disorder or controlled for comorbidities. Nevertheless, these EMSs would appear to be associated with the symptoms of depression and anxiety across the range of psychological disorders. Moreover, research suggests that focus on schemas may be especially efficacious for patients with personality disorders and other longstanding emotional problems, including chronic or recurrent depression and anxiety.

Gonzalez, Diez, in Bizkaia (Basque Country) in 2012, 539 students aged between 18 and 25 years were studied, measures were social anxiety (Caso-A30; Caballo et al., 2010), Early Maladaptive Schemas (YSQ-3; Young, 2005) and coping styles (YRAI-1 and YCI-1 -1; Young, 2003). The results showed that social anxiety is associated with several schemas: Subjugation, Pessimism, Emotional Inhibition, Grandiosity (negative relationship), Abandonment, Enmeshment, and Self-Sacrifice. Moreover, the relationship between the schema of emotional deprivation and social anxiety moderated by the coping style of overcompensation, whereas the relationship between enmeshment and sacrifice schemas and social anxiety is moderated by avoidance (Diez et al., 2012).

Pinto-Gouveia et al. 2006 in Portugal ,in a cross-sectional study have studied, the Early Maladaptive Schemas and Social Phobia compared core beliefs between a group of patients with social phobia (n=62), other anxiety disorders (n=41), and a group of non-psychiatric controls (n=55). The Mean age was 28.71. Participants completed measures to assess social anxiety and the Young's Schema Questionnaire (123-items version) that is designed to assess 15 early maladaptive schemas (EMSs). Results suggest that the schematic structure of patients with social phobia differs one of patients with other anxiety disorders and from normal controls'. Patients with social phobia show higher levels of EMSs, particularly in the area of disconnection/rejection than patients with other anxiety disorders. Regression analysis identified the EMSs of mistrust/abuse, social undesirability/defectiveness, entitlement, emotional deprivation, unrelenting standards and shame, as the ones that explain most of the variance in the sample subject's anxiety. The cross-sectional nature of research makes it impossible

to determine the relationship and influence anxiety and EMS together (Pinto-Gouveia et al., 2006).

Hedley et al. 2001 in Norway have investigated the relationships among Early Maladaptive Schemas (EMS), beliefs about the loss of control, a fear of bodily sensations, and avoidance in patients undergoing cognitive therapy. Fifty-nine patients (43 women and 16 men) with a Mean age (38.4) being treated for panic disorder with agoraphobia (PDA) base on DSM-V participated in the study. The Mean age was 38.4. Measures were Mobility Inventory for Agoraphobia(MI), Agoraphobia Cognition questionnaire

Two EMSs that are seen as being central in PDA [vulnerability to harm (VH) and functional incompetence/dependency (DI)], beliefs about the loss of control, fear of bodily sensations, and avoidance were measured treatment start and at six month follow-up. The data were analyzed using structural modeling techniques. The VH schema influenced beliefs about loss of control ($r=.66$, $p<.001$, effect size $=.96$) on DI ($r=.78$, $p<.001$, effect size $=.98$,) fear of bodily sensations ($r=.55$, $p<.001$, effect size $=.83$), and avoidance ($r=.42$, $p<.001$, effect size $=.86$). Beliefs about loss of control, in turn, predicted a fear of bodily sensations. DI was predicted by VH and did not influence other aspects of PDA. VH also indirectly affected the fear of bodily sensations through VHs effect on a loss of control $r=.21$, $p<.01$, effect size $=.81$. limitations are sample size was small. and structural equation modeling is used for testing (Hedley et al., 2001).

Mammad et al. 2017 conducted a cross-sectional study, among 212 students, aged 17 to 25 years, to diagnose the prevalence of anxiety disorders using early maladaptive schemas and Beck's anxiety inventory among students. and randomly selected from different institutions of the IBN TOFAIL University, (NW of Morocco). Two neurocognitive tests were used: The Beck Anxiety Inventory to evaluate anxiety & the short version of the early maladaptive schema questionnaire of Schmidt, Joiner, Young and Telch (1995), which was translated in French by Rusinek & Hautekéete (2000) to evaluate schemas. The obtained results of measure of anxiety show that the inadequate early maladaptive schemas positively correlated with the Beck Anxiety Inventory: Emotional deprivation ($r = 0.1635$, $p < 0.05$) Isolation ($r = 0.2305$, $p = 0.001$) and Insufficient self-control ($r = 0.1819$, $p < 0.01$), Abandon ($r = 0.2514$, $p = 0.001$) Vulnerability ($r = 0.1505$, $p < 0.05$), Fear of losing control ($r = 0.1510$, $p < 0.05$). A band

appears between early maladaptive schemas and Beck anxiety inventory ,revealing the existence of anxiety in university students, which has appeared in some maladaptive schemas, especially: Emotional deprivation, Isolation, Insufficient self-control, Abandon, Vulnerability, Fear of losing control. Deeper investigations need to understand this relationship and to study other possible factors that could affect this important neurocognitive function. This result limits related to Generalizability due to samples and the nature the research (Mammad et al., 2017).

In descriptive-correlational research, **Jafari et al. 2015** investigated the relationship between early maladaptive schemas, and death anxiety and referential thinking. The research population consisted of MA female students of Azad University, South Tehran branch, of whom 360 subjects were selected through cluster sampling method and 328 (age 26-40) of them were analyzed. Young Schema Questionnaire Short Form (2005), Templer Death Anxiety Scale (1870), and Referential Thinking Questionnaire (2010) were used. Data were analyzed through simultaneous multiple regression analysis. The results indicated that early maladaptive schemas are predictors of negative thinking of referential thinking dimensions $P = 0.039$ and $F(5, 322) = 2.37$ and 3.6% of the variance of negative thinking is related, and early maladaptive schemas are not predictors of death anxiety $P = 0.413$ and $F(5, 322) = 1.007$ (Jafari et al., 2016).

Shariati et al.2014, studied the correlation between anxiety and the early maladaptive schemas and predicting this disorder with early maladaptive. schemas questionnaires were Schema Questionnaire Short Form (SQ-SF) designed by Young and Kettle's Anxiety Questionnaire. 144 female students of the third year of high school. Research results analyses participated in this research. The results analyzed by using, SPSS20 software and the Pearson's correlation coefficient, one-way ANOVA test and stepwise regression. Results indicate a significant correlation between the early maladaptive schemas and the symptoms of anxiety, and they predict that the early maladaptive schema of defectiveness/shame predicts anxiety, and the early maladaptive schema of self-sacrifice has an inverse correlation with students' anxiety. According the Pearson's correlation test, there are a significant and direct correlation($r>0$) exists between the anxiety (overt & covert) and the early maladaptive schemas (except for self-sacrifice schema) of students at 99% level

(Sig. <0.01). On the other hand, an inverse correlation ($r < 0$) exists between anxiety (overt & covert) and the self-sacrifice schema (Shariati, 2014) .

María Cámara & Esther Calvete 2012 studied the Early Maladaptive Schemas as Moderators of the Impact of Stressful Events on Anxiety and Depression in University Students on 510 sample of first- and second year college students at the University of Deusto and the University of the Basque Country, both in Northern Spain. 374 completed measures at time 1 (T1) and time 2 (T2). The Life Stress Questionnaire (LSQ; Wadsworth et al. 2005) and the Social Stress Questionnaire (SSQ; Connor-Smith and Compas 2002) were used. Two-wave prospective study showed that the presence of EMS constitutes a vulnerability factor for both, depressive and anxiety symptoms, and this effect was also moderated by sex. Moreover, the EMS's content specificity revealed which schemas were more relevant to each symptom, providing valuable information for prevention and intervention programs. Two EMS, vulnerability to harm and dependence, predicted increases in anxiety symptoms.

The association between stressors and T2 anxiety symptoms was higher among participants high in dependence, $\beta = .21$, $t(98) = 2.51$, $p = .014$, than among participants low in dependence, $\beta = -.08$, $t(123) = -.84$, ns. For the Abandonment \times sex interaction we estimated the regressive path from abandonment to T2 anxiety in women and men separately. this association was higher for women, $\beta = .19$, $t(249) = 2.99$, $p = .003$, than for men, for whom it was no significant, $\beta = -.16$, $t(122) = -1.57$, ns. Finally, the same procedure was used to examine the Dependence \times sex interaction. In this case, and as displayed in Fig. 2c, the association between dependence and T2 anxiety was higher for men, $\beta = .27$, $t(122) = 3.26$, $p = .014$, than for women, $\beta = .01$, $t(249) = 0.20$. due to it was based on an undergraduate student sample. The findings may not be reproducible in clinical populations that have permanently activated EMS and measuring the schemas only at T1 may have excluded the possibility of testing whether symptoms and stressors influence the cognitive structures and not vice versa. Indeed, it has been found that both distress and stressors can modify cognitive style (Cámara & Calvete, 2012).

Ghasemi and Elahi 2019. investigated the mediating role of experiential avoidance in the relationship between the early maladaptive schemas and illness anxiety. by using correlation method on 308 students of Qazvin University who were selected with the convenience sampling method. The measures were Early Maladaptive Scheme

(Young), hypochondriasis (Evans), and Acceptance and Action Questionnaires. Data analysis with stepwise regression method showed a significant role of schemas of impaired autonomy and performance and impaired limits domains in illness anxiety $p=0.00$. Also, vulnerability to harm or illness and entitlement/grandiosity schemas could significantly predict illness anxiety. $P=0.00$. The limitations of the present study can be attributed to the lack of generalization of results to other communities and collect data in the form of a questionnaire (Ghasemi & Elahi, 2019).

In the study by **Pauwels 2016** was investigated early maladaptive schemas (EMSs) in function of the eating disorder (ED) subtypes (restrictive/bulimic) and the presence/absence of non-suicidal self-injury (NSSI). Female inpatients ($N = 491$) completed the Young Schema Questionnaire and the Self-Injury Questionnaire. The influence of ED subtype and the presence/absence of NSSI and their interaction on the EMS were investigated through MANCOVA. The results showed main effects of ED subtype and the presence of NSSI on EMS. Pearson correlation analyses showed significant positive associations between all YSQL2 scales, NSSI and ED severity indexes (all $p < .003$), except for entitlement that showed no significant correlations. Six of the 16 YSQL2 scales showed significant differences between the different ED subtypes. Patients with bulimia scored significantly higher on insufficient self-control, and emotional deprivation compared with restrictive patients, whereas restrictive patients scored significantly higher on social undesirability, failure to achieve, subjugation and unrelenting standards compared with patients with bulimia Overall, higher YSQL2 scores were associated with more severe NSSI and more severe ED

Limitations of this study are: The study did not include all ED subtypes such as binge eating disorder) and the patients with ED were not equally distributed over the different ED subtypes, and did not control for axis I comorbidity, Finally , it was a female-only sample and there is no information about previous treatment experiences that could have influenced the identification of EMSs and the prevalence of recent NSSI (Pauwels et al., 2018).

Shorey et al. 2015, USA, studied the Relationship Between Early Maladaptive Schemas, Depression, and Generalized Anxiety among Adults Seeking Residential Treatment for Substance Use Disorders. In cross-sectional by using pre-existing patient records of 122 adults (The majority of were male ($n = 81, 66.4\%$) and the mean age, 37.36) diagnosed with a substance use disorder from a residential substance use

treatment facility with psychiatric diagnoses, based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) Patients most frequently identified themselves as Caucasian (93.6%), followed by African American (3.2%), and “Other” (e.g., Indian; 3.2%) studied. Measures were Young Schema Questionnaire long-form, psychiatric Diagnostic Screening Questionnaire (PDSQ) the Alcohol Use Disorders Identification Test (AUDIT), DUDIT test (Shorey et al., 2015).

The EMS domains of disconnection and rejection and impaired limits were associated with symptoms of MDD and the domain of impaired autonomy and performance was associated with symptoms of GAD even after controlling for age, gender, years of education, alcohol use, drug use, and symptoms of MDD (when predicting GAD) and GAD (when predicting MDD). The first model by Hierarchical Regression Analysis accounted for 48% of the variance in GAD. Specifically, gender and symptoms of MDD were significant predictors of GAD. GAD was associated with the EMS domain of impaired autonomy and performance. In the second model, the five schema domains were entered as additional predictors. This second model accounted for 63% ($R^2 = .15$) of the variance in symptoms of GAD. Specifically, symptoms of MDD and the EMS domain of impaired autonomy and performance were significant predictors of symptoms of GAD. due to the cross-sectional nature of the study design, no causal inferences can be made. Longitudinal research is needed that examines the relationship identified in the current study. Second, the facility where charts were reviewed does not conduct structured diagnostic interviews and this may somewhat reduce confidence in the participants’ substance use diagnoses. Moreover, limitations included, a sample of mostly non-Hispanic Caucasian individuals, lack of generalizability to more diverse populations ,and sample size was relatively small.

Schema therapy in anxiety

Schema therapy is a psychological treatment which has had increasing popularity over the last ten years. At first described schema therapy to help treat pervasive, long-term psychological difficulties unresponsive to traditional cognitive therapy. Interest in applying schema therapy to other disorders has increased over recent years. There is empirical support for the role of maladaptive schemas in psychopathology. ST focuses on felling and thoughts that are out of the people's awareness. Preliminary research suggests that schema therapy may be successfully extended to mood and anxiety disorders.

Also Talbot et al. (2015) suggest that positive treatment results can be obtained with group ST-based inpatient treatment for patients who did not respond to previous psychotherapeutic interventions (Talbot et al., 2015).

Hoffart et Sexton (2002), Norway, investigated The role of optimism in the process of schema-focused cognitive therapy of personality problems has examined schema change with ST in co-occurring agoraphobia and personality traits and disorder. There were 35 participants (80%) women and seven (20%) men—the mean age was 40.1 years) in the study although not all met the criteria for Cluster C, and PD. Significant changes were found during the schema-focused phase in reducing panic/agoraphobia symptoms. There were significant improvements in panic/agoraphobia symptoms comparing the assessment to follow-up on the Mobility Inventory for Agoraphobia Alone version (MI-AAL; Chambless et al. 1985) $d = 0.68$ and the accompanied version (MI-ACC; Chambless, et al., 1985) $d = 0.47$ with small-to-medium effect sizes. The PD-Cluster C Index also demonstrated reductions in symptoms that met the criteria for Cluster C PD (SCID-II; First, Spitzer, Gibbon, Williams & Benjamin, 1994) with a small effect size $d = 0.39$. There were also reductions in schema ratings on the schema questionnaire with a medium effect size ($d = 0.6$). This study is the first to examine schema reduction and symptom reduction with a group format approach for agoraphobia for individuals with personality disorder combined with CBT and ST intervention. Limitations are lack of control group, and independent randomization and a lack of blinding (Hoffart & Sexton, 2002).

Cockram et al. (2010) investigated the Role and the treatment of Early Maladaptive Schemas in Vietnam Veterans with PTSD examined Treatment of Early Maladaptive Schemas in Vietnam Veterans with PTSD in Australian and New Zealand Vietnam war veterans ($n = 220$). Mean age of 52 years. The study measured at baseline, termination, and three months the early maladaptive schemas, PTSD, anxiety and depression of war veterans ($n = 54$) participating in a PTSD group treatment program that included schema-focused therapy. Measured were PTSD Checklist, the Hospital Anxiety, and Depression Scale, YSQ. Change scores for the schema treatment compared with change scores of war veterans ($n = 127$) who had completed a manualized cognitive-behavioral therapy program without schema-focused therapy. Pre-treatment measures were similar in both groups. The Significant difference between intake and three month follow-up, and, PTSD and anxiety improved more

significantly for the schema-focused therapy group. The effect size was large for the ST group (Cohen's d between 0.61 and 0.82) and small to medium in the CBT comparison group (between 0.3 and 0.53) (Cockram et al., 2010)

In the ST group, 17 of 18 EMSs were significantly reduced at post-treatment, the only exception being Enmeshment. The reduction of EMS scores was maintained at three months, whereas five EMSs continued to fall even lower in the follow-up period (Self-Sacrifice, Unrelenting Standards/ Hypercriticalness, Insufficient Self-Control, Approval-Seeking/Recognition-Seeking, and Punitiveness). The degree of change in the EMSs of the Impaired Autonomy domain predicted change in PTSD symptoms, explaining 26.3% of the variance. The results limit to generalizability, and the use of a historical control group. While SFT within the second study PTSD treatment program may have weakened EMS content and reduced psychopathology, the discrete or moderating role or influence of other factors on the outcome is not clear.

Hamidpour et al. 2011 in Iran conducted a study about The Efficacy of Schema Therapy in Treating Women's Generalized Anxiety Disorder, three women with Generalized Anxiety Disorder (GAD) (25,30,34 years) were selected using Structured Clinical Interview for DSM-IV (SCID) based on disorders axis I. Subjects were selected using purposeful sampling, and underwent the treatment process after obtaining treatment requirements. Multiple baseline experimental single case study used as the method of the present study. The treatment program was carried out for 20 weekly sessions, with a follow-up period of three months after treatment termination. Subjects completed Pennsylvania State Worry Questionnaire (PSWQ), Worry Domain Questionnaire (WDQ) and Young Schema Questionnaire (YSQ). Results: Results showed that schema therapy is significantly efficient on treatment's target. Schema therapy has appropriate efficacy in the treatment of women suffering from Generalized Anxiety Disorder. This research limits to generalizability, randomization, small size, and lack of control group (Hamidpour et al., 2011).

Gewelt, Silje Engedal, 2017 in the RCT in Norway studied Early Maladaptive Schemas in Anxiety Disorders and comparing the effects of metacognitive therapy (MCT) and cognitive behavioral therapy (CBT) for complex anxiety disorders. The participants were randomized to either diagnosis-specific CBT or trans diagnostic MCT. Current analyses are based on computer-administered self-report questionnaires at pre-treatment, post-treatment, and 1-year follow-up. Schemas, meta-cognitions and

symptoms were assessed by the Young Schema Questionnaire-Short Form (YSQ-S1), Metacognitions Questionnaire-30 (MCQ-30), and Beck Anxiety Inventory (BAI), respectively. Multilevel models were used to analyze the data. Data were disaggregated into within- and between person effects when applicable. The current study is the first to compare between- and within-person effects of schemas and metacognitions on anxiety symptoms. Results showed Schemas are related to anxiety symptoms in complex anxiety disorders. There were significant concurrent between- and within-person relationships between symptoms and schema-endorsement. The within-person relationship of schema- endorsement and concurrent anxiety symptoms upheld even when between- and within person effects of metacognitions were included in the analysis. The within-person effect of metacognitions was also significant. This indicates that within-person changes in both EMSs and metacognitions uniquely impact concurrent anxiety symptoms. Treatment condition significantly impacted the degree of decline in symptoms and metacognitions during treatment, and showed a trend towards affecting decline in EMSs in the same direction. In these analyses, patients receiving MCT showed more declines than those receiving CBT. However, this effect was not apparent in analyses across treatment and follow-up. The lack of lasting difference between treatment conditions implies that both EMSs and metacognitions can be changed by different interventions.

The result limits the generalizability due to, sample characteristics, the timeframe of measurements, treatment-characteristics, and a limited number of measurements participant. Secondly, the use of self-report poses considerable limitations. Self-report questionnaires are subject to several possible biases, and overlap of concepts and unclear causal direction between the variables in the current study, and lack of control over therapy in the time between post-treatment and follow-up must be considered (Gewelt, 2017).

GUDE and ASLE HOFFART 2008 in Norway compared cognitive agoraphobia and schema-focused therapy and treatment as usual” according to psychodynamic principles in panic disorder with agoraphobia and co-occurring Cluster C Traits in a quasi-experimental study. Two cohorts of patients were followed through three months’ in-patient treatment programs and assessed at follow-up one year after the end of treatment. The one cohort comprised 18 patients treated with “treatment as usual” according to psychodynamic principles, the second comprised 24 patients

treated in cognitive agoraphobia and schema-focused therapy program. Measures were Checklist-90 (Derogatis, Lipman & Covi, 1973) Mobility Inventory for Agoraphobia - MI (Chambless, Caputo, Jasin, Gracely & Williams, 1985) measures agoraphobic avoidance of a range of situations. The result has shown, Effect sizes from pre-treatment to follow-up on the IIP and SCL-90 phobic anxiety sub-dimension were large in the group of those having completed CT 1.18/0.59/1.82, whereas the TAU group exhibited low to moderate effect sizes 0.24/-0.29/0.01 on both interpersonal and symptomatic distress. When controlling for difference score in phobic anxiety from pre-treatment to follow-up, the time \times intervention interaction was maintained ($F = 11.41$, $df = 1$, $p < 0.01$). For instance, working upon maladaptive schemas in a closed group setting, as is mentioned above in describing the CT condition, may have yielded group support and social acceptance to make it easier for the members to expose shameful topics. The limitation of this study have been The samples are small and the patients were not randomly assigned for treatment, the samples were collected in different periods (TAU in 1992-4, CT in 1995-7), different selection criteria were used, and possible differences in the patients' expectations to and motivation for therapy may have been present. The different follow-up procedures may also have influenced the results (Gude & Hoffart, 2008).

Schemas and schema therapy in chronic diseases

Patients tended to experience depression or anxiety as a consequence of being diagnosed with a chronic disease. Multiple consequences of a chronic disease diagnosis can contribute to depression or anxiety: the loss of a sense of self, anxiety and uncertainty about the future, loss of relationships and social isolation, and feelings of guilt, trapped in a different life", because the limitations of the disease, such as fatigue and a lack of energy in day activities. Functional limitations also lead to feelings of frustration and sadness (DeJean et al., 2013). Then this situation can be provoked the sensations and schemas .some researches have conducted in this issue till now.

In a cross-sectional study, Nazemiyeh **et al. 2018** in Iran have studied Early maladaptive schemas and asthma: Disconnection and rejection domains may have an effect on the severity of asthma on Fifty asthmatic patients (Mean age was 30.6 years, and 52% male /48 female) were measured the personality schema of patients by using the Young Schema Questionnaire – Short Form (YSQ-SF)And patients' clinical

findings and severity of asthma were assessed by spirometry and the Asthma Control Test (ACT) questionnaire.

Uncontrolled and controlled asthma had a significant defect in the 'Disconnection domain' ($p = 0.001$). Also, significant reverse linear correlation was found between FEV1 and 'Disconnection domain', 'Rejection' schema area ($r = -0.29$, $p = 0.03$), and 'Over vigilance domain' ($r = -0.36$, $p = 0.01$). Whereas, a significant reverse linear correlation was revealed between FEV1/FVC and Over vigilance domain ($r = -0.41$, $p = 0.003$). limitations: The first socio-economic situation and education of the patients did not consider. Second, the participants in the study were only the cases of stable asthma.

In the research by **Saariaho 2010** in Finland studied Early maladaptive schemas in Finnish adult chronic male and female pain patients. Samples were 158 Finnish chronic pain patients, rang of age 18-64 years (of men 56.7%; of women 59.7%. Measures were pain variables and EMS. In men the scores for Unrelenting Standards/Hypercriticalness (US) and Self-Sacrifice (SS) EMSs and in women SS and US EMSs showed the highest occurrence in that order of magnitude. The meaningful and non-meaningful schema groups did not differ by sex, age or length of education. However, patients scoring on one or more EMSs as meaningful had more intense, longer duration and more disabling pain. The pain sites or the number of pain locations did not differ between these groups. According to the data, Emotional Deprivation schema was associated with pain disability as much as pain intensity and the number of pain sites. In female patients, pain disability was also associated to a significant degree with SS schema. the result limit to unable to determine the specific causal relationship between EMS, lack of control group, and generalizability (Saariaho et al., 2010).

Mizara, et al. 2011 were investigated Core beliefs and psychological distress in patients with psoriasis and atopic eczema attending secondary care: The role of schemas in chronic skin disease investigated the presence of early maladaptive schemas (EMS) in patients with psoriasis and eczema and to explore their links with psychological distress. A sample of 185 adults Men and women age 23-75, in the Dermatology Department, Royal Free Hospital (London, U.K.) (psoriasis $n = 55$, atopic eczema $n = 54$, chronic disease control $n = 23$, normal control $n = 53$) completed validated, self-administered questionnaires. Hospital Anxiety and Depression Scale

(HADS), Young Schema Questionnaire-Short Form, (YSQ), Demographic information questionnaire Differences were found between dermatology patients and control groups. Patients with psoriasis differed on seven EMS from the normal control group: Emotional Deprivation ($P = 0.011$), Social Isolation ($P < 0.001$), Defectiveness ($P < 0.001$), Failure ($P < 0.001$), Vulnerability to harm ($P < 0.001$), Subjugation ($P = 0.009$) and Emotional Inhibition ($P = 0.002$). They differed from the chronic disease group on vulnerability to harm ($P = 0.002$) only. Patients with eczema differed from the normal control group on eight EMS: Emotional Deprivation ($P < 0.001$), Social Isolation ($P < 0.001$), Defectiveness ($P < 0.001$), Failure ($P < 0.001$), Dependence ($P = 0.010$), Vulnerability to harm ($P = 0.002$), Subjugation ($P = 0.006$) and insufficient self-control ($P = 0.010$). EMS were strongly positively related to psychological distress experienced by dermatology patients. Hierarchical regressions demonstrated two schemas, vulnerability to harm ($P < 0.001$) and defectiveness ($P = 0.029$), to be predictive of anxiety, and social isolation ($P = 0.012$) and vulnerability to harm ($P = 0.018$) to be predictive of depression, irrespective of age and years of coping for dermatology patients. A cross-sectional structure does not allow causal inferences to be drawn. There was no reliable measurement of disease seriousness in this research (Mizara et al., 2012).

Manavipour, Laya Sadat Miri 2020 were studied the Early Maladaptive Schemas in Patients with Psychosomatic Disorder and Multiple Sclerosis. In the one ex post facto study, evaluated 100 patients (men and women) (50 with MS and 50 with psychosomatic disorder) and compared them to 50 healthy people that completed Young Schema Questionnaire (short form). The study was causal-comparative. The results showed that the average score of vulnerability to harm or illness subscale in people with the psychosomatic disorder was higher than healthy people, and the average score of emotional deprivation, dependence/incompetence, and failure subscale in patients with MS was higher than the healthy group, then Early maladaptive schemas should be considered as an important element when comparing patients with psychosomatic disorders and MS with healthy people. The limitations were: sample size, generalizability, and assessment (Manavipour & Miri, 2017).

Pust et al. 2020, in Germany examined the association of childhood adversities, specific trait characteristics, and MS disease characteristics with fatigue symptoms

utilizing path analysis. 571 PwMS participated in an online survey. psychometric tools were applied. The Childhood Trauma Questionnaire (CTQ), Trait variables were alexithymia (Toronto Alexithymia Scale; TAS-26) and early maladaptive schemas (Young Schema Questionnaire; YSQ). Beck's Depression Inventory Fast Screen; BDI-FS, anxiety symptoms State-Trait Anxiety Inventory; (TAI-state), Patient determined Disease Steps; (PDDS), and Fatigue Scale for Motor and Cognitive Functions (FSMC). PwMS displayed high levels of fatigue and depression (mean FSMC score: 72; mean BDI-II score: 18). Higher alexithymia scores, higher perceived disconnection and rejection, higher impairments in autonomy and performance, and higher other-directedness predicted more severe anxiety symptoms. The result showed emotional neglect and emotional abuse have the significant childhood adversity variables associated with fatigue. There were differential associations for the trait variables and current pathology: TAS-26, the YSQ domain impaired autonomy and performance, and all current pathology measures had direct effects on fatigue symptoms, accounting for 28.2% of the FSMC variance. The limitation of this study is that data were obtained cross-sectionally and use of correlational and the path model's hierarchical structure cannot infer a cause effect relationship. study was web-based and all MS diagnoses and clinical data rely on participants' self-reports. A selection bias for the PwMS sample must also be considered (Pust et al., 2020).

Karbasdehi et al. 2018 in Iran in a true experimental with pretest/posttest design and a control group studied the effectiveness of schema therapy integrated with rehabilitation on CER and existential anxiety in patients with CHF. The study sample consisted of 25 patients The age range of the participants was 40-45 years with CHF that selected by the convenience sampling method and assigned into two groups (one experimental and one control). Data was collected by cognitive emotion regulation questionnaire (CERQ), and existential anxiety inventory (EAI) were used before and after the intervention. Ten-session young schema therapy was performed for the experimental group. Two-way ANOVA was used for data analysis and Cohen's d test measured effect extent. The results of analysis showed that the group schema therapy integrated with rehabilitation improved CER and existential anxiety in patients with CHF ($p < 0.001$). limitations of this study were: the therapist and the researcher were the same person, ,lack of follow up ,small sample size (Karbasdehi et al., 2018).

Gojani et al. 2017 were studied , effects of the Schema Therapy and Mindfulness on the Maladaptive Schemas Hold by the Psoriasis Patients with the Psychopathology

Symptoms in Iran in 2017 . ($n = 24$, 11 males, 13 females, age range 20-50 years) In the semi-experimental study with post- and pre-tests by using the convenience sampling in 2014. The patients had a low general health score. The experimental groups included two treatment groups, schema-based ($n = 8$) and mindfulness ($n = 8$). Both groups received eight 90-min sessions of therapy once a week; they were compared with 8 patients in the control group. To evaluate the psoriasis patients' maladaptive schema, Young schema questionnaire was used. Data were analyzed through the covariance analysis test. the results of the covariance analysis of the pretest scores on the mental health and incompetence schema among the psoriasis patients ($P \leq 0.05$). The findings revealed significant difference between the schema-based therapy and mindfulness with the control group consisting of the defeated schema, dependence/incompetence schema, devotion schema; stubbornly criteria schema, merit schema, restraint/inadequate self-discipline schema and general health the control group revealed significant difference ($P \leq 0.05$), but for the defect/schema, the difference between the three groups were insignificant. The limitations of this research are, generalizability due to factors related to sample characteristics, and the sample size as well as focusing study to Isfahan city population in Iran (Gojani et al., 2017).

Schema therapy on anxiety in MS

Like all the other cognitive processes, patients' cognitive reaction to their disease is formed by integrating their information from the internal and external previous and current stimuli. Patients process their diseases actively. In fact, they gain knowledge of what threatens them and predict or estimate their vulnerability the internal or external risks that are either uncontrollable or whose control is not enough for ensuring their health and safety. According to Beck (2007), the feelings are experienced by evaluation of events. Those who evaluate their feelings as more negative are more anxious or more depressed (Leihi, 2015). The deviated behaviors and perceptions cause a distortion of the situation and estimation of the level of vulnerability. Accordingly, relying on the concept of loss and devaluation, as different types of logical errors, the individual experiences anxiety. Based on James Longe's theory, this knowledge is influenced by emotions. The individual's emotions become active when s/he perceives a threat in the important area of life, both physical and social, with the purpose of helping survival and adaptability under these complicated situations.

Normally, in a fraction of a second, emotional processing happens earlier than cognitive processing. Therefore, emotions can influence our perception and interpretation of the conditions. According to the emotional schema, individuals have different cognitive views about their emotions. These schemas reflect the way they experience emotions and the belief they have in mind once undesirable emotional experiences about an appropriate plan of action are stimulated. They are schemas that cause negative interpretation and evaluation of emotions. Therefore, according to Leihl's theory, non-adaptive schemas lead to negative interpretation and evaluation of the emotions, which causes anxiety. This anxiety appears due to the reactive and problematic relationship with internal experiences (thoughts, feelings, images, bodily senses) (Romer) and can affect the cognitive reactions.

Besides the physical problems, such factors as individual differences, controllability, and predictability of the harmful event affect perception of the disease and its effect on the individual. Therefore, individuals interact with the disease based on their cognition and schemas. Non-adaptive schemas, by creating cognitive vulnerability, prepare the patient for inefficient attitudes, desperation, and mental disorders.

Like any other threat, the MS disease leaves deep effects on attitude to oneself, others, and the world and experiencing the disease disturbs their conceptualization of the world as a secure predictable and controllable place and of themselves and the latent fears and anxieties and schemas are reactivated. For example, inability—needing others' help and the interference of the disease in one's daily life—can activate the non-adaptive schemas. As a result, whether the person experiencing inability or the person expecting inability has to adapt to the disease as a real threat that is absolutely inconsistent with his/her perception of life before the disease and this cognitive mismatch and real risk leads to anxiety and selection of a confrontational lifestyle. Giving in to the disease is like being frozen. In this state, the person gives in cause reduced motivation, which gradually makes him/her feel separate. According to Freud, anxiety is the consequence of desperation.

In the state of avoidance, the person avoids experiencing many of his/her useful activities to reduce his/her anxiety or even ignores the disease and treatment. This avoidance leads to increased anxiety, indirect development of the disease and irresponsiveness to treatment, which causes a vicious circle.

In the state of excessive compensation, the person does disproportionate activities beyond his/her ability and even changes his/her physician; some even refer to amulet makers.

Stimulation of non-adaptive schemas and disturbance of the cognitive coordination in these patients leads to the selection of the confrontational lifestyle causing increased anxiety and desperation. For instance, in a person who has the schema of dependence, any change even positive ones causes suffering and anxiety and even influences the trend of his treatment and disease. Inflexibility or not regulating the emotions, as the core of mental vulnerability causes different forms of mental vulnerability including anxiety disorders and depression (Kashden et al., 2006).

All patients with MS face uncertainty (Alschuler & Beier, 2015). However, there is significant variability in how individuals cope with that uncertainty and not everyone develops pathological anxiety symptoms, which questions the reason of this difference.

presence of the continuous illness as big stressor in life without decisive treatment and disabilities can justify the anxiety. Bearing in mind that MS is a progressive and debilitating disease can affect all aspects of life. However These concerns which elicit anxiety do not affect everyone. The factors impact on this difference not only is not definite but its debatable. Some factors have investigated, for instance , personality factors and maladaptive schemas maybe play an important role, as well as common underlying factors. Also, paying attention to stressful childhood experiences as an essential element that affects cognition, perception and emotions, may be one of the important components of therapeutic interventions for anxiety. (Lähdepuro 2019). Then focus on these factors can be benefit ,given that no study was done in this issue ,it would have worth a try.

Chapter 3

Methodology

3-1-Aims of The Current Study

Main objective:

The study of the effect of schema therapy on anxiety in patients with MS

Secondary objectives

The study of the effect of schema therapy on depression in patients with MS .

The study of the effect of schema therapy on Fatigue patients with MS.

The study of the effect of schema therapy on quality of life in patients with MS

The study of the effect of schema therapy on quality of sleep in patients with MS

The study of the effect of schema therapy on EDSS in patients with MS

3-2-Hypotheses

Schema therapy decreases BAI score in experimental group more than the control group in patient with MS.

Secondary hypothesis

Schema therapy decreases HADS-A score in experimental group more than the control group in patient with MS

Schema therapy decreases BDI score in experimental group more than the control group in patient with MS

Schema therapy decreases HADS-D score in experimental group more than the control group in patient with MS

Schema therapy decreases PSQI score in experimental group in more than the control group patient with MS

Schema therapy decreases MSIS score in experimental group more than the control group in patient with MS

Schema therapy decreases FFS score in experimental group more than the control group in patient with MS

Schema therapy decreases EDSS score in experimental group more than the control group in patient with MS.

3-3- Method

Study design and setting: This parallel-arm randomized controlled trial (RCT) was conducted at Multiple Sclerosis (MS) clinics of Kashani Hospital (located at Isfahan, a center of Iran)receiving ,either schema therapy or none.

3-4-Sample size and randomization:

The aim of this research was the study of effectiveness of schema therapy on anxiety in patient with MS .

we used this formula to calculate the sample size $P=0.45$, $Z=1.96$, $d=0.1$. With respect to previous studies, (Hashemi & Darvishzadeh, 2016) Given that study and according to

$$n = \frac{Nz^2p(1-p)}{Nd^2 + z^2p(1-p)}$$

the following formula 106 samples were calculated using the information provided

3-5-inclusion and exclusion criteria

Participants were recruited via a advertisement by available sampling (in the Iran) all individuals are registered with confirmation a neurologist. Individuals who responded and indicated they were interested in participating were screened for suitability according to psychological inclusion criteria by a psychologist interview. individuals were enrolled from those who met the study criteria, and call them for recruited to the RTC. Inclusion Criteria were: Age between 18 and 55 years old, the ability of writing and reading, diagnosed as relapsing-remitting MS and anxiety score greater than 26 using the BAI scale; Expanded Disability Status Scale (EDSS) score less than 6 and having at least high school education level. Exclusion criteria were a history of psychotic disorders, a history of cognitive deficiency, the use of anti-depressants in the past three months, history of relapse in the past three months, and hospitalized at the time of the study. All participants completed some questionnaires for eligibility which was explained later.

The structure of recruitment

To recruit eligible patients into the trial, MS patients were recalled, and 120 patients responded. Of those, seven patients were ineligible, five patients declined to consent, and two patients were excluded for other reasons. Finally, One hundred and six patient were enrolled in the experiment. The age range was narrow: 18-55 years old. The participants were divided into two groups of 53 participants

To randomize patients, block randomization was performed using a computer randomization program (<https://www.sealedenvelope.com/simple-randomiser/v1/lists>). The program created 27 blocks of 4 which sealed.

This sample size which included a 10% attrition rate, ensured us to have 80% power to detect the 40% of the standard deviation of mean difference in anxiety score at 5% significance level between trial and control group. Finally, patients were divided into experimental and control groups. In the experimental group, patients changed their psychotherapy groups according to their place of work and other programs in order to be able to attend the sessions. While the patients were randomly divided into control and experimental groups, the treatment groups were formed at the patients' discretion

3-6-Overview of the study

The consent patients were visited by the neurologists that was involved in the program. The patients who were neurologically eligible were evaluated for psychological criteria and then fill out the BAI Questionnaire. The participants were told that they would participate in a research project investigating the effectiveness of psychological interventions for anxiety and its effect on their illness. The patients who consent enrolled for the study, before starting the treatment period, all participants completed the questionnaire. After checking the inclusion and exclusion criteria, databases were achieved by filling the questioners, a research assistant divided the patient randomized the patients to the group control or ST group condition. participants randomize into either the schema therapy or control arm, using randomization. after finishing 20 sessions retest was performed and after six months the follow-up will be performed. Participants gave their informed consent to attend six months' research and six months follow up., Also informed that they would be randomly assigned to a condition and that the control. Control participants were offered the opportunity treated afterward with the technique that would prove to be effective at the end of the present investigation. The participants were told they have the right to leave the research at any time. participants were also informed that they would fully be debriefed at the end of the follow-up period. For the two groups, an evaluation would be administrated the pretest at the beginning , post-test after 20 session ST , and follow up six months later at the same time for those in the control group. The main criteria are the impact of schema therapy on anxiety evaluated by the (BAI) Back anxiety inventory at six months after the start program. Secondary criteria are: an impact on the psychological dimensions assessed by Hospital Anxiety and Depression Scale (HAD), intensity of fatigue assessed by Fatigue Severity Scale (FSS), sleep quality evaluated by the

Pittsburgh Sleep Quality Index (PSQI) depression by (BDI) beck depression inventory and quality of life evaluated by Multiple sclerosis impact scale (MSIS29). Sampling and data collection steps were performed by the researcher with scientific background and assistant neurologist involved in the research.

3-7-Experimenter assignment to treatment conditions

The experimenter is a clinical psychologist (the main investigator) .The therapist has a certificate of schema therapy course from ISST(International schema therapy Society), and also has a history of holding schema therapy workshops and has undergone ST treatment.

3-7-Treatment procedure:

Clinical condition: ST. It consists of 20 sessions. Once-weekly sessions of 90 minutes (with a 15 min break), with homework activities. It is designed for a group of 6 people and will be delivered by one psychologist. PowerPoint presentations support each session and a detailed therapist manual and companion patient workbook accompany the program. The sessions were organized based on the clinicians' Guide of Farrel, Reiss, Shaw. (index 1)

The ST's content is: general: identify their schemas and become aware of their childhood memories, emotions, bodily sensations, cognitions and coping styles associated with them. Once patients understand their schemas and coping styles, they can then begin to exert some control over their responses (Young et al., 2014).

3-8-Sessions Include:(Summary of schema therapy group Protocol in Index)

Session 1: The Welcome Group Session

Sessions 2-6:Five Schema Therapy Education (STE)

Session 7-13: learn to be aware of their own modes in daily life

Session 14-19:Mode Management Sessions:

The last session (20): post-test and welcoming

3-9-Control condition.

These participants did not receive any treatment and only came to the evaluation sessions. And they had the right to leave the research whenever they wanted and needed treatment for anxiety

3-10-Measures:

Demographic information.

Participants were asked to identify their gender, age, level of education, marital status medical data, date of diagnosis, disease type, level of disability and information on relapses and treatments, are evaluated.

3-11-Expanded disability status scale (EDSS)

The most popular and widely used instrument is the Expanded Disability Status Scale (EDSS) of (Kurtzke, 1983).The EDSS is a clinician-administered assessment scale evaluating the functional systems of the central nervous system. The EDSS is used to describe disease progression in patients with MS and to assess the effectiveness of therapeutic interventions in clinical trials .It consists of ordinal rating system ranging from 0 (normal neurological status) to 10 (death due to MS (Meyer-Moock et al., 2014)

3-12-Measures

3-12-1-Beck Anxiety Inventory (BAI)

Anxiety Measure is obtained by Beck Anxiety Inventory. This scale is a self-report measure of anxiety. Items: 21 Reliability: Internal consistency for the BAI = (Cronbach's $\alpha=0.92$) Test-retest reliability (1 week) for the BAI = 0.75 (Beck, Epstein, Brown, & Steer, 1988). The BAI (Beck, 1990) is a 21-item self-report measure of anxiety sensitive to prolonged state anxiety (Kabacoff et al., 1997). Item responses on the BAI range from 0 to 3, and each item rating is accompanied by a statement describing the severity of a given anxiety symptom, with 0 indicating no self-reported symptoms and 3 indicating more severe symptoms. A total score of 0-7 on the BAI indicates minimal anxiety; 8-15 indicates mild anxiety and a score of 16+ indicates

moderate or greater anxiety. Item-level responses are totaled to provide an overall BAI score indicating the severity of self-reported anxiety. Respondents are asked to consider how they have been feeling in the past week, Findings showed that the Persian version of BAI proved an acceptable test-retest reliability ($r = 0.67$), an internal consistency ($\alpha = 0.88$), convergent validity (0.40-0.44), and divergent validity ($r = 0.216$) with BDI-II. We found a clear cut point for our society and these findings confirmed the confirmatory factor analysis results and suggested that the factor structure for the BAI-Iranian is valid and stable.(Gojani et al., 2017).

3-12-2-Beck Depression Inventory (BDI)

Beck Depression Inventory (BDI)- self-report questionnaires,21-question multiple-choice Developed by Beck et al. in 1961, each answer being scored on a scale value of 0 (not at all) to 3 (severely), total scores indicate more severe depression symptoms. Score between 0-63. BDI-II scores are classified as minimal (0-13), mild (14-19), moderate (20-28), and severe (29-63). Studies have reported that the BDI has high internal consistency Cronbach's alpha 0.89 Criterion validity of the BDI-II is positively correlated with the Hamilton Depression Rating Scale ($r = 0.71$) with a high one week test-retest reliability $r = 0.93$ (Jackson-Koku 2016)

The BDI-II-Persian had high internal consistency (Cronbach's $\alpha = 0.87$) and acceptable test-retest reliability ($r = 0.74$). The instrument correlated strongly with the Automatic Thoughts Questionnaire (Ghassemzadeh et al., 2005).

3-12-3-Multiple sclerosis impact scale - 29 items(MSIS29)

Multiple sclerosis impact scale - 29 items .Self -reported questionnaires (MSIS29):29-item self-report measure with 20 items associated with a physical scale and 9 items with a psychological scale ,each of the two scales is scored by summing the responses across items, then converting to a 0-100 scale where 100 indicates greater impact of the disease on daily function (worse health)

All estimates of reliability using Cronbach's alpha were more the recommended 0.80 The 95% confidence intervals for the MSIS-29 physical scales The convergent validity of the MSIS-29 physical scale with other measures of physical impairment is indicated

by the high correlations found with the Kurtzke EDSS (0.704) (McGuigan & Hutchinson, 2004).

Persian version of the MSIS-29 had high internal consistency (Cronbach's alpha coefficients > 0.70) and test-retest reliability (intra-class correlation coefficients >0.70) and a good validity. Conclusion: The Persian version of the MSIS-29 is a reliable and valid instrument for measuring MS outcomes in Iranian patients (AYAT et al., 2006).

3-12-4-Pittsburgh Sleep Quality Index (PSQI)

The PSQI was developed in 1988, by Buysse and his colleagues, to create a standardized measure designed to gather consistent information about the subjective nature of people's sleep habits.

Self-report questionnaire that assesses sleep quality over a one-month time interval the self-report questionnaire that assesses sleep quality over a one-month time interval. The measure consists of 19 individual items, each item is weighted on a 0-3 interval scale The global PSQI score is then calculated by totaling the seven component scores, providing an overall score ranging from 0 to 21, where lower scores denote a healthier sleep quality.

A global PSQI score greater than 5 yielded a diagnostic sensitivity of 89.6% and specificity of 86.5% (kappa = 0.75, p less than 0.001) in distinguishing good and poor sleepers.

The Persian version of PSQI was evaluated in the study with regard to its internal consistency and factor structure. The result showed an excellent item content validity index (≥ 0.78) and an excellent scale content validity index (≥ 0.90). The result of the Cronbach alpha coefficient was 0.65 (Mezerji et al.2017).

3-12-5-Fatigue Severity Scale (FSS)

Fatigue Severity Scale (FSS) was developed by Krupp et al. f (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989). The FSS, a nine-item questionnaire, primarily focuses on the motor aspects of fatigue, the main emphasis is assessing the severity of fatigue symptoms and their impact on an individual's daily functioning. Each item of the questionnaire is scored on a seven-point Likert scale ranging from 1 ("completely disagree") to 7 (completely agree). The mean score of the nine items is used as the

FSS score. Originally, the cut-off score for fatigue was set to be ≥ 4 . Validation of a fatigue scale in a large sample size demonstrates that the FSS is a simple and reliable instrument to assess and quantify fatigue for clinical and research purposes. Item analysis showed an excellent internal consistency and reliability (Cronbach $\alpha = 0.93$). Test-retest variability was assessed in 104 healthy subjects, showing stable values over time (2.94 ± 0.90 vs. 2.90 ± 0.74 ; $P = 0.27$). (Valko et al. 2008) the study revealed that the FSS-P is an appropriate psychometric instrument to assess people with Multiple Sclerosis. The ICC was reported 0.93 for the total score and 0.88 for VAS, The Cronbach's alpha was reported 0.96. The total score and the VAS were significantly correlated with the SF-36 vitality subscale ($r = -0.69$ and $r = -0.73$, respectively). Correlations with other SF-36 subscales were a moderate level ($r = -0.43$ to $r = -0.65$, all $P < 0.001$ (A'zimian et al., 2013).

3-12-6-The Hospital Anxiety and Depression Scale (HADS)

The Hospital Anxiety and Depression Scale (HADS) was devised by Zigmond and Snaith (1983) The HADS is a questionnaire intended for the diagnosis and evaluation of anxiety and depression in non-psychiatric patients (Reda, 2011).

Guidelines are recommended for the interpretation of scores: 0-7 for normal or no anxiety, 8-10 for mild anxiety, 11-14 for moderate anxiety, and 12-21 for severe anxiety. In some rheumatologic conditions, a cut score for the HADS-A of 9 was recommended as useful for diagnosing an anxiety disorder (Julian, 2011).

A review of the 747 identified papers that used HADS was performed to address the validity of HADS. the analyses demonstrated, the correlations between the two subscales varied from .40 to .74 (mean .56). Cronbach's alpha for HADS-A varied from .68 to .93 (mean .83) and HADS-D from .67 to .90 (mean .82). The sensitivity and specificity for both HADS-A and HADS-D of approximately 0.80 were very similar to the sensitivity and specificity achieved by the General Health Questionnaire (GHQ) Correlations between HADS and other commonly used questionnaires were in the range .49 to .83 (Bjelland et al., 2002).

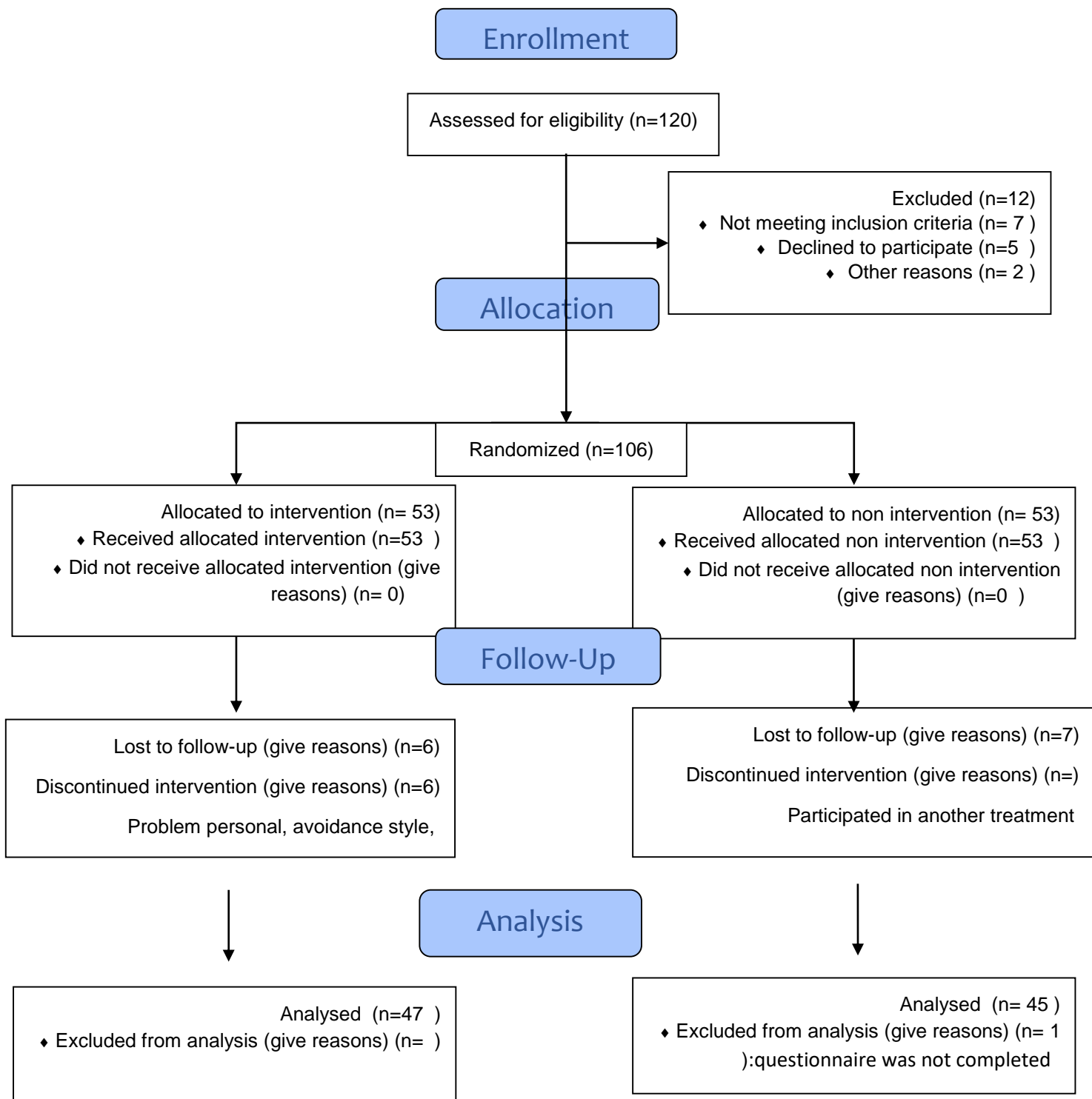
The Iranian version of the HADS was found to be acceptable to almost all patients (99%). Cronbach's alpha coefficient (to test reliability) is 0.78 for the HADS anxiety sub-scale and 0.86 for the HADS depression sub-scale (Montazeri et al., 2003).

3-12-7-The Young Schema Questionnaire (YSQ):

The Young Schema Questionnaire (YSQ), Young, 1994 was developed to assess Maladaptive Schemas (EMS), which account for the dysfunctional beliefs in individuals with personality disorders or maladaptive personality traits (Pauwels et al., 2018). These maladaptive schemas are thought to be important in the development and maintenance of psychiatric symptoms, such as anxiety and depression. The Schema Questionnaire–Short Form (SQ-SF) was designed by Young, 1998 to measure 15 maladaptive schemas and is a briefer (75 item) instrument (Welburn et al., 2002). Emotional Deprivation (ed). 1-5, Abandonment/Instability(ab) 11-15, Mistrust/Abuse(ma),16-20 Social Isolation/Alienation(si),21-25. Defectiveness/Shame(ds) ,25-30. Failure(fa) 31-35. Dependence/Incompetence(di),36-40, Vulnerability to Harm or Illness(vh) 41-45, Enmeshment/Undeveloped Self(em), 46-50 Subjugation(sb) 51-55, Self-Sacrifice(ss) 56-60, Emotional Inhibition(ei) 61-65, Unrelenting Standards/Hypercriticalness(us) ,66-70 Entitlement/Grandiosity(et) 71-75, Insufficient Self-Control and/or Self-Discipline(is).

The items are rated on a 6-point Likert scale ranging from 1 “Completely untrue for me” to 6 “Describes me perfectly.” we generally consider any score of 5 or 6 on a schema to be meaningful. The first comprehensive investigation of its psychometric properties was conducted by Schmidt, Joiner, Young, and Telch (1995). Results from this study produced alpha coefficients for each Early Maladaptive Schema that ranged from .83. The primary subscales demonstrated high test-retest reliability and internal consistency. The questionnaire also demonstrated good convergent and discriminant validity on measures of psychological distress, self-esteem, cognitive vulnerability to depression, and personality disorder symptomatology (Young et al., 2003). For Persian version, the results showed that the internal reliability of the YSQ-SF in terms of Cronbach’s alpha were found to be good. Criterion, predictive, and discriminant validity of the scale was confirmed to be acceptable. The findings suggest that among the proposed models of YSQ-SF, the 75-item YSQ-SF with 15-factor first-order and five-factor second-order models has acceptable fits among Iranian psychiatric patients (Khosravani et al., 2018).

3-13-CONSORT 2010 Flow Diagram



3-14-schedule of assessment:

	Pre assessment	T0 (before)	T1 (at 6 months)	T2 Follow up
BAI	X	x	X	X
HADS		X	x	x
BDI		X	x	x
FSS		X	x	x
MSIS		X	X	x
PSQI		x	x	x
EDSS	X	X	X	X
YSQ		X	X	

3-15-ETHICAL CONSIDERATION

The studies included in this thesis were all approved by the Committee research at Isfahan university of medical sciences, approval no.396479 and ethics code 30475.

Chapter 4

Analyses

4-1-Statistical Analyses

Descriptive statistics were reported as mean (standard deviation [SD]) for continuous variables and frequency (percentage) of patients for categorical variables. A Kolmogorov-Smirnov test was performed to analyze data distribution. Repeated-measures ANOVAs were performed for each measure (MSIS, SLEEP, BAI, HA, HD, BDI, HADS, FSS, EDSS) considering between-subject's factors "group" (intervention and control) and the within-subject factor "Time" (Pre, Post, and F). The results of repeated measure analyses were recorded as eta square (Eta) and p-value. The level of significance was set at 0.05 (2-tailed). All statistical analysis procedures were performed using IBM SPSS Statistics (version 18; IBM Corporation, Armonk, NY, USA). Also control variable were: Sex, Age, marriage status and education, which were removed from the final model due to lack of significant meaning.

One hundred- six adults with Multiple sclerosis (MS) volunteered to participate in the study. They were 81 patients (76.4%) women, and 25 patients (23.6%) were men.

Table1. Descriptive statistics including mean (standard deviation) and n (%) for numerical and categorical variables respectively. n=106

Table1: The frequency distribution of the participants based on the demographic characteristics

	Variables	Intervention (N=56)		Control (N=56)		Total		P value
		Frequency	Relative frequency	Frequency	Relative frequency	Frequency	Relative frequency	
Age (years)	Less than 30	6	31.6	13	68.4	19	17.9	0.150
	30 to 40	29	50.9	28	49.1	57	53.8	
	Higher than 40	18	60.0	12	40.0	30	28.3	
Education level	Diploma and lower	5	50	5	50	10	9.4	0.714
	Bachelor of Science	38	48.1	41	51.9	79	74.5	
	Master of science	9	56.3	7	43.8	16	15.1	
	Doctor of Philosophy and higher	1	100	0	0	1	0.9	
Gender	Female	41	50.6	40	49.4	81	76.4	0.819
	Male	12	48.0	13	52.0	25	23.6	
Marital status	Married	43	49.4	44	50.6	87	82.1	0.800
	Single	10	52.6	9	47.4	19	17.9	

‡ EDSS, Expanded Disability Status Scale; BS, Bachelor of Science; MA, Master of Arts; PhD,

Descriptive statistics including means and standard deviations for numerical variables as well as number (percentage) for class variables are presented in Table 1. According to the results, women and men comprised 76.4% and 23.6% of the sample, respectively. The average age of the participants was 36.22. The classification of participants based on their level of education was as follows: 9.4% with diploma, 75.5% with bachelor's degree, 14.2% with master's degree and 0.9% with doctorate. Among the participants, 17.9% were single and 82.1% were married. The average EDSS score was 1.35.

Table 2. Association between background variables and schema therapy

Variables	Level	Mean (SD)		P
		n (%)		
		Intervention n=53	Control n=53	
Gender; n (%)	Female			
	Male			
Age; mean (SD)				
	Diploma	5 (9.4)	5 (9.4)	
Education; n (%)	BS	38 (71.7)	41 (77.4)	0.714
	MA	9 (17)	7 (13.2)	
	PhD	1 (1.9)	0 (0)	
Marital; n (%)	Single	44 (83)	43 (81.1)	0.5
	Married	9 (17)	10 (18.9)	
EDSS; mean (SD)				

‡ EDSS Expanded Disability Status Scale; BS Bachelor of Science; MA Master of Arts; PhD

Table 2 shows the relationship between contextual variables and treatment. The results indicate no significant difference between the control and intervention groups in terms of any of the contextual variables. Thus, in terms of all contextual variables, the control and intervention groups are homogeneous

Table 3: the status of the disorders in the participants

	Variable	Control, n (%)	Intervention, n (%)
BAI	None	0 (0.0)	0 (0.0)
	Mild	0 (0.0)	0 (0.0)
	Moderate	0 (0.0)	0 (0.0)
	Severe	53 (100.0)	53 (100.0)
BDI	Normal	0 (0.0)	0 (0.0)
	Mild	0 (0.0)	0 (0.0)
	Borderline	0 (0.0)	0 (0.0)
	Moderate	31 (58.5)	32 (60.4)
	Severe	22 (41.5)	19 (35.8)
HA	Extreme	0 (0.0)	2 (3.8)
	Normal	0 (0.0)	0 (0.0)
	Borderline	50 (94.3)	46 (86.8)
HD	Abnormal	3 (5.7)	7 (13.2)
	Normal	0 (0.0)	0 (0.0)
FSS	Borderline	46 (86.8)	45 (84.9)
	Abnormal	7 (13.2)	8 (15.1)
MSIS	Low	0 (0.0)	4 (7.5)
	High	53 (100.0)	49 (92.5)
PSQI	Low	29 (54.7)	35 (66.0)
	High	24 (45.3)	18 (34.0)
PSQI	Low	0 (0.0)	0 (0.0)
	High	53 (100.0)	53 (100.0)

Table 4. Correlation between EDSS and measurements study n=106.

Measures		EDSS‡					
		Pre		Post		F	
		R	P	r	P	r	P
BAI	Pre	0.152	0.121	-	-	-	-
	Post	-	-	0.325	0.002	-	-
	F	-	-	-	-	0.251	0.016
HA	Pre	0.203	0.036	-	-	-	-
	Post	-	-	0.321	0.002	-	-
	F	-	-	-	-	0.110	0.296
HD	Pre	0.088	0.367	-	-	-	-
	Post	-	-	0.052	0.621	-	-
	F	-	-	-	-	0.069	0.514
BDI	Pre	0.083	0.083	-	-	-	-
	Post	-	-	0.043	0.684	-	-
	F	-	-	-	-	0.078	0.461
HADS	Pre	0.190	0.052	-	-	-	-
	Post	-	-	0.253	0.015	-	-
	F	-	-	-	-	0.170	0.105
F	Pre	0.010	0.916	-	-	-	-
	Post	-	-	-0.045	0.669	-	-
	F	-	-	-	-	-0.015	0.887
MSIS	Pre	-0.103	0.292	-	-	-	-
	Post	-	-	-0.046	0.665	-	-
	F	-	-	-	-	-0.043	0.681
Sleep	Pre	-0.145	0.138	-	-	-	-
	Post	-	-	-0.172	0.103	-	-
	F	-	-	-	-	-0.098	0.354

‡ EDSS Expanded Disability Status Scale; Pre previous intervention; post post intervention; F follow up;

Table 3 illustrates the relationship between the EDSS variable and different dimensions of research. According to the results, the relationship between EDSS and variable A was significant in the post-test and follow-up stages alike. In case of HA variable, it had a significant relationship with EDSS variable in both pre-test and post-test stages. The HADS variable also indicated a significant relationship with EDSS in the post-test stage.

Table 5 summarizes the results of the repeated analysis of variance. According to the results, the group effect was significant for HA, HD, BDI and HADS variables. Furthermore, the time effect and interaction effect of group \times time were also significant for BAI, HD, BDI and HADS variables. None of the effects included in the table of analysis of variance were significant for MSIS, Sleep, F and EDSS variables.

The comparison of the mean scores of BAI, HD, BDI and HADS indices in each stage of the experiment revealed that there was no significant difference between the control and intervention groups in terms of the mentioned traits in the pre-test, while a significant difference was observed between the control and intervention groups in the post-test and follow-up stages. The effect size of Cohen's d also disclosed that the treatment effect was considerable in reducing BAI, HD, BDI and HADS scores ($d > 0.5$). The results showed there are significant different between subject (HA) $\text{Eta} = 0.129$; $p < 0.001$, (HD) $\text{Eta} = 0.092$; $p = 0.003$, (BDI) $\text{Eta} = 0.037$; $p = 0.047$ (HADS) $\text{Eta} = 0.155$; $p < 0.001$. Moreover, the result within subject showed the variables (BAI) $\text{Eta} = 0.100$; $p < 0.001$, (HA) $\text{Eta} = 0.092$; $p < 0.001$, (HD) $\text{Eta} = 0.155$; $p < 0.001$, (BDI) $\text{Eta} = 0.251$; $p < 0.001$ و (HADS) $\text{Eta} = 0.092$; $p = 0.001$ have had significant change during time.

And the Time*group for (BAI) $\text{Eta} = 0.135$; $p < 0.001$, (HA) $\text{Eta} = 0.099$; $p < 0.001$, (HD) $\text{Eta} = 0.078$; $p = 0.001$, (BDI) $\text{Eta} = 0.238$; $p < 0.001$ و (HADS) $\text{Eta} = 0.150$; $p < 0.001$ have had significant different in follow up.

Table 5: Mean and standard deviation values of the studied variable between two groups in different times

Variables	Intervention (N=53)		Control (N=53)		P value	
	Mean	Standard deviation	Mean	Standard deviation		
BAI	Pre	27.66	1.39	27.66	1.53	0.999
	Post	26.96	1.49	27.73	1.75	0.024
	Follow up	27.14	1.47	28.07	1.60	0.005
	P value	> 0.001		> 0.001		-
BDI	Pre	30.30	4.67	30.26	3.26	0.962
	Post	27.38	4.40	29.89	3.67	0.004
	Follow up	28.15	4.12	30.53	3.33	0.003
	P value	> 0.001		0.003		-
HADS	Pre	19.75	1.07	19.70	0.82	0.761
	Post	18.68	0.98	19.78	1.20	< 0.001
	Follow up	18.72	1.10	19.80	1.08	< 0.001
	P value	> 0.001		0.564		-
HD	Pre	9.89	0.87	9.89	0.64	0.999
	Post	9.17	0.70	9.69	0.60	< 0.001
	Follow up	9.17	0.84	9.73	0.58	< 0.001
	P value	> 0.001		0.318		-
HA	Pre	9.85	0.72	9.81	0.52	0.757
	Post	9.26	0.49	9.82	0.65	< 0.001
	Follow up	9.51	0.69	10.11	0.86	< 0.001
	P value	> 0.001		0.022		-
FSS	Pre	42.96	3.42	42.81	2.48	0.795
	Post	42.43	3.44	42.91	3.44	0.500
	Follow up	42.57	3.73	43.07	3.77	0.531
	P value	0.613		0.770		-
MSIS	Pre	71.32	6.62	71.66	8.59	0.820
	Post	70.34	6.55	70.80	8.23	0.767
	Follow up	70.36	6.57	70.82	8.25	0.767
	P value	0.187		0.786		-
PSQI	Pre	9.06	1.13	8.89	0.99	0.414
	Post	8.98	0.97	8.66	0.68	0.073
	Follow up	9.00	1.000	8.70	0.67	0.099
	P value	0.931		0.743		-

Table 6: effect of schema therapy on schema in case group

	Schema	N		P value
		N0 (0)	Yes (1)	
T1	No (0)	41	0	1
	Yes (1)	0	6	
T2	No (0)	45	0	1
	Yes (1)	0	2	
T3	No (0)	44	0	1
	Yes (1)	0	3	
T4	No (0)	44	0	1
	Yes (1)	1	2	
T5	No (0)	46	0	1
	Yes (1)	0	1	
T6	No (0)	34	0	0.250
	Yes (1)	3	10	
T7	No (0)	46	0	1
	Yes (1)	0	1	
T8	No (0)	35	1	0.375
	Yes (1)	4	7	
T9	No (0)	41	0	0.5
	Yes (1)	2	4	
T10	No (0)	33	0	0.31
	Yes (1)	6	8	
T11	No (0)	24	0	.002
	Yes (1)	10	13	
T12	No (0)	45	0	1
	Yes (1)	1	1	
T13	No (0)	44	0	1
	Yes (1)	1	2	
T14	No (0)	40	0	1
	Yes (1)	0	7	

Figure 1: Score on the BAI between T0,T1,T2 for intervention and control group

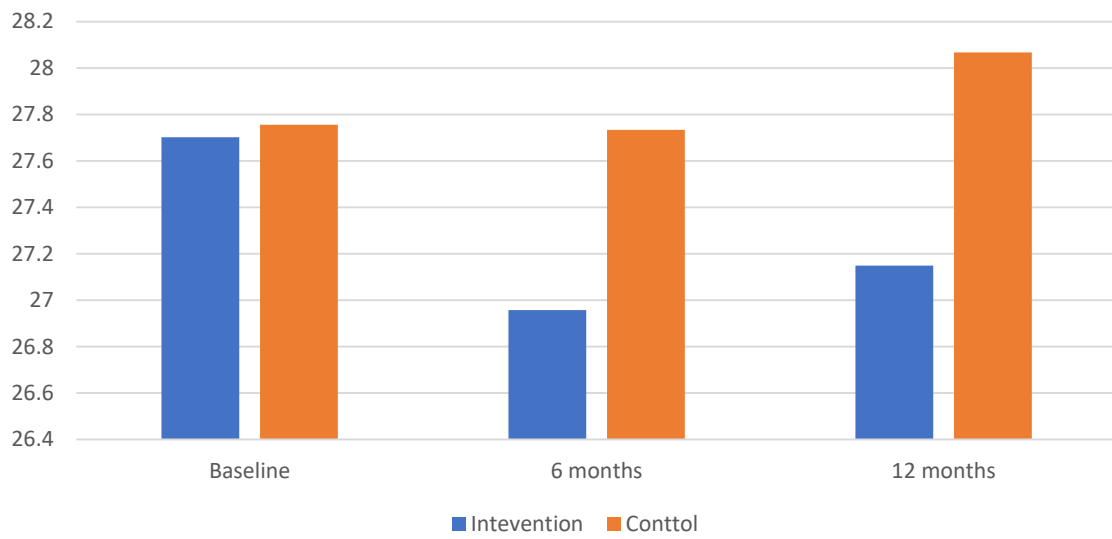


Figure 2: Score on the HA between T0, T1, T2 for intervention and control group

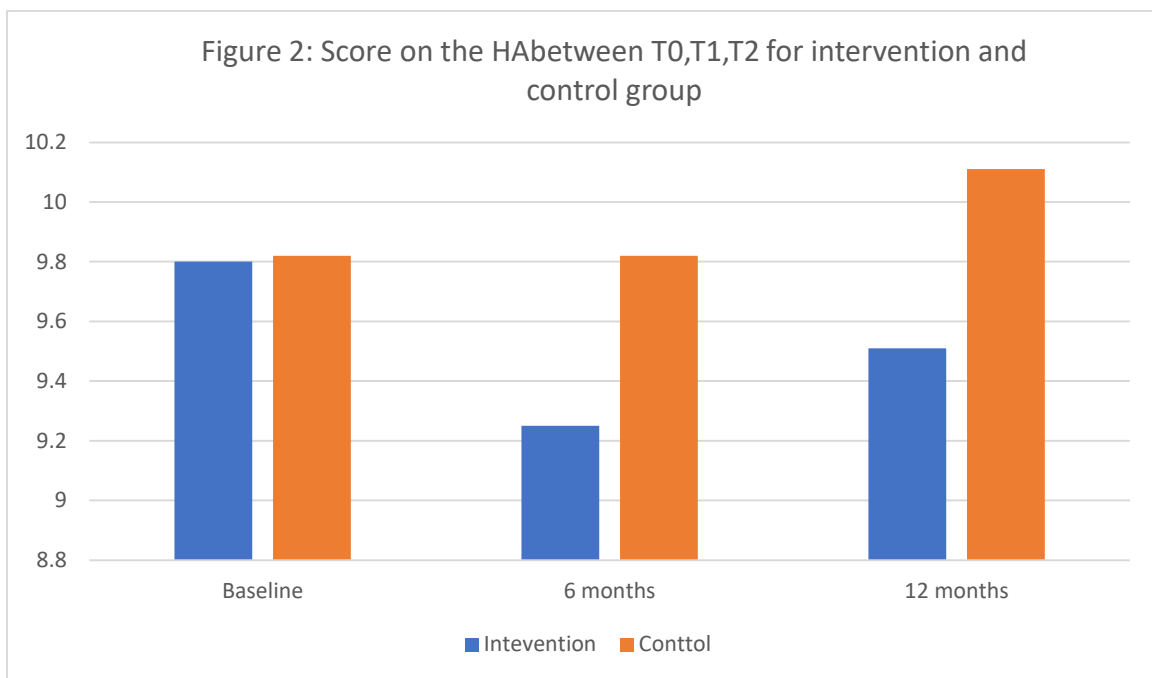


Figure 3: Score on the BAI between T0,T1,T2 for intervention and control group

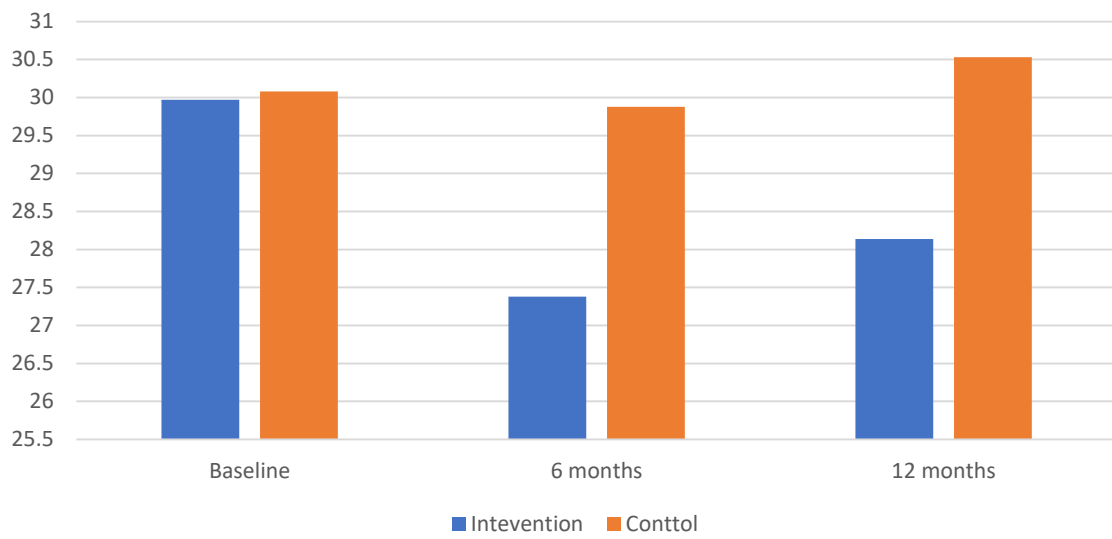


Figure 4: Score on the HD between T0,T1,T2 for intervention and control group

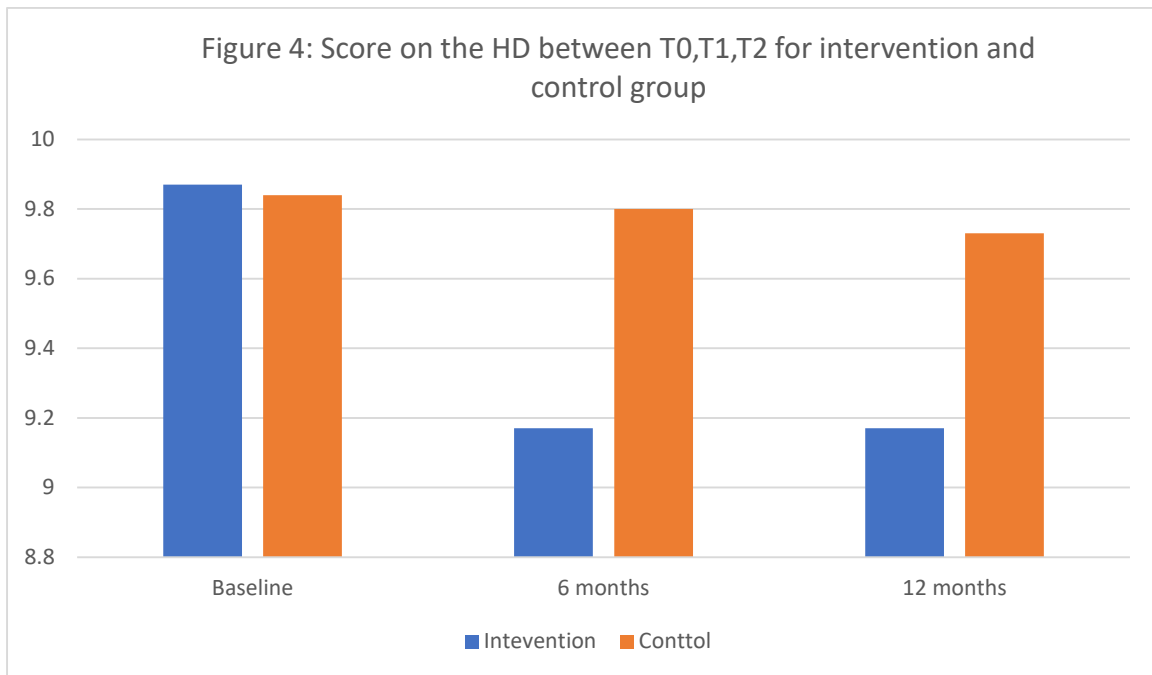


Figure 5: Score on the HADS between T0,T1,T2 for intervention and control group

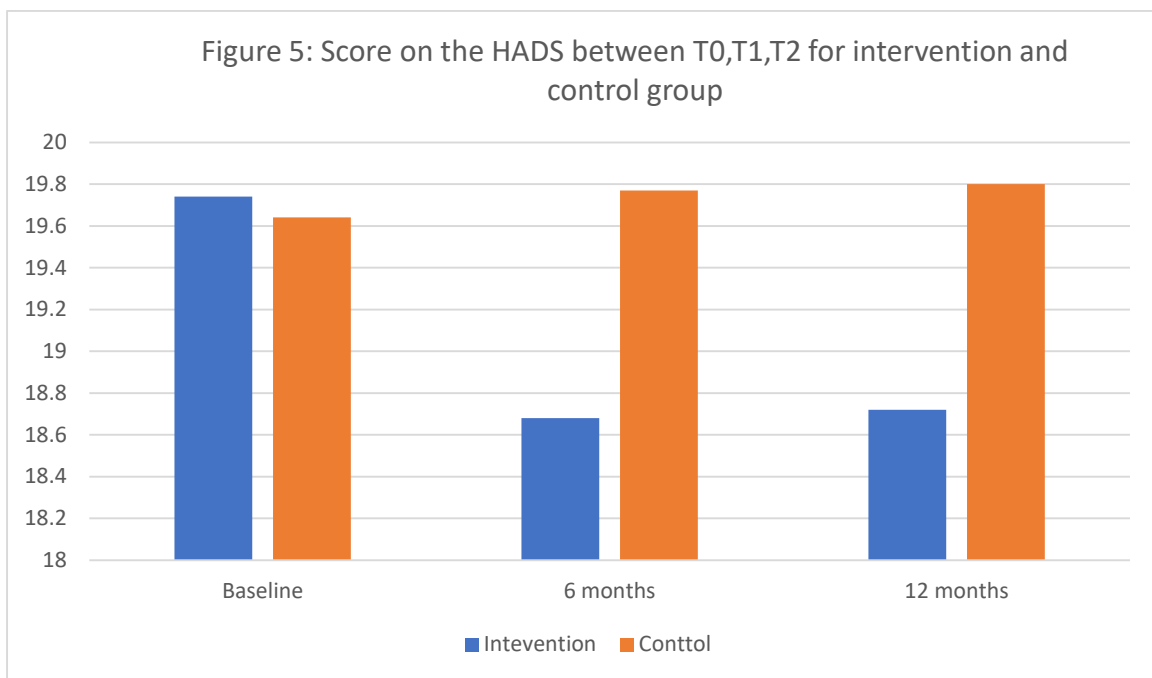


Figure 6: Score on the FSS between T0,T1,T2 for intervention and control group

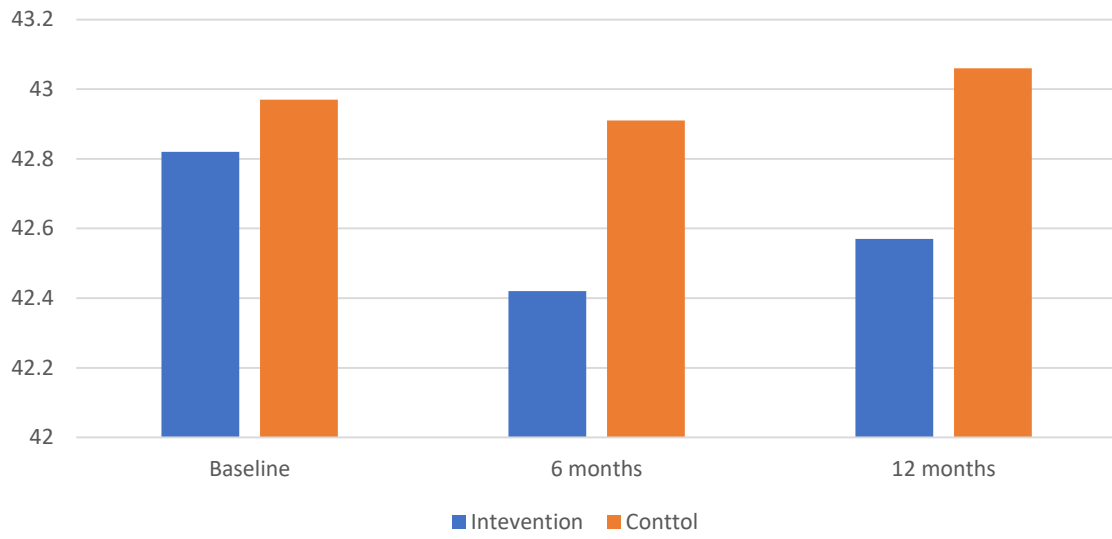


Figure 7: Score on the MSIS between T0,T1,T2 for intervention and control group

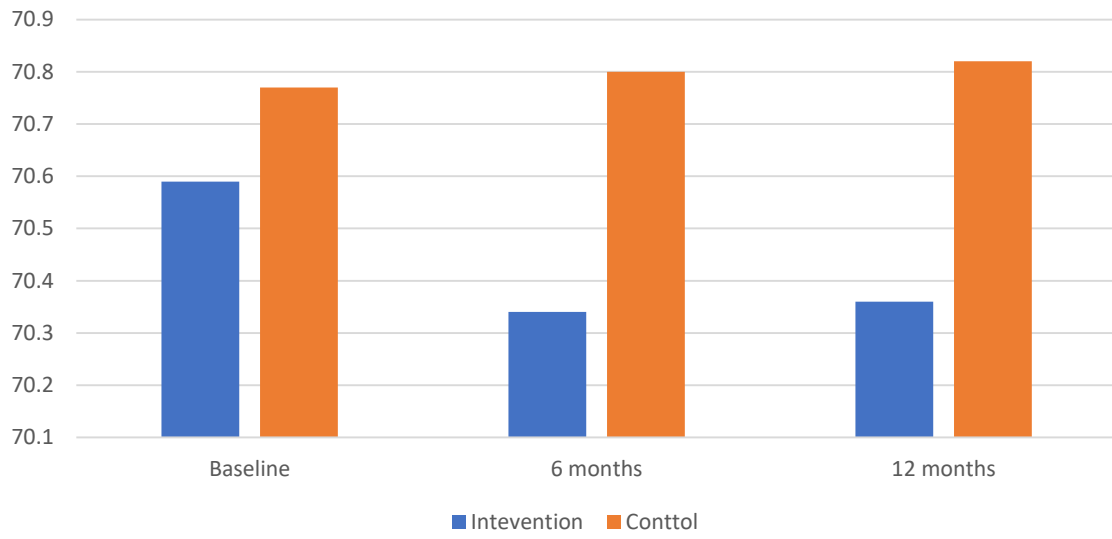
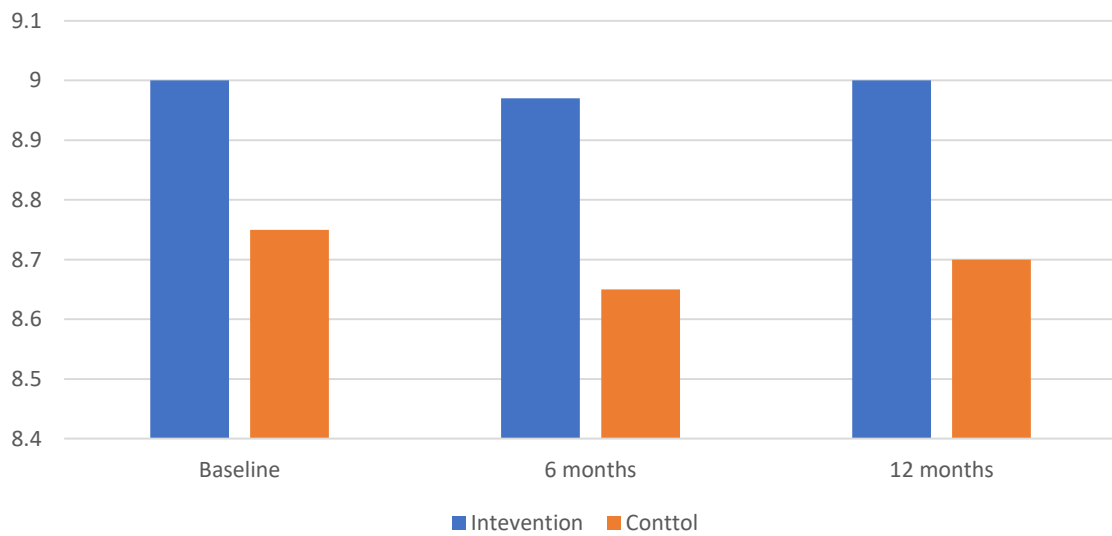


Figure 8: Score on the PSQI between T0,T1,T2 for intervention and control group



Chapter 5

Discussion

Up to now there is no research related to schema therapy and anxiety in the patients with MS.

5-1-Effect of schema therapy on anxiety in MS patient

The first aim of the study, was to assess the efficacy of schema therapy on anxiety in patients with multiple sclerosis. In this study, the present data revealed that schema therapy is effective as it reduced

Anxiety after 20 weeks of sessions. This reduction was maintained up to the 6-month follow-up and was significantly different from the control group. Up to now there is no research related to schema therapy and anxiety in patients with MS. However, Hunsley 2013, and Hawke & Provencher, 2011 showed in other samples, schema therapy affects reducing anxiety. The results related to the first hypothesis showed that the posttest mean scores and anxiety in the experimental group are significantly higher than the control group.

Anxiety is 35% in the MS patients, which reaches 69% with the onset of the disease. So far, no study has examined the effectiveness of schema therapy on anxiety in these patients and in other studies anxiety has been less focused upon; in a single clinical study on anxiety by Moher (2004), the effect of injection has been examined in these patients with the results showed no effectiveness for cognitive therapy. However, in the studies on the patients without MS infliction, different results have been reported. Some have confirmed the effectiveness of other treatments including cognitive therapy while others have shown medium effects or lower effects than what was expected. In a meta-analysis by Woten (2015), the effectiveness of cognitive therapies has been confirmed and in another meta-analytical study by Lorince, the efficiency of cognitive therapies has been lower than expected.

The studies show the effectiveness of schema therapy as a treatment for those who do not respond to cognitive methods. It seems that the unpredictable trend and uncertainty about the future in MS patients

instigates negative feelings in the patients and initial non-adaptable schemas. The studies have also shown a relationship between adaptable schemas such as abandonment, failure, obedience, and sacrifice and anxiety (Treep, 2006). In the first sessions of treatment when the schemas were identified by the patients, they emphasized the treatment of a suffering caused by not being understood, being controlled by others, inability to express their feelings and demands on fear of being rejected or upsetting others and also serving and helping others and receiving nothing instead. Some considered their disease as the result of these sufferings feeling that this trend should change, but they did not know how this change should occur. In the treatment schemas, the patients gained insight into their problems. In other words, the patient's level of unconsciousness decreased and with effective intervention and presenting explanations to the patient, the causes of harmful behaviors were made consistently predictable and controlled. With a feeling of dominance, the patient's anxiety level decreased. Besides, by adjusting the center of control and training the patient to express his/her needs without feeling guilty, fear of being rejected or fear of the occurrence of a bad event, the patient was helped to experience a higher sense of control over his/her destiny. Feeling more powerful and reducing excessive responsibility toward others helped to improve situational understanding, as one of the effective factors in anxiety. Therefore, controlling feelings based on knowledge and prior to knowledge led to reduced anxiety with lasting effects. These findings are to some extent consistent with those of Yalom, Rank, Jerome. (Yalom, 1931) Studies on anxiety and its treatment have yielded different results with some showing the effectiveness of cognitive therapy and some others indicating lower than expected effectiveness. However, few studies have examined the effectiveness of schema therapy. The present study is in line with Farhadi et al.'s study.

5-2-Effect of schema therapy on depression in MS patient

The results showed schema therapy was significantly effective as it reduced depression. Our findings showed that ST changes in cognition and emotion can have effect on abiding change.

ST is a potentially effective treatment for chronic depression (Renner et al., 2014). Koruk, ozabac ,2018 In a meta-analysis showed that schema therapy had a high level of efficacy in the treatment of depressive disorders.

Future with disabilities and limitations caused by the disease leads to negative thoughts and low mood evocating. Also, researches show that people with chronic depression have higher degrees of maladaptive central beliefs.(Keefe et al.2016) With a lack of insight and an apparent reason for depression, chronically depressed people have change-resistant thinking and behavior patterns. They may report that they logically understand that their cognitions are distorted, but their emotional reactions have not changed.(young 2004). However, in MS patients, in addition to this, there is an apparent reason for depression and low mood, which makes treatment conditions more difficult for them. Different situations, such as waiting in the doctor's office and going through various tests, preparing drugs and inability to perform certain activities, and in some cases even requiring the help of others, activate the schemas of these .patients

Given that periods of depression may coincide with the side effects of the disease, they may be perceived as unpleasant experiences, and these experiences seem to create dysfunctional beliefs about depression and its consequences. Outcomes consistent with these schemas (such as negative mood swings, lack of concentration, and fatigue) lead to the activation of schemas and the formation of a new period of depression and lead to the curability reduction. In the cognitive dimension, schema therapy helps patients become aware of the root of their thoughts by using the inner voice of the parents and the deepest level of cognition, i.e., schemas. People suffering from depression highlight information consistent with the schema, ignore information inconsistent with it for many years and perpetuate this trend at all levels of life. Schema therapy, which is one of the healthy answers of the individual, identifying the root of the schema and dysfunctional thoughts, is the best tool to help the individual identify the provocative schematic situation, the negative behaviors, and how to substitute the schema and dysfunctional beliefs healthy and positive behaviors. They provide the

context for change in the individual and, consequently, the interpersonal and intrapersonal relationships. Experimental techniques also help the patient improve schemas by organizing emotional self-examination, new learning, regulation of .interpersonal emotion, and self-relaxation

On the other hand, patients can use these techniques to test the hypothesis of schemas, and by arousing schemas and their relation to current issues, the context is prepared for emotional insight and subsequent improvement of schemas. Mental imagery helps individuals recognize the original schemas, understand their evolutionary roots, and relate these roots to one's current life, and it promotes the patient's understanding and helps him move from rational cognition to emotional experiencing.

5-3-Effect of schema therapy on fatigue in MS patient

This research shows no differences in participants regarding their fatigue. Fatigue is the most common symptom, and one of the most debilitating symptoms in MS patients. Despite its high prevalence and significant impact, fatigue is still poorly understood and often under-emphasized because of its complexity and subjective nature (Braley & Chervin, 2010). According to Pust et al. 2020 fatigues associated with childhood adversities, and It was expected ST be effective on fatigue in this research. Fatigue in MS patients may be multifactorial. In addition to immunologic abnormalities, multiple sclerosis is associated with an increased risk of other conditions that contribute to fatigue, including depression and several sleep disorders. These terms may be interpreted differently depending on cultural or educational backgrounds.

Based on the symptomatology, it is suggested that fatigue in MS is the outcome of excess axonal activity in the demyelinated CNS. There is now strong evidence to suggest that fatigue results from reduced voluntary activation of muscles through central mechanisms. Given that axonal demyelination is a pathological hallmark of MS, activity-dependent conduction block [ADCB] has been proposed as a mechanism underlying fatigue in MS (Vucic et al., 2010). Notwithstanding, MS fatigue is a multifactorial phenomenon, which can also increase by medical side effects or due to inactivity, and its subjective character in self-reported questionnaires is difficult to evaluate (Christogianni et al., 2018). Akker et al. 2016 found that the use of CBT for

the treatment of fatigue in patients with MS has a moderately positive short-term effect. However, this effect decreases with the cessation of treatment. Because fatigue likely results from different underlying causes treatment proceed, by trial and error with limited success, probably due to the presence of multiple different underlying mechanisms. Further studies are needed to explore the long-term effect of this therapy (Manjaly et al., 2019).

5-4-Effect of schema therapy on quality of sleep in MS patient

The result showed no significant difference in an individual's sleep quality. Sleep problems are prevalent in patients with MS. Individuals who had clinically significant anxiety levels were roughly two times more likely to have sleep troubles when compared to people without anxiety (Garland et al., 2017). we expected the reduced anxiety has been positive on the quality of sleep.

Moreover, the quality of sleep could be affected by much variables age- gender- physiologic, hormonal, pharmacologic, and naturalistic probes (Reynolds & Kupfer, 1987). brain volume, metabolism (Branger et al., 2016), and Seasonal changes in sleep duration (Suzuki et al., 2019). Available literature data regarding sleep quality studies indicate that many factors may influence sleep quality such as diabetes mellitus, cardiac diseases, menopause, and eating and drinking habits. one of the important factors in MS is pain, that we did not consider it.

External factors that would affect sleep quality and patterns include environment and consumption of caffeine and alcohol, and amount of exercise. Given this research performed in summer, that could be affected by weather, habitual, cultural, and fasting month, that in general causes sleep disturbances.

5-5-Effect of schema therapy on quality of life in MS patient

The result showed no significant difference in the quality of life in this study. Also, research by Ghodsipour et al.2018 have showed no significant difference was found between the two groups MBSR and CBT in terms of overall Quality of Life in IRAN.

QoL in patients with MS is determined by several factors beyond the more obvious; including coping with the MS diagnosis, understanding the disease and the disease process, dealing with so-called 'hidden' symptoms such as fatigue, cognitive impairments, and sexual disturbances, and managing the many associated personal challenges such as social isolation, family issues, and work difficulties. Evidence is emerging that psychological interventions may be beneficial in MS patients although more research is required to confirm their utility (Lysandropoulos & Havrdova, 2015).

Sleep disturbances may be highly prevalent yet under-recognized contributors to fatigue in persons with MS (Braley et al., 2014). Fatigue is considered one of the main causes of impaired quality of life among MS patients, independent of depression or disability (Braley & Chervin, 2010). The researches have shown the poor sleep is associated with fatigue and quality of life (Chirstabel et al 2017).

5-6-Effect of schema therapy on Demographic Variable in MS patient

We expected the treatment to have more positive effects in married patients but, there was no significant association between marital status, Age, Sex, education. These may due to :

- 1) Lack of sufficient knowledge about MS and its complications and lack of understanding of the patient by the partners because of high levels of anxiety and distress in the first years after diagnosis in the partners pwMS (Janssens et al., 2006),
- 2) Treatment-induced changes, especially during breaking patterns, made resistance and challenge in some families. For example, after a patient asked her mother-in-law not to enter her house in their absence, the mother-in-law became upset and broke off the relationship for a long time. Another example, when a woman did not accept her husband's request for a party of the family due to fatigue." he said sarcastically. "oh guys, your mother is making the breaking pattern.

There was also no significant relationship between age, gender, education. This may be due to common pain in patients who were interested in research. And increasing general knowledge about psychology, and a common view in patients who continued treatment.

5-7-Effect of schema therapy on EDSS in MS patient

The result showed there is no significant difference in EDSS in patients before and after schema therapy. The presenting symptoms and rate of progression of multiple sclerosis (MS) are very heterogeneous. low vitamin D levels, smoking (Hempel et al., 2017). seasonal factors. (Harding et al., 2017; Nikolenko et al., 2019) stress, extreme temperatures (Çinar & Yorgun, 2018). Although schema therapy did not have a positive effect on EDSS, but, lack of change in EDSS can be considered as good result.

5-8-Effect of schema therapy on schemas in MS patient

The result showed schema therapy modified Subjugation and Self-Sacrifice inpatient. In 20session schema therapy some schemas were changed. The healing of schemas specially Subjugation, Self-Sacrifice led to feel of having more control over the individuals, and the situation and belief of hopelessness were changed.

These result is consistent with locus of control theory Lazarus and Folkman (Atkinson et al., 1996; Dilmac, 2009) and research carol et al,2013 showed the people who believe that their lives are in the control of other forces than their selves are characterized as external locus of are more anxious, aggressive, and depress. subjugation schema significantly is effected by therapy (Young et al., 2014).

Also with healing from self-sacrifice schema, they learned to live more and better for them self. According to school existentialism, the self can be a prison, a trap, and a source of great anxiety. By the time we realize where and what we are, according to restrictive categories of historical thought and language, we are already in world, inescapably bound to our conditions, forced to perform roles for which we never auditioned. Some of schemas has changed, and it seems some of them need more therapeutic sessions specially under challenging situations.

5-9-Conclusion

The aim of this study is to investigate the effects of schema therapy on anxiety in patients with MS. The result indicated a significant effect of schema therapy on anxiety, depression and it modified some schema. Maybe schema therapy heals somehow anxiety arise from stage of development .for instance anxiety of fragment because of not meeting needs or losing love or approval of loved object and felling guilty .it seems

fading subjugation and self-scarified modify locus of control and interpersonal relationship and leads to decrease anxiety .the patient learn not to inhibit their felling ,also they learn to turn a one- sided relationship into a desirable one by reducing responsibility for others and paying more attention to their own needs, and to overcome the feelings of loneliness and helplessness that Fromm considered as the main source of anxiety.

Moreover, it showed no significant effect on fatigue, quality of life and quality of sleep, other conducted researches have shown other treatments which were effective on anxiety. Factors associated with MS sexual dysfunction estimated prevalence of 40% to 80% in women and 50% to 90% in men (Domingo et al., 2018) pain 50-86%, (Murphy et al., 2017) Bladder dysfunction up to 75% of patients (DasGupta & Fowler, 2003) are an important factor can be affected on sleep, quality of life and fatigue dramatically .Also undesirable minor events, hassles and major daily stress significantly predict psychological symptoms and they have a reciprocal effect on psychotherapy.

However, when one person has a phobia of dogs, we can interpret it with all theories. Treatment of a person with a phobia of the dog through psychological theories is one thing, anxiety and fear in a patient who suffers from a chronic illness with features of the disabling process is a horse of different color. It seems in chronic illness that has potential for recurrence and relapse like MS, due to the unpredictable course of the disease and relapses, patients with Relapsing-Remitting MS (RRMS) may deal with the stress of anticipation of relapse and its unpredictable consequences. They have no information regarding the timing, severity, and consequences of their next relapse. This disability is directly related to the level of uncertainty regarding future events, and it propels these patients towards chronic fear or, as one might call, fear of progression as well as anxiety by reducing their opportunity to efficiently prepare for the future. (Khatibi et al., 2020). So the patient with MS experiences fear and anxiety simultaneously. The patients experience different levels of anxiety in cognition and emotion. Schema therapy with explaining as the reason for behaviors and events and emotions and formation of cognition changes some roles in the life of patients. although patients cannot remove the source of anxiety they can control it. schema therapy with self-awareness is an opportunity to learn schemas and overcame them, and in the end, be responsible for self. According to existentialism, awareness of the reason for the behavior and cause control and dominance that can reduce anxiety and

fear of death and The feeling of power and control arise of awareness is effective, even in the existing situation. ST increases insight and awareness and Creates controls but create a life outlook and create meaning is very important,

As Pole Tillich says: the only thing we can do about anxiety is to put it in the proper place. we can put anxiety in right place and encourage the patients to Courage Be in their lifetime. The Courage To Be is the power of man to affirm himself in spite of the dominating anxieties he faces in his contemporary existence, and gain the power of life (Tillich, 1952).

Overall, this research included some strengths, weaknesses and limitations. According to criteria of Ingram, (Ingram et al., 2000), stability and acceptability are strengths of the research. Anxiety and depression reduction were maintained after six months. Also, 10 percent of the attrition rate shows the patients were interested in the treatment.

Lack of safety was one of the weakness because of making trouble in the family. Another one which I can bring up is lack of generality of change. Short time and patient tendency to the treatment of subjugation and self-sacrifice cause not enough time for other schemas. The tendency may be due to the fact that when people experience loss and grief and become aware of non-being, they become more eager to change and live for themselves.

Limitation :In the last few years, a number of interesting studies have done. With these limitations in mind, the present results suggest a number of directions for future research. First . First, Interest in the type of treatment and insist on the specific schema, also availability of the therapist during the follow-up can be effected on the resul. Second , there is no research about schema therapy in MS up to now. Then access to literature further was limited.

Third during follow-up periods, confounding factors may have threatened the validity of our long term effect estimates we confront with intervening variables, as this research was being conducted, people were experiencing a social, economic, and political crisis in Iran. Patients have disease-related problems besides all these social issues, including procurement drugs for treatment and sometimes they have problems preparing MS medicine. It is well known that mental health problems are related to

deprivation, poverty, inequality, and other social and economic determinants of health. Economic crises are therefore times of high risk to the mental well-being of the population and of the people affected and their families (https://www.euro.who.int/data/assets/pdf_file/0008/134999/e94837.pdf). However, At the clinical level, patients can benefit from schema therapy treatment for reducing anxiety and depression. Treatment is likely to have different results in communities with higher levels of economic and social well-being. Another point should be considered among people with medical conditions is often difficult to differentiate clearly psychological symptoms from those attributable to physical.

Then further studies with regard to important symptom like pain ,bladder and sexual dysfunction in other culture are suggested. Also, maybe is better than added Existentially psychotherapy to schema therapy and disability anxiety could be considered separately as an important concept and should be studied

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Appendix

Summary of research about schemas and anxiety

Name(s)	Date	Country	N	Main criteria (DSM, ...)	Method (ECR,...)	Age	Gender	Assessment tools	Results	Comments (interest; limits; bias...)
Early Maladaptive Schemas in Patients with Psychosomatic Disorder and Multiple Sclerosis	2020	Iran	100	Diagnosed by psychiatrist	causal comparative.	20-40	Female Male	SQ-SF	average score of emotional deprivation, dependence/incompetence, and failure subscale in patients with MS was higher than healthy group	sample size, generalizability and assessment
Role and Treatment of Early Maladaptive Schemas in Vietnam Veterans with PTSD	2010	Australian and New Zealand	54+127	diagnosed PTSD by psychiatrist	compare Schema Therapy (ST) with traditional CB	mean age of 52 years	Male+ 2female	PTSD Checklist Military; Young Schema Questionnaire-L3; Hospital Anxiety.	effect size was large for the ST group (Cohen's d between 0.61 and 0.82) and small to medium in the CBT comparison	results limit to generalizability and the use of a historical control group, data collection base on memory

									group (between 0.3 and 0.53)	
<p>Early Maladaptive Schemas in Anxiety Disorders</p> <p>An Investigation of Schemas' Relation to Symptoms in a Complex Sample</p>	2017	Norway	90	DSM	RCT comparing	18 and more	Female Male	<p>Young Schema Questionnaire-Short Form (YSQ-S1), Metacognitions Questionnaire-30 (MCQ-30), and Beck Anxiety Inventory (BAI),</p>	<p>There were significant concurrent between- and within-person relationships between symptoms and schema-endorsement in patients receiving MCT showed greater declines than those receiving CBT. However, this effect was not apparent</p>	<p>use of self-report poses</p> <p>overlap of concepts and unclear causal direction between the variables</p> <p>the lack of control</p>

									t in analyse s across treatme nt and follow- up.	
Early Maladaptiv e Schemas and Social Phobia	20 06	Portugal	158(3 group)	(ADIS-IV).	cross- sectional	a mean age of years= 28.71	Femal e Male	social anxiety and the Young's Schema Questio nnaire (123- items version)	Patients with social phobia show higher levels of EMSs particula rly in the area of disconn ection/re jection than patients with other anxiety disorder s.	impossibil ity to determine the relationshi p and influence anxiety and EMS together.
P-129 - EARLY MALADAP TATIVE SCHEMAS AND SOCIAL ANXIETY: THE	20 12	Basque Country	539	college students	cross- sectional	18-25	Femal e Male	social anxiety (Caso- A30; Caballo et al., 2010), Early Maladap tative Schema	that social anxiety is associat ed with several schema s: Subjuga tion,	Generaliz ability due to based on an undergrad uate student sample

MODERATING EFFECT OF AVOIDANT VS. OVERCOMPENSATION COPING								s (YSQ-3; Young, 2005) and coping styles (YRAI-1 and YCI-1 - 1; Young, 2003)	Pessimism, Emotional Inhibition, Grandiosity (negative relationship), Abandonment, Enmeshment, and Self-Sacrifice	
Early Maladaptive Schemas as Moderators of the Impact of Stressful Events on Anxiety and Depression in University Students	2012	Basque Country	374	first- and second year college students at the University of Deusto and the University	longitudinal design,	mean age =19.16	Female male	Life Stress Questionnaire (LSQ; Wadsworth et al. 2005) and the Social Stress Questionnaire (SSQ; Connor-Smith and Compas 2002)	distress can modify cognitive style. certain early maladaptive schemas are risk factors for the development of depressive and anxiety	Generalizability was based on an undergraduate student sample, measuring the schemas only at T1 may have excluded the possibility of testing whether symptoms

									symptoms in undergraduate students	and stressors influence the cognitive structures and not vice versa. and stressors can modify cognitive style
the mediating role of experiential avoidance in the relationship between early maladaptive schemas and illness anxiety	2019	IRAN	308	students of Qazvin University	Correlation	Mean =22	Female male	Early Maladaptive Scheme (Young), hypochondriasis (Evans) and Acceptance and Action Questionnaires	a significant role of schemas of impaired autonomy and performance and impaired limits domains in illness anxiety. Also, vulnerability to harm or illness	limitations of the present study can be attributed to the lack of generalization of results Refer to other communities and collect data in the form of a questionnaire.

									and entitlement/grandiosity schemas could significantly predict illness anxiety	
early maladaptive schemas (EMSs) in function of eating disorder (ED) With or Without Non-Suicidal Self-Injury	2016	Belgium	491	DSM-IV	Cross sectional	mean age 21.44	Female	Young Schema Questionnaire and the Self-Injury Questionnaire	a strong association between lifetime prevalence of NSSI and higher levels of EMS within the ED sample. I	generalizability sample size include criteria lack of information about past history
The efficacy of schema therapy in treating women's Generalized Anxiety disorder	2011	Iran	3	DSM-IV	experimental single case study	25,30, 34 years	Female	Pennsylvania State Worry Questionnaire (PSWQ), Worry Domain Questionnaire	significantly efficient	generalizability randomization, small size and lack of control group.

								(WDQ) and Young schema Questionnaire (YSO).		
effects of the Schema Therapy and Mindfulness on the Maladaptive Schemas Hold by the Psoriasis Patients with the Psychopathology Symptoms	2017	Iran	25	psoriasis symptoms with dermatologist's diagnosis.	semi-experimental study with post-and pre-tests	Adulthood (18 yrs & older) Middle Age (40-64 yrs)	Male Female	cognitive emotion regulation questionnaire (CERQ) and existential anxiety inventory (EAI)	Similar and significant effects of both the schema and mindfulness-based therapies on the maladaptive schemas in improving the psoriasis patients with the psychopathologic symptoms	generalizability due to factors related to sample characteristics, and the sample size

effects of the Schema Therapy and Mindfulness on the Maladaptive Schemas Hold by the Psoriasis Patients with the Psychopathology Symptoms	2017	Iran	16	Referred by specialist	semi-experimental	20-50	Male female	Young schema questionnaire	significant difference between the schema-based therapy and mindfulness with the control group	to generalizability due to factors related to sample characteristics, and the sample size
Core beliefs and psychological distress in patients with psoriasis and atopic eczema attending secondary care	2011	uk	185	Diagnosis by dermatologist	cross-sectional	23-75	Male female	Hospital Anxiety and Depression Scale Young Schema Questionnaire-Short Form, Demographic information questionnaire	Differences were found between dermatology patients and control groups. Patients with psoriasis differed on seven EMS	A cross-sectional structure Measurement

									from the normal control group:	
Change in interpersonal problems after cognitive agoraphobia and schema-focused therapy versus psychodynamic treatment as usual of inpatients with agoraphobia and Cluster C personality disorders	2008	Norway	24+13	DSM-III-R (DSM-IV)	Cohort comparison quasi-experimental study	Tau=3 9.1 ± 8.3 st= 40.8 ± 7.7 yrs	Male female	Symptom Checklist-90 SCL-90 IIP Mobility Inventory for Agoraphobia - MI	ST group showed greater improvement in interpersonal function than treatment as usual.	small sample not randomly assign, the samples collection in different time periods (TAU in 1992-4, CT in 1995-7), different selection criteria, and possible differences in the patients' expectations to and motivation. The staff's motivation and competence the different

										follow-up procedure
the association of childhood adversities, specific traits, and MS disease characteristics with fatigue symptoms utilizing path analysis.	2020	Germany	571	MS outpatient	cross-sectional based on web	Mean=43.4	Male Female	Childhood Trauma Questionnaire (CTQ) Toronto Alexithymia Scale; TAS-26) YSQ).; BDI-FS) (State-Trait Anxiety Inventory; STAI-state), determined Disease Steps; PDDS). Functions (FSMC)	higher perceived disconnection and rejection, higher impairments in autonomy and performance, and higher other-directedness predicted more severe anxiety symptoms.	study was web-based and all MS diagnoses and clinical data rely on participants' self-reports. A selection bias for the PwMS sample can also not be excluded.
relationships among Early Maladaptive Schemas (EMS), beliefs about loss of control, a	2001	Norway	59	DSM-V	Cross-sectional	Mean=38.4	Male Female	Mobility Inventory for Agoraphobia - MI, Agoraphobia	EMS predict changes in beliefs about loss of control,	limitations are sample size was small. and structural equation modeling

fear of bodily sensations, and avoidance in patients undergoing cognitive therapy								Cognition questionnaire ACQ	a fear of bodily sensations	is used for testing
Early maladaptive schemas in Finnish adult chronic male and female pain patients	2010	Finland	271	Referred by specialist	Correlation study	age 18-64	Male Female	pain variables and EMS	chronic pain patients may suffer from early maladaptive schemas which have an effect on their current pain situation and may reflect underlying emotional maltreatment.	the result limit to unable to determine the specific causal relationship between EMS, lack of control group, and generalizability
the relationship between early maladaptive	2015	IRAN	328	students were selected in accordance	descriptive-correlational	Age 26-40.	Female	Young Schema Questionnaire Short	early maladaptive schemas are	Generalizability due to sample size

e schemas and death anxiety and referential thinking				with Plant formula				Form (2005), Templer Death Anxiety Scale (1870), and Referential Thinking Questionnaire (2010)	predictors of negative thinking of referential thinking dimensions early maladaptive schemas are not predictors of death anxiety	And population
the Relationship Between Early Maladaptive Schemas, Depression, and Generalized Anxiety among Adults Seeking Residential Treatment for Substance Use Disorders	2015	USA	122	psychiatric diagnoses, based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR	cross-sectional	mean age 37.36)	Male Female	Young Schema Questionnaire—long form, psychiatric Diagnostic Screening Questionnaire (PDSQ) the Alcohol Use Disorders	GAD was associated with the EMS domain of impaired autonomy and performance.	Generalizability due to sample size And population

								Identification Test (AUDIT)		
The role of optimism in the process of schema-focused cognitive therapy of personality problems ,schema change with ST in co-occurring agoraphobia and personality traits and disorder	2002	Norway	35	DSM-IV	post design)	mean age =40.1	(80%) women and seven (20%) men—the	the Structured Clinical Interview for DSM IV; Panic Rating Scale; the State-Trait Anxiety Inventory; Schema Questionnaire; the Inventory of Interpersonal Problems	Effect sizes from pre-treatment to follow-up on the MI-AAL was 0.52, the STAI was 0.32 and the Personality Disorder cluster C index was 0.39	lack of control group and independent randomization and a lack of blinding.
effectiveness of schema therapy integrated with rehabilitation on CER and	2018	IRAN	25	congestive heart failure	true experimental with pretest/posttest design	40-45 years	Female Male	Cognitive Emotion Regulation Questionnaire (CERQ; Garnefs	the group schema therapy integrated with rehabilitation improve	both the therapist and the researcher were the same person, ,lack of follow up

existential anxiety in patients with CHF								ki et al. 2001) Existential Anxiety Inventory (EAI; Good and Good 1974)	d CER and existential anxiety in patients with CHF (p < 0.001).	,small sample size
Early maladaptive schemas and asthma: Disconnection and rejection domains may have an effect on the severity of asthma	2018	IRAN	50	Referred by specialist	cross-sectional study	Mean 30.6	Female Male	Asthma Control Test (ACT) questionnaire. EMS	EMSs have potential effects on clinical characteristics and severity of asthma in asthmatic patients.	socio-economic situation and education of the patients didn't consider. second, the participants in the study were only the cases of stable asthma,
Diagnosis of Anxiety Disorders in University Students through the Early	2017	Morocco	2012	Student of IBN TOFAIL University,	cross-sectional	17-25	Female Male	Questionnaire of early maladaptive schemas short version	The activation of certain schemas influenced the	Generalizability due to samples and nature of research

Maladaptive Schemas and Beck's Inventory								of Young - Beck Anxiety Inventory (BAI)	development of anxiety disorders among students	
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3 Young Schema Questionnaire - Short Form (YSQ)

Listed below are statements that a person might use to describe him or herself. Please read each statement and decide how well it describes you. When you are not sure, base your answer on what you emotionally feel, not on what you think to be true. Choose the highest rating from 1 to 6 that describes me perfectly .

1. ____ Most of the time, I haven't had someone to nurture me, share him/herself with me, or care deeply about everything that happens to me.
 2. ____ In general, people have not been there to give me warmth, holding and affection.
 3. ____ For much of my life, I haven't felt that I am special to someone.
 4. ____ For the most part, I have not had someone who really listens to me, understand me, or is tuned into my true needs and feelings.
 5. ____ I have rarely had a strong person to give me sound advice or direction when I'm not sure what to do.
- *ed
6. ____ I find myself clinging to people I'm close to, because I'm afraid they'll leave me.
 7. ____ I need other people so much that I worry about losing them.
 8. ____ I worry that people I feel close to will leave me or abandon me.
 9. ____ When I feel someone I care for pulling away from me I get desperate.
 10. ____ Sometimes I am so worried about people leaving me that I drive them away.
 11. ____ I feel that people will take advantage of me.
 12. ____ I feel that I cannot let my guard down in the presence of other people, or else they will intentionally hurt me.
 13. ____ It is only a matter of time before someone betrays me.
 14. ____ I am quite suspicious of other people's motives.
 15. ____ I'm usually on the lookout for people's ulterior motives.

*ma

- 16. _____ I don't fit in.
- 17. _____ I'm fundamentally different from other people.
- 18. _____ I don't belong; I'm a loner.
- 19. _____ I feel alienated from other people.
- 20. _____ I always feel on the outside of groups.

*si

- 21. _____ No man/woman I desire could love me once he/she saw my defects.
- 22. _____ No one I desire would want to stay close to me if he/she know the real me.
- 23. _____ I'm unworthy of the love, attention, and respect of others.
- 24. _____ I feel that I'm not loveable.
- 25. _____ I am too unacceptable in the very basic ways to reveal myself to other people.

*ds

- 26. _____ Almost nothing I do at work (or school) is as good as other people can do.
- 27. _____ I'm incompetent when it comes to achievement.
- 28. _____ Most other people are more capable than I am in areas of work and achievement.
- 29. _____ I'm not as talented as most people are at their work.
- 30. _____ I'm not as intelligent as most people when it comes to work (or school).

*di

3

- 31. _____ I do not feel capable of getting by on my own in everyday life.
- 32. _____ I think of myself as a dependent person, when it comes to everyday functioning.
- 33. _____ I lack common sense.
- 34. _____ My judgement cannot be relied upon in everyday situations.

35. _____ I don't feel confident about my ability to solve everyday problems that come up.

*di

36. _____ I can't seem to escape the feeling that something bad is about to happen.

37. _____ I feel that a disaster (natural, criminal, financial, or medical) could strike at any _____ moment.

38. _____ I worry about being attacked.

39. _____ I worry that I'll lose all my money and become destitute.

40. _____ I worry that I'm developing a serious illness, even though, nothing serious has been diagnosed by a physician.

*vh

41. _____ I have not been able to separate myself from my parent (s) the way other people my age seem to.

42. _____ My parents and I tend to be over involved in each other's lives and problems.

43. _____ It is very difficult for my parent(s) and me to keep intimate details from each other without feeling betrayed or guilty.

44. _____ I often feel as if my parent(s) are living through me - I don't have a life of my own.

45. _____ I often feel that I do not have a separate identity from my parent(s) or partner.

*em

46. _____ I think that if I do what I want, I'm only asking for trouble.

47. _____ I feel that I have no choice but to give in to other people's wishes, or else they will retaliate or reject me in some way.

48. _____ In relationships, I let the other person have the upper hand.

49. _____ I've always let others make choices for me, so I really don't know what I want for myself.

50. _____ I have a lot of trouble demanding that my rights be respected and that my feelings be taken into account.

4

*sb

51. _____ I'm the one who usually ends up taking care of the people I'm close to.

52. _____ I am a good person because I think of others more than of myself.

53. _____ I'm so busy doing for the people that I care about that I have little time for myself.

54. _____ I've always been the one who listens to everyone else's problems.

55. _____ Other people see me as doing too much for others and not enough for myself.

*ss

56. _____ I am too self-conscious to show positive feelings to others (e.g. affection, showing I care).

57. _____ I find it embarrassing to express my feelings to others.

58. _____ I find it hard to be warm and spontaneous.

59. _____ I control myself so much that people think I am unemotional.

60. _____ People see me as uptight emotionally.

*ei

61. _____ I must be the best at most of what I do; I can't accept second best.

62. _____ I try to do my best; I can't settle for "good enough".

63. _____ I must meet all my responsibilities.

64. _____ I feel there is constant pressure for me to achieve and get things done.

65. _____ I can't let myself off the hook easily or make excuses for my mistakes.

*us

66. _____ I have a lot of trouble accepting "no" for an answer when I want something from other people.

67. _____ I'm special and shouldn't have to accept many of the restrictions placed on other people.

68. _____ I hate to be constrained or kept from doing what I want.

69. _____ I feel that I shouldn't have to follow the normal rules and conventions other people do.

70. _____ I feel that what I have to offer is of greater value than the contributions of others.

*et

5

71. _____ I can't seem to discipline myself to complete routine or boring tasks.

72. _____ If I can't reach a goal, I become easily frustrated and give up.

73. _____ I have a very difficult time sacrificing immediate gratification to achieve a long-range goal.

74. _____ I can't force myself to do things I don't enjoy, even when I know it's for my own good.

75. _____ I have rarely been able to stick to my resolutions.

Beck Anxiety Inventory (BAI)

Below is a list of common symptoms of anxiety. Please carefully read each item in the list. Indicate how much you have been bothered by that symptom during the past month, including today, by circling the number in the corresponding space in the column next to each symptom.

	Not at all	Mildly, but it didn't bother me much	Moderately - it wasn't pleasant at times	Severely - it bothered me a lot
Numbness or tingling	0	1	2	3
Feeling hot	0	1	2	3
Wobbliness in legs	0	1	2	3
Unable to relax	0	1	2	3
Fear of worst happening	0	1	2	3

Dizzy or lightheaded	0	1	2	3
Heart pounding / racing	0	1	2	3
Unsteady	0	1	2	3
Terrified or afraid	0	1	2	3
Nervous	0	1	2	3
Feeling of choking	0	1	2	3
Hands trembling	0	1	2	3
Shaky / unsteady	0	1	2	3
Fear of losing control	0	1	2	3
Difficulty in breathing	0	1	2	3
Fear of dying	0	1	2	3
Scared	0	1	2	3
Indigestion	0	1	2	3
Faint / lightheaded	0	1	2	3
Face Flushed	0	1	2	3
Hot / cold sweats	0	1	2	3

Beck's Depression Inventory

This depression inventory can be self-scored. The scoring scale is at the end of the questionnaire.

1.

0 I do not feel sad.

1 I feel sad

2 I am sad all the time and I can't snap out of it.

3 I am so sad and unhappy that I can't stand it.

2.

0 I am not particularly discouraged about the future.

1 I feel discouraged about the future.

2 I feel I have nothing to look forward to.

3 I feel the future is hopeless and that things cannot improve.

3.

0 I do not feel like a failure.

1 I feel I have failed more than the average person.

2 As I look back on my life, all I can see is a lot of failures.

3 I feel I am a complete failure as a person.

4.

0 I get as much satisfaction out of things as I used to.

1 I don't enjoy things the way I used to.

2 I don't get real satisfaction out of anything anymore.

3 I am dissatisfied or bored with everything.

5.

0 I don't feel particularly guilty.

1 I feel guilty a good part of the time.

2 I feel quite guilty most of the time.

3 I feel guilty all of the time.

6.

0 I don't feel I am being punished.

1 I feel I may be punished.

2 I expect to be punished.

3 I feel I am being punished.

7.

0 I don't feel disappointed in myself.

1 I am disappointed in myself.

2 I am disgusted with myself.

3 I hate myself.

8.

0 I don't feel I am any worse than anybody else.

1 I am critical of myself for my weaknesses or mistakes.

2 I blame myself all the time for my faults.

3 I blame myself for everything bad that happens.

9.

0 I don't have any thoughts of killing myself.

1 I have thoughts of killing myself, but I would not carry them out.

2 I would like to kill myself.

3 I would kill myself if I had the chance.

10.

0 I don't cry any more than usual.

1 I cry more now than I used to.

2 I cry all the time now.

3 I used to be able to cry, but now I can't cry even though I want to.

11.

0 I am no more irritated by things than I ever was.

1 I am slightly more irritated now than usual.

2 I am quite annoyed or irritated a good deal of the time.

3 I feel irritated all the time.

12.

0 I have not lost interest in other people.

1 I am less interested in other people than I used to be.

2 I have lost most of my interest in other people.

3 I have lost all of my interest in other people.

13.

0 I make decisions about as well as I ever could.

1 I put off making decisions more than I used to.

2 I have greater difficulty in making decisions more than I used to.

3 I can't make decisions at all anymore.

14.

0 I don't feel that I look any worse than I used to.

1 I am worried that I am looking old or unattractive.

2 I feel there are permanent changes in my appearance that make me look unattractive

15.

0 I can work about as well as before.

1 It takes an extra effort to get started at doing something.

2 I have to push myself very hard to do anything.

3 I can't do any work at all.

16.

0 I can sleep as well as usual.

1 I don't sleep as well as I used to.

2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.

3 I wake up several hours earlier than I used to and cannot get back to sleep.

17.

0 I don't get more tired than usual.

1 I get tired more easily than I used to.

2 I get tired from doing almost anything.

3 I am too tired to do anything.

18.

0 My appetite is no worse than usual.

1 My appetite is not as good as it used to be.

2 My appetite is much worse now.

3 I have no appetite at all anymore.

19.

0 I haven't lost much weight, if any, lately.

1 I have lost more than five pounds.

2 I have lost more than ten pounds.

3 I have lost more than fifteen pounds.

20.

0 I am no more worried about my health than usual.

1 I am worried about physical problems like aches, pains, upset stomach, or constipation.

2 I am very worried about physical problems and it's hard to think of much else.

3 I am so worried about my physical problems that I cannot think of anything else.

21.

0 I have not noticed any recent change in my interest in sex.

1 I am less interested in sex than I used to be.

2 I have almost no interest in sex.

3 I have lost interest in sex completely.

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.

Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			feel as if I am slowed down:
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy.			I get a sort of frightened feeling like 'butterflies' in the stomach:
0		Definitely as much	0		Not at all
1		Not quite so much	1		Occasionally
2		Only a little	2		Quiet often

3		Hardly at all	3		Very Often
		I get a sort of frightened feeling as if something awful is about to happen			I have lost interest in my appearance:
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			I feel restless as I have to be on the move:
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind :			I look forward with enjoyment to things :
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all

		I feel cheerful:			I get sudden feelings of panic:
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			I can enjoy a good book or radio or TV
					Program:
	0	Definitely		0	Often
	1	Usually		1	Sometimes
	2	Not often		2	Not often
	3	Not at all		3	Very seldom

Multiple Sclerosis Impact Scale (MSIS-29)

• The following questions ask for your views about the impact of MS on your day-to-day life

during the past two weeks.

- For each statement, please **circle** the **one** number that **best** describes your situation
- Please answer **all** questions

In the past two weeks, how much has your MS limited your ability to...	Not at all	A little	Moderately	Quite a bit	Extremely
1. Do physically demanding tasks?	1	2	3	4	5
Grip things tightly (e.g. turning on taps)?	1	2	3	4	5
Carry things?	1	2	3	4	5

In the past two weeks, how much have you been bothered by...	Not at all	A little	Moderately	Quite a bit	Extremely
4. Problems with your balance?	1	2	3	4	5
5. Difficulties moving about indoors?	1	2	3	4	5
6. Being clumsy?	1	2	3	4	5
7. Stiffness?	1	2	3	4	5
8. Heavy arms and/or legs?	1	2	3	4	5

9. Tremor of your arms or legs?	1	2	3	4	5
10. Spasms in your limbs?	1	2	3	4	5
11. Your body not doing what you want it to do?	1	2	3	4	5
12. Having to depend on others to do things for you?	1	2	3	4	5

In the past two weeks, how much have you been bothered by...	Not at all	A little	Moderately	Quite a bit	Extremely
13. Limitations in your social and leisure activities at home?	1	2	3	4	5
14. Being stuck at home more than you would like to be?	1	2	3	4	5
15. Difficulties using your hands in everyday tasks?	1	2	3	4	5
16. Having to cut down the amount of time you spent on work or other daily activities?	1	2	3	4	5
17. Problems using transport (e.g. car, bus, train, taxi, etc.)?	1	2	3	4	5
18. Taking longer to do things?	1	2	3	4	5
19. Difficulty doing things spontaneously (e.g. going out on the spur of the moment)?	1	2	3	4	5
20. Needing to go to the toilet urgently?	1	2	3	4	5
21. Feeling unwell?	1	2	3	4	5

22. Problems sleeping?	1	2	3	4	5
23. Feeling mentally fatigued?	1	2	3	4	5
24. Worries related to your MS?	1	2	3	4	5
25. Feeling anxious or tense?	1	2	3	4	5
26. Feeling irritable, impatient, or short tempered?	1	2	3	4	5
27. Problems concentrating?	1	2	3	4	5
28. Lack of confidence?	1	2	3	4	5
29. Feeling depressed?	1	2	3	4	5
Please check that you have answered all the questions before going on to the next page					

FATIGUE SEVERITY SCALE (FSS)

Please circle the number between 1 and 7 which you feel best fits the following statements. This refers to your usual way of life within the last week. 1 indicates “strongly disagree” and 7 indicates “strongly agree.”

Read and circle a number.	Strongly Disagree → Strongly Agree						
	1	2	3	4	5	6	7
1. My motivation is lower when I am fatigued.							
2. Exercise brings on my fatigue.							
3. I am easily fatigued.							
4. Fatigue interferes with my physical functioning.							
5. Fatigue causes frequent problems for me.							

6. My fatigue prevents sustained physical Functioning.	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
8. Fatigue is among my most disabling symptoms.	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7

Summary of schema therapy group Protocol

Session 1

The Welcome Group Session

Explain the purpose of this group

welcome patients to the ST program .

The Group Connection

Patients and therapists toss the ball of yarn back and forth, each person connecting to the yarn by wrapping it around their hand so that a web of connections is constructed within the group circle. After all are connected once with the yarn, we have them make another connection around the circle from person to person. Then we comment on the added connections.

The Bubble-Safety Technique

The first safety image that we present to patients is a simple image

This is an imagery exercise in which we put a huge “magical safety-bubble” around the whole group. This fits with the developmental approach of ST which suggests that safety and protection initially need to come from the therapists.

Ice breaking

Introducing the therapist and her role and introduce each member

The goals of the group sessions and information

- providing a new way to understand the anxiety

problems you have and how you can recover from them;

- how to make changes in your life to function better, be happier

and more fulfilled;

- helping to increase feeling of emotional stability,

comfort level, and ability to tolerate distress without acting

in ways that are harmful

- And giving Information about schema therapy Group exploration of how schemas and modes developed through early family

- Teaching and present imagery

The ground rules for the group

1. **Attendance:** Members are expected to attend all sessions and be on time.
2. **Your Responsibility as a Group Member:** Part of patient responsibility as a group member is to try. The exercises have been developed to help patient learn about their emotions and modes and come to feel that you have some control over them. Members are expected to try to take care of themselves in the session.
3. **Respect for Other Members :**Members are expected to respect other members' physical and emotional space

4. **The Role of the Group Therapists** :All members need to know that the therapists will maintain safety and set limits. At times, this will mean reminding you of the ground rules and asking you to stop a behavior that breaks them.
5. **Confidentiality** :is expected of all members for the privacy and safety of all concerned. Whatever comes up in the group that is of a personal nature about another member cannot be repeated outside the group except with your individual psychotherapist.
6. **Medication/Leaving the Group** :

try not to take sedating PRN medications before the group.

do not leave the group except for real emergencies.

7. **Your Commitment to the Group**: You are asked to consider seriously your commitment to the Schema

Therapy program.

Wrap and feedback

10 min at the end of session is for wrap and taking feedback

Five Schema Therapy Education (STE) Sessions 2-6

At the beginning of ST treatment, patients need to learn about the core concepts of Schema Therapy, such as schemas and modes and how to understand their presenting problems in ST terms. The materials of the ST Education group give patients and therapists the needed exercises and handouts to accomplish this. Generally the ST Education group is the one that begins treatment.

In Session 1 of ST Education patients learn what schemas and modes

are and how they develop. On the handout **Schema Therapy Education Session 1: What Is a Schema?** core childhood needs are identified and patients are encouraged to talk about how these needs were or were not

fulfilled in their childhoods. And how EMS make anxiety

Session 2 focuses on the MCMs, Innate Child Modes and DyPMs.

Modes we will focus on

1. Maladaptive Coping Modes are the survival strategies we used in childhood to protect ourselves from the emotions that go along with hurt, pain, neglect and abuse:

Avoidant Modes

When patients utilize avoidance as a coping style, they try to arrange their lives so that the schema is never activated. They attempt to live without awareness, as though the schema does not exist. They avoid thinking about the schema. They block thoughts and images that are likely to trigger it: When such thoughts or images loom, they distract themselves or put them out of their minds.

Overcompensation Modes

When patients overcompensate, they fight the schema by thinking, feeling, behaving, and relating as though the opposite of the schema were true. They endeavor to be as different as possible from the children they were when the schema was acquired.

Surrender Modes

When patients surrender to a schema, they yield to it. They do not try to

avoid it or fight it. They accept that the schema is true. They feel the emotional pain of the schema directly. They act in ways that confirm the schema. Without realizing what they are doing, they repeat schema-driven patterns so that, as adults, they continue to relive the childhood experiences that created the schema.

2. Child Modes occur in response to our needs not being met:

Vulnerable Child Mode

The mode in which our needs for attachment and safety are not met

The Vulnerable Child is the mode that usually experiences most of the core schemas: It is the Abandoned Child, the Abused Child, the Deprived Child, or the Rejected Child.

Angry/Impulsive Child Mode

The Angry Child is the part that is enraged about unmet emotional needs and that acts in anger without regard to consequences.

The Impulsive/Undisciplined Child expresses emotions, acts on desires, and follows natural inclinations from moment to moment in a reckless manner, without regard to possible consequences for the self or others.

3. Dysfunctional Parent Modes are the internalization of the negative aspects of our childhood caretakers and the feelings that went along with our childhood experience of them.

Punitive Parent Mode: the patient becomes

like the parent who has been internalized. The Punitive Parent punishes one of the child modes for being “bad,”

Demanding Parent Mode: Demanding Parent

continually pushes and pressures the child to meet excessively high standards

Session 3 describes the healthy modes, the HCM and the HAM.

4. Healthy modes are adaptive responses to our adult environment and the ability to access creative joyful aspects of childhood:

Healthy Adult Mode

Happy Child Mode :The Happy Child is one whose core emotional needs are currently met

Session 4 of ST Education describes the main interventions used in ST.

ST integrates cognitive, experiential, and behavioral pattern-breaking work and this integration is one of the unique features of the model.

In this session we explain all techniques for patient

Techniques

Cognitive techniques

1.Cognitive techniques are methods that use our thinking and reasoning

- Pro and Con lists: what are the advantages or benefits and disadvantages

or costs of my present mode?

- What cognitive distortions are operating to maintain my mode

(e.g., all-or-none thinking, catastrophizing, mind-reading)?

- Dialogues between different modes. In groups these dialogues

include therapists and peers playing the role of my mode

behaviors and in individual sessions empty-chair work is used

for me to take all my mode roles.

- Mode flashcards.

- Mode monitoring: recording times when you notice modes

occurring.

2. Experiential techniques are methods that help us to experience our emotions

The Vulnerable Child Mode holds the painful emotions and memories

from situations that we refer to as “roots.” We are asking patient to be aware of the “root” experiences of modes. Patients tend to be familiar with cognitive and behavioral interventions, so the focus here is on the experiential interventions and the work that integrates the three. Work with imagery, including imagery rescripting, is explained and discussed. We use an exercise that demonstrates to patients that they are able to “do imagery” and that it is not a painful or overwhelming experience. This is described in detail in the therapist notes for this session.

Behavioral techniques are methods to break our old habits and develop new

Skills.

We chose one behavior base of modes that patient want change it we ask the patient do Role-play and they do it in real situation and share experience in group

Session 5 focuses on the HCM. Learning about the modes continues,

using games as the vehicle. In this session we try exercise Identified Modes with game .in this session we show some clips and ask patient try to guess modes .we sure patients after this sessions can identified their modes

Discusses anxiety etiology , schema focus anxiety Conceptualization

Wrap and feedback

In the end of session 10 min at the end of session is for wrap and taking feedback

Session 7-13

After the introduction to the concept of modes in the ST Education group, patients must learn to be aware of their own modes in daily life. Awareness has a cognitive component (“What am I thinking?”), an emotional component (“How am I feeling?”), a physiological component (“Can I notice any changes in my body?”), and a behavioral component (“What action(s) do I take?”). The goal of these sessions is to make patients aware that a mode has been triggered before they act. The first five sessions focus on awareness of the cognitive, emotional, and physiological components of modes, their current trigger situations, and the past experiences the mode is linked to.

The two last session focus on the HAM.

Accessing My Healthy Adult Mode focuses on changing mode behaviors. We try to shift the focus now to the adaptive modes a patient has and try to increase

their awareness of the HAM behaviors in their repertoire.

Session 1 focuses on the MCMs. To allow for the considerable differences

that are possible in patient groups, we did not specify which MCM. Patients

can simply write in their mode, referring back to the ST Education material if needed.

Session 2 focuses on the Dysfunctional Parent Modes (Punitive Parent Mode and Demanding Parent Mode).

focuses on the Dysfunctional Parent Modes . We provided two handouts for this session, version a focusing on Punitive Parent Mode and version b focusing on Demanding Parent Mode.

Session 3 focuses on the Vulnerable Child mood

focuses on the VCM. The ST concept of Vulnerable Child varies somewhat, based upon the feelings present and the nature of the missed childhood need that creates the vulnerability.

Session 4 focuses on the Angry Child Modes. For the ACM it is especially helpful if patients learn to be aware of physical signals

focuses on the ACM. For the ACM it is especially helpful if patients learn to be aware of physical signals such as heat waves, hot head, agitation, tense muscles, clenching the jaw, and so on. When a patient is in his/her ACM it is usually difficult to think, so physical signals are particularly helpful to use as awareness cues.

Session 5 focuses on the Happy Child Modes and the handout changes a bit. Patients with psychological difficulties often have difficulty allowing themselves to experience the HCM.

Sessions 6 and 7 focus on the Healthy Adult Modes

Mode Management Sessions 14-19

The goal for coping modes in ST is not to get rid of them completely, but to be aware of when they are triggered and to be able to make a choice about whether the old response will get your need met in the current situation or a different

copying strategy is needed. Session 1 starts with a short introduction on MCMs and ST's goal regarding these modes. Then we employ an experiential exercise that asks patients to imagine a situation in which they hear a message from an MCM (Mode Management

Session 1: Reducing the Power of the Maladaptive Coping Modes (MM

1-MCM1)). This is done to make patients more aware of the mode. We then ask patients what their HAM could say to their MCM in that situation. After that, we work on behavioral and cognitive skills to use with MCMs in the short term.

Session 2: Fighting Your Punitive and Demanding Parent Modes.

focuses on the DyPMs. The same steps are gone through as for the previous modes. The only difference is that this time we ask patients what their HAM can say to their DyPM

Session 3: Caring for Your Vulnerable Child Mode's Feelings of Sadness and Anxiety

focuses on the VCM. Again a short introduction to the VCM is given, distinguishing the sad and the anxious child versions. The experiential exercise of this session asks patients to imagine a VCM situation.

Some patients are likely to choose a sad and others an anxious VCM situation.

Session 4: Managing Your Angry Child Mode

Focuses on the ACM. For this mode it is important to be aware that skills need to fit two goals. A patient in the ACM needs to vent the anger in a non-damaging way, and to learn social competencies or interpersonal skills to be able to better fulfill their needs. The session follows the same procedure. We ask what the ACM needs to hear to feel attended to and heard

Session 5: Developing Your Happy Child Mode

focuses on the HCM and the goal is to develop a short-term plan either to access that mode or to stay in it.

Session 6: Strengthening Your Healthy Adult Mode

focuses on the HAM and the same format is followed. This time we are looking at the triggering of healthy behaviors

the last session(20)

post tests and welcoming

in session 20 all test repeated and if the patient have question or problem it answered and we thank of them for participate in this session

the terms

1. Maladaptive Coping Modes (**MCM**)
2. Dysfunctional Parent (**DyPM**), Punitive Parent (**PPM**), and Demanding Parent (**DePM**) Modes
3. Vulnerable Child Mode (**VCM**)
4. Angry and/or Impulsive Child Modes (**ACM, ICM**)
5. Happy Child Mode (**HCM**)
6. Healthy Adult Mode (**HAM**)
7. Schema Therapy Education (STE)

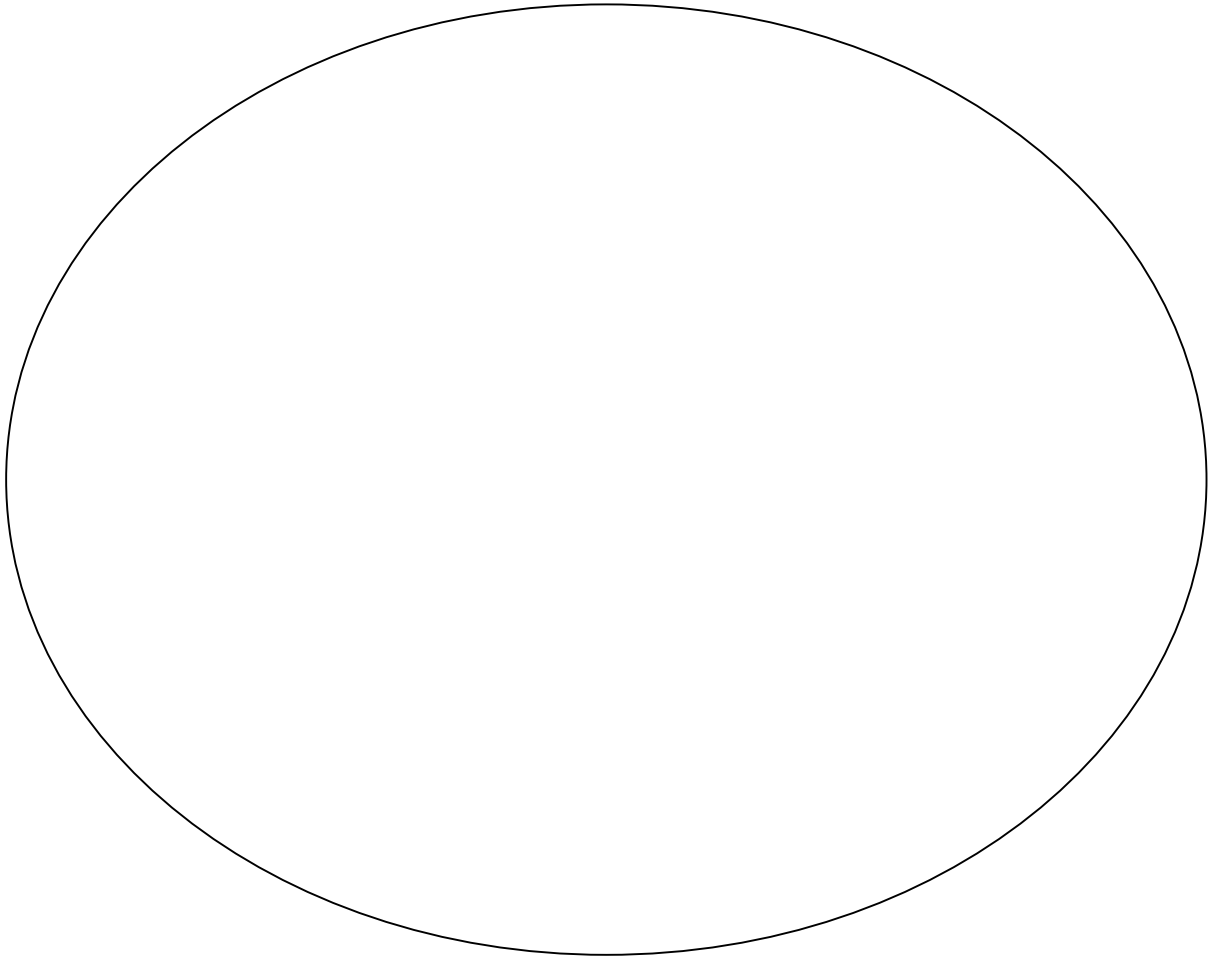
WORK SHEET ABOUT SCHEMA THERAPY

Mode Awareness Assignment(session 7-13)

Day	Situation What situation were you in?	Thoughts	Feelings	Physical	Need	Childhood memories related to situation
Sunday						
Saturday						
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						

Homework

A picture of my mode distribution today: draw lines to represent the approximate size of the six modes or parts of yourself):



The need of children (session 2 STE)

Look at the following list of core child hood needs. childhood how were theses need met in adolescence . (age1-18) for the needs that still exist,how do you try to meet them now?

1.safety and attachment predictability and love

Child hood experience with this need?

Adolescent experience with this need?

How I try to meet this need now?

2. autonomy, competence, identity development

Child hood experience with this need?

Adolescent experience with this need?

How I try to meet this need now?

3. freedom to express your own feelings and needs

Child hood experience with this need?

Adolescent experience with this need?

How I try to meet this need now?

4.freedom to play and be creative

Child hood experience with this need?

Adolescent experience with this need?

How I try to meet this need now?

5.realistic limits and self-control

Child hood experience with this need?

Adolescent experience with this need?

How I try to meet this need now?

Identify Your Mode Experiences (session 3 STE)

If I am in a Maladaptive Coping Mode, I feel (feelings):

If I am in a Maladaptive Coping Mode, I think (thoughts):

Typical actions that I take in the Maladaptive Coping Mode:

Typical situations that trigger the Maladaptive Coping Mode:

Vulnerable Child Mode

If I am in my Vulnerable Child Mode, I feel (feelings):

If I am in my Vulnerable Child Mode, I think (thoughts):

Typical actions that I take in my Vulnerable Child Mode:

Typical situations that trigger my Vulnerable Child Mode:

Angry/Impulsive Child Mode

If I am in my Angry/Impulsive Child Mode, I feel (feelings):

If I am in my Angry/Impulsive Child Mode, I think (thoughts):

Typical actions that I take in my Angry/Impulsive Child Mode:

Typical situations that trigger my Angry/Impulsive Child Mode:

Identify Mode Experiences (session 3 STE)

If I am in my Punitive/Demanding Parent Mode, I feel (feelings):

If I am in my Punitive/Demanding Parent Mode, I think (thoughts):

Typical actions that I take in the Punitive/Demanding Parent Mode:

Typical situations that trigger the Punitive/Demanding Parent Mode:

Healthy Adult Mode

If I am in Healthy Adult Mode, I feel (feelings):

If I am in Healthy Adult Mode, I think (thoughts):

Typical actions that I take in the Healthy Adult Mode:

Typical situations that pull for the Healthy Adult Mode:

Happy Child Mode

If I am in Happy Child Mode, I feel (feelings):

If I am in Happy Child Mode, I think (thoughts):

Typical actions that I take in Happy Child Mode are:

Typical situations that pull for Happy Child Mode:

Session 4 (STE)

Teaching Techniques of Schema Therapy

Cognitive techniques

Experiential techniques :imagery , the Mode Dialogue

Role-Play

Why is that necessary?

What happens in imagery

exercises?

How do imagery exercises work?

Behavioral techniques

Exercise with imagery and role play

Doing in real situation

Session 5 (STE)

Try to identify the modes that characters in the movie clips that we show you are in. If you are not sure, feel free to guess ...

Movie clip

I saw the following behaviors and physical reaction:

I believe the person felt and thought:

The person could be in the following mode:

Session 1 (Mode Management)

Situation	Reducing the Avoidant Protector	Reducing the Compliant Surrendered	Reducing the Over compensator
Your strategy			
Related schema:			
cognitive strategies			
Experiential			

techniques			
behavioral pattern breaking			
Your strategy			

Session 2: Mode Management)

Imagine a situation in which you heard a message from your

Dysfunctional Parent Modes.

What can your Healthy Adult Mode say to your Punitive Parent

Mode?

What can your Healthy Adult mode say to your Demanding

Parent Mode?

Record what you can say or do, when you notice that you are stuck

in your Punitive or Demanding Parent Mode and recognize that

this is not good for you.

Punitive Parent Mode	Demanding Parent Mode
<p>Add more techniques to your plan as you try things and find out what works best for you.</p>	

Session 3 (Mode Management)

Imagine a situation in which you were in the VCM and felt sad.

What has your VCM heard from your therapists that felt comforting?

What could the Good Parent part of your HAM say to

your VCM to comfort him/her?

Imagine a situation in which you were in the VCM and felt anxious or scared.

What has your VCM heard from your therapists that made you feel safe? What could the Good Parent part of your HAM say to your VCM to help him/her feel safe?

It is our goal that your HAM is strengthened to become able to recognize

the VCM's needs and be able to comfort and reassure his/her sadness or anxiety.

	Comforting sadness the Vulnerable Child	Reducing anxiety in the Vulnerable Child
Situation or example		

Your strategy		
cognitive strategies		
experiential techniques		
Behavioral techniques		

Plan with your preferred

strategies and techniques that you can keep with you as a flashcard

For comforting sadness	For reducing anxiety

--	--

Add more techniques to your plan as you try things and find out what works best for you.

--	--

Session 4 (Mode Management)

Imagine a situation in which you are in your Angry Child Mode.

What does your Angry Child Mode need to hear so that he/she feels heard and attended to? How can you say this from your Healthy Adult Mode?

	Managing Your Angry Child Mode
Situation	
cognitive strategies	
Experiential techniques	

behavioral strategies	

Plan with your preferred

strategies and techniques that you can keep with you as a flashcard

Angry Child Mode
Add more techniques to your plan as you try things and find out what works best for you.

Session 5 (Mode Management)

What does your Happy Child Mode enjoy?

What does your Happy Child need to hear from your Healthy Adult Mode so that he/she is able to come out to play and enjoy life?

Situation	
Your strategy	
cognitive strategies	

Experiential techniques	
behavioral strategies	

happy Child Mode
Add more techniques to your plan as you try things and find out

what works best for you.

Seesion 6 (Mode Management)

What can your Healthy Adult Mode say to:

1. Your Maladaptive Coping Modes

2. Your Vulnerable Child Mode

3. Your Angry/Impulsive Child Mode

4. Your Punitive Parent Mode

5. Your Demanding Parent Mode

6. Your Happy Child Mode

Situation	
Your strategy	

cognitive strategies	
Experiential techniques	
behavioral strategies	



École doctorale 139 :
Université des sciences
**Connaissance, langage,
Modélisation**

médicales Ispahan,Iran

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*l'efficacité du schéma thérapeutique sur l'anxiété des malades atteints par le
SEP*

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Résumé de la thèse

La SEP est une maladie inflammatoire chronique auto-immune médiée par les cellules T du système nerveux central (Kumar & Clark's, 2012) avec une variété de symptômes de la maladie qui interfèrent avec les activités quotidiennes et la vie familiale, sociale et professionnelle, perturbent le bien-être émotionnel et réduisent la qualité de vie (Munoz et al.2015). La SEP a une évolution variable et imprévisible, avec des symptômes qui peuvent inclure la faiblesse, la perte visuelle, l'incontinence intestinale et vésicale, la fatigue, les troubles cognitifs et les symptômes de l'humeur. Les patients atteints de SEP semblent présenter une prévalence plus élevée de plusieurs symptômes et troubles psychiatriques. La dépression et l'anxiété, en particulier, ont été associées à une moindre adhésion au traitement, ainsi qu'à un statut fonctionnel et une qualité de vie inférieurs (Chwastiak et al.2007)

Les estimations les plus récentes de la charge mondiale de l'anxiété révèlent que les troubles anxieux expliquent 10 % des années de vie corrigées de l'incapacité pour tous les troubles mentaux, neurologiques et liés à l'utilisation de substances, ce qui les place en deuxième position après la dépression majeure. Malgré leur charge élevée, les troubles anxieux ont la plus faible proportion de traitement professionnel de toutes les classes de troubles mentaux (Sadock, 2017). Cela vaut également pour .l'anxiété chez les patients atteints de SEP

Les troubles anxieux sont fréquents chez les patients atteints de SEP au cours du cycle de vie, avec une prévalence à vie supérieure à 35 % (Korostil et Feinstein, 2007) et des niveaux élevés d'anxiété (69 %) enregistrés dès le début de la maladie (Janssens et al. 2006). Selon Marrie et al.(2015), l'anxiété toucherait plus souvent la population atteinte de SEP que la population générale. L'anxiété peut être une conséquence des dysfonctionnements neurologiques et physiologiques dus à l'évolution de la maladie. Selon Boeschoten et al. (2017), il s'agit également d'une réaction naturelle à l'évolution imprévisible de cette maladie débilite et chronique. L'incapacité liée à la SEP, les niveaux plus élevés de fatigue et les exacerbations de la SEP sont liés à des niveaux d'anxiété plus élevés et peuvent signaler un risque

accru d'aggravation des symptômes d'anxiété au fil du temps dans la dépression des pwMS (Hartoonian et al.2015).

L'anxiété est un facteur prédictif de la dépression chez les personnes atteintes de SEP (Gay, 2010, 2017) et est liée à un plus grand nombre de plaintes somatiques, de dysfonctionnements sociaux et à une augmentation des pensées suicidaires (Korostil, .(2007)

Tous les patients atteints de SEP connaissent l'incertitude. (Alschuler,Beier, 2015). Cependant, il existe une variabilité importante dans la façon dont les individus font face à cette incertitude, et tous ne développent pas des symptômes d'anxiété pathologique, ce qui interroge la raison de cette différence

Malgré sa forte prévalence et ses conséquences néfastes, l'anxiété est fréquemment négligée et insuffisamment traitée. Deux catégories de traitements sont proposées. Les traitements pharmacologiques, qui ont montré une efficacité dans la réduction de l'anxiété et l'amélioration des symptômes mais qui présentent de nombreux effets secondaires tels que l'insomnie, les nausées, l'hyperhidrose, la fatigue, la somnolence, les céphalées, la baisse de la libido, l'anorgasmie et les troubles de l'éjaculation. Ils n'entraînent pas non plus de rémission durable de l'anxiété dans de nombreux cas (Elizabeth et al. 2017) et ne font rien pour traiter la situation de vie ou ses corrélats internes qui ont induit l'état d'anxiété (Sadok, 2015). C'est pourquoi les traitements non-pharmacologiques ont été considérés comme une alternative intéressante. Plusieurs méta-analyses ont examiné l'efficacité des interventions psychologiques dans le traitement de l'anxiété. De nombreuses données démontrent que la psychothérapie, en particulier la TCC, peut être efficace pour un large éventail de problèmes de santé et de santé mentale courants, dont l'anxiété (Hunsley, 2013). Bien que la thérapie cognitivo-comportementale (TCC) soit efficace pour les troubles anxieux, (Bandelow et al. 2015, Olatunji, Cisler, & Deacon, 2010), son efficacité est modeste puisque seulement la moitié environ des personnes souffrant d'anxiété répondent avec succès à la TCC (Hofmann et al. 2012). Les rechutes et les symptômes résiduels sont également fréquents (Martin et al. 2005). Dans le cas d'une maladie chronique comme la SEP, où les sources d'anxiété sont multiples et liées à l'évolution de la maladie, la TCC peut ne pas être la meilleure option pour le traitement de l'anxiété, car elle se concentre sur l'anxiété aiguë et sur des cibles spécifiques, qui

suscitent l'anxiété. Malheureusement, il n'existe pas de documentation sur le traitement de l'anxiété dans la SEP (Turner, 2016). Des recherches (par exemple, Arntz, 1999 ; Kindynis et al. 2013 ; Gewalt, 2017) suggèrent que la thérapie des schémas peut être étendue avec succès aux troubles de l'humeur et de l'anxiété.

La thérapie des schémas peut constituer un traitement alternatif intéressant, car elle est plus souple et permet de traiter plus facilement un large éventail de préoccupations concernant l'évolution des symptômes, le moment et la manière dont ils vont évoluer, Comme l'anxiété n'affecte pas tous les quelle que soit l'évolution de la maladie. pwMS, on peut s'interroger sur les facteurs de personnalité et les schémas inadaptés .comme facteurs sous-jacents communs

Plusieurs études ont montré que les schémas ou domaines de schémas inadaptés précoces sont liés aux symptômes généraux d'anxiété dans les troubles psychiatriques ou dans des échantillons non cliniques. Dans une méta-analyse, 13 des 15 SGE évalués étaient significativement corrélés aux symptômes d'anxiété (Hawke & Provencher, 2011). Il est donc logique de recommander la thérapie par les schémas aux pwMS qui souffrent d'anxiété .

La présente étude tente d'évaluer l'effet de la thérapie des schémas sur l'anxiété chez les patients atteints de SEP.

Sclérose en plaques

La sclérose en plaques (SEP) est une maladie chronique, neurodégénérative et auto-immune qui cible le système (SNC) avec des cicatrices gliotiques, une démyélinisation et une perte axonale. Les facteurs médiateurs de la de la maladie sont des lymphocytes autoréactifs qui dépassent la barrière hémato-encéphalique (BHE) et pénètrent dans l'organisme. cerveau (BBB), pénètrent dans le SNC et créent une inflammation locale (HUANG 2016). Cliniquement, elle se manifestée dans les zones de destruction du cerveau. (Sontheimer, 2015) La nature de la SEP en fait une maladie imprévisible avec une présentation clinique variable ; cependant, les signes et les symptôme dépendent des parties du SNC, notamment le tronc cérébral, les nerfs optiques, le cervelet, et la moelle épinière cervicale. (Karussis, 2017). La SEP présente une variété de symptômes qui interfèrent avec les activités quotidiennes et

la vie familiale, sociale et professionnelle, perturbent le bien-être émotionnel et réduisent la qualité de vie

Inflammation chronique, démyélinisation et dégénérescence neuronale, dommages axonaux. Greenberg et al. 2012) entraînent des pertes de mémoire, une dépression, des problèmes cognitifs et un handicap chez les jeunes adultes (Robert b. et al. 2012). Les manifestations de la SEP varient d'une maladie de l'être

à une maladie rapidement évolutive et invalidante nécessitant une adaptation profonde du mode de vie(Pucak, 2007)..

Parmi les caractéristiques frustrantes de la maladie, on trouve des symptômes tels que "faiblesse, perte visuelle, l'incontinence intestinale et vésicale, les troubles cognitifs et les symptômes de l'humeur, et la fatigue.

Il est possible que ces caractéristiques de la SEP prédisposent les patients atteints de .cette maladie à une plus grande prévalence de certains symptômes psychiatriques prévalence plus élevée de certains symptômes et troubles psychiatriques. En raison l'adhésion des patients au traitement et le statut ,de la dépression et de l'anxiété fonctionnel diminuent ainsi que la qualité de vie(chwastiak, et al. .2007

Anxiété

Par définition, l'anxiété est la réponse à une menace ou à un danger. L'expérience est liée à perception du danger, à la réflexion sur le mal, et aux processus physiologiques d'alarme et d'activation (Moss, 2002).

Il en va de même pour l'anxiété chez les patients atteints de SEP. Les troubles anxieux sont généralement présents chez les patients atteints de SEP tout au long de leur vie, avec une prévalence à vie dépassant 35 % (Korostil, 2002).

prévalence au cours de la vie dépassant 35 % (Korostil et Feinstein, 2007) et des niveaux élevés d'anxiété (69 %) enregistrés dès le début de la maladie.

enregistrés dès le début de la maladie (Janssens et al.2006). Selon Marie et al.

,(2015)il est reconnu que l'anxiété touche plus souvent la population atteinte de SEP que la population générale. générale. En plus de l'aspect psychologique de la SEP,

l'anxiété peut être une conséquence de dysfonctionnements neurologiques et physiologiques dus à la progression de la maladie. Boeschoten et al.

2017) expliquent que l'anxiété est une réaction naturelle à l'évolution imprévisible de cette maladie et de la maladie chronique. Selon Morrow 2018 . L'anxiété est également associée aux pensées suicidaires, pensées et actions autodestructrices chez les PwMS. L'anxiété est également liée à plusieurs symptômes " invisibles " courants chez les SMSP. chez les personnes atteintes de SPM. Comme l'indique la recherche, l'anxiété est liée à des problèmes de sommeil plus graves, et elle est plus répandue que les autres. problèmes de sommeil, et elle est plus répandue chez les personnes atteintes de SP qui ressentent une fatigue liée à la SP (Morrow 2018).

Il existe une relation unique entre l'anxiété et une qualité de vie élevée ou faible. Elle est aussi notamment liée à la dépression (Butler 2016). L'anxiété est un prédicteur de la dépression dans la SEP (Gay, 2010,)

,(2017 est liée à des problèmes somatiques plus robustes, à un dysfonctionnement social plus élevé et à des pensées suicidaires plus profondes (korostil, 2007)

La dépression et l'anxiété sont des réponses normales à des événements imprévisibles, invalidants et chroniques. nature de la SEP. En outre, les patients peuvent être prédisposés à la dépression ou à l'anxiété en raison de nombreux facteurs de risque psychosociaux, tels qu'une capacité d'adaptation ou un soutien social inadéquats, ou par des processus biologiques liés à la SEP, tels que des modifications de la structure du cerveau ou des voies inflammatoires (Boeschot et al 2017).

L'anxiété dans les maladies chroniques

"Si peu de choses peuvent être prédites avec certitude, une chose qui semble certaine est que l'avenir des soins de santé sera dominé par le défi des troubles chroniques complexes"(Nolte et al 2008).

Le mot chronique vient du grec chorons qui signifie pendant une longue période de temps. L'élément du temps est un concept principal dans la description de la maladie chronique. La maladie représente une menace fondamentale pour la survie et le bien-être et peu d'événements de la vie sont plus capables de susciter l'anxiété et la peur (Cameron et Leventhal, 2003). Les stimuli liés à la maladie (symptômes corporels)

suscitent des processus cognitifs et émotionnels pour le traitement de la santé et l'anxiété en parallèle. Une maladie chronique ou un handicap peut constituer une menace en raison de la perte potentielle de fonction, d'indépendance amoureuse et de sécurité financière. La maladie représente une menace fondamentale pour la survie et le bien-être.

La nature de la maladie chronique en fait une source d'anxiété : "de longue durée - souvent avec une longue période de latence et une évolution clinique prolongée ; d'étiologie multifactorielle ; sans remède défini ; changements graduels dans le temps, évolution asynchrone et hétérogénéité de la susceptibilité de la population". (Martin 2007). Selon la théorie de la construction, l'anxiété est ressentie lorsque votre système de construction ne s'applique plus à la situation à laquelle vous êtes confronté. Vous ne pouvez pas interpréter (donner un sens) à ce qui se passe. Se retrouver dans une nouvelle situation entraîne une certaine anxiété. (Laster 2009, Feeist 2002). Selon Kelly (1955), les processus psychologiques d'une personne sont dirigés (ou, selon les termes de Kelly, "canalisés") par la façon dont elle anticipe les événements. Ainsi, il a théorisé l'anxiété comme une prise de conscience que les constructions d'une personne ne l'équipent pas de façon adéquate pour prédire les événements auxquels elle est confrontée. (Norton 2010). Les taux de prévalence des troubles anxieux chez les patients atteints de maladies médicales sont élevés, avec des pourcentages allant jusqu'à 29 % chez les patients épileptiques, 48,9 % chez les patients atteints de sclérose en plaques, 30,1 % chez les patients atteints de la maladie de Parkinson, 30 % chez les patients atteints de maladies cardiovasculaires, 47,0 % chez les patients atteints de diabète sucré, etc. après un accident vasculaire cérébral (AVC) varie entre 20 % et 25 % et reste un problème courant plusieurs années après l'accident. (Burton, 2011).

Les troubles anxieux cooccurrents avec des maladies médicales ont un certain nombre d'implications cliniques, notamment la plus grande sévérité des deux et l'impact négatif sur le résultat du traitement des maladies médicales et des troubles anxieux. Les patients atteints de maladies chroniques déclarent que leur qualité de vie est détériorée par les restrictions physiques, la chronicité, les symptômes et l'escalade des maladies, ainsi que leurs effets sur les activités et les relations quotidiennes (Kristofferzon, 2018 ; Omranifard et al. 2006).

Les recherches sur les maladies chroniques ont conduit à l'élaboration d'un modèle, selon lequel la détresse profuse peut résulter de l'interaction de la nature inhérente avec plusieurs facteurs, tels que les schémas préformés, les expériences de vie antérieures, la difficulté à supporter l'incertitude et les croyances métacognitives concernant l'inquiétude. La détresse qui en résulte peut déclencher des processus cognitifs dont les caractéristiques sont la vigilance, l'inquiétude et l'introspection. Les activités visant à faire face à la reprise du contrôle et à un modèle de vigilance à l'égard des signes de la maladie peuvent accroître l'anxiété, dans le contexte d'un spectre de plusieurs facteurs systémiques qui peuvent soit intensifier soit atténuer l'anxiété (Curren et al., 2017). L'anxiété est une partie invisible mais intégrante de l'expérience quotidienne des patients atteints de maladies chroniques.

L'anxiété est construite sur les ruines de la peur, et la source de la peur dépend de l'affection sous-jacente. La peur de la maladie est due aux attentes du patient quant à l'influence de la douleur sur sa vie personnelle et sociale et à la façon dont la douleur à long terme entraîne un handicap dans les deux cas. La peur de la progression s'est avérée être le pilier des problèmes d'anxiété des patients souffrant de maladies chroniques (Katibi et Moradi, 2018), car environ 50% de ces patients redoutent la perspective d'être handicapés ou estropiés (Herschbach et al., 2005). Les maladies chroniques nécessitent une réponse complexe, sur une période de temps prolongée. Cette réponse doit découler d'un système d'autonomisation soigneusement orchestré à l'aide des données obtenues auprès de plusieurs professionnels de la santé, des médicaments nécessaires et, si nécessaire, des équipements de surveillance. Une maladie organique chronique nécessite généralement un changement dans le mode de vie du patient, rend la vie plus compliquée et souvent moins agréable, et oblige ainsi le patient à s'adonner à moins d'activités et d'intérêts par rapport à sa vie antérieure (Armstrong, 2014). Ces changements sont incompatibles avec l'imagerie et les schémas du patient et peuvent provoquer de l'anxiété. Les maladies chroniques n'affectent pas seulement tous les aspects de la vie du patient ; elles réduisent également la qualité de vie des membres de la famille du patient. Golics et al. (2013) ont mené plusieurs entretiens semi-structurés avec 133 membres de la famille des patients atteints de maladies chroniques issus de 26 domaines médicaux et ont identifié les principales façons dont la vie de la famille peut être affectée par la maladie et les points communs entre toutes les maladies. Les résultats ont été classés dans les catégories suivantes : impact émotionnel (mentionné par 92% des sujets), activités

quotidiennes (91%), relations familiales (69%), sommeil et santé (67%), vacances (62%), implication dans les soins médicaux et soutien apporté aux membres de la famille (61%), travail et études (52%), impact financier (51%), vie sociale (37%) et planification du temps (14%).

L'anxiété dans la SEP

La sclérose en plaques est l'une des causes d'invalidité et la deuxième après les traumatismes. Elle présente un large éventail de symptômes et a des effets sur toutes les parties du corps. Vivre avec la sclérose en plaques a été décrit par le philosophe Toombs (1955) qui a souffert de la sclérose en plaques comme "un trouble global. Un trouble qui incorpore une relation modifiée avec soi-même et les autres, une transformation du monde environnant, une menace pour soi-même et un changement dans sa relation avec les autres (Reenen, et al. 2019). L'une des séquences les plus importantes de ce changement est l'anxiété, environ trois fois supérieure à celle de la population générale (Gascoyne, 2020). Dans l'étude la plus approfondie menée jusqu'en 2012, Jones et al. ont montré que les taux d'anxiété étaient particulièrement élevés, avec plus de la moitié (54,1 %). D'autres recherches ont montré le taux élevé d'anxiété dans la SEP (Boeschoten et al. 2017, Korostil et Feinstein 2007, Janssens et al. 2006) Il existe une relation réciproque entre le trouble anxieux et l'inflammation (Rossi et al. 2017). De plus, des études ont suggéré que "l'atteinte des cortex frontaux et temporaux, le manque de connectivité fonctionnelle entre deux aires préfrontales et l'amygdale joue un rôle important dans la genèse des troubles émotionnels dans la sclérose en plaques." (Passamonti, 2009). Aussi, les événements biologiques, qui ne sont pas moins importants que les facteurs psychosociaux traditionnels. Les chercheurs ont identifié les facteurs affectant l'anxiété chez les patients atteints de SEP. La dépression, les faibles niveaux d'auto-efficacité, le handicap et le stress (Garfield 2012), les facteurs cognitifs et sociaux (Butler 2016), le soutien social (Hanna & Strober, 2020). Ensuite, l'anxiété et la SEP ont une relation réciproque, la SEP peut développer l'anxiété, et l'anxiété influence les rechutes. (Potagas et al. 2008, Hartonian et al. 2015).

L'incertitude est l'un des facteurs de risque de l'anxiété dans la SEP. L'incertitude est le facteur commun des troubles anxieux (Boswell et al. 2013). De plus, l'incertitude est une partie inévitable de l'expérience de la SEP. Ils ne savent jamais s'il y aura une exacerbation, quelle sera la gravité des symptômes ou à quelle vitesse ils

progresseront (Beier 2016). Tous les patients atteints de SEP sont confrontés à l'incertitude. (Alschuler, Beier, 2015).

L'incertitude selon la théorie de Merle Mishel, est un état mental caractéristique pour un être humain, signifiant le sentiment de perte de contrôle, le manque de connaissances sur les changements qui peuvent survenir dans le futur, et le sentiment de doute. Des études antérieures ont identifié les corrélats suivants de l'incertitude : stress et anxiété, perte de contrôle, manque d'information et attente. (Kurta - Nowicka & Jaracz, 2019). La nature imprévisible de la SEP peut être une source d'anxiété

Les patients diagnostiqués avec la SEP ne savent pas quand ils pourraient avoir leur prochaine poussée et n'estiment pas la gravité de la poussée et ses conséquences. En général, il est bien accepté qu'une nouvelle poussée est un signe de la progression de la maladie et a ses complications. Il a également été suggéré que la peur de la progression (dans son terme général et en tant que réponse émotionnelle) est liée à la dépression observée chez les patients atteints de SEP. Dans le même temps, elle n'est pas corrélée avec le sexe, l'âge, la durée de la maladie et le stade de la maladie (Nielsen, Saliger, et al. 2018).

La SEP a des effets considérables sur tous les aspects de la vie, et chacun d'entre eux augmente l'anxiété à lui seul. L'anxiété a été associée à de nombreux autres symptômes " invisibles " courants chez les personnes atteintes de SP. Des études ont révélé que l'anxiété est associée à des problèmes de sommeil plus importants, et qu'il existe une prévalence plus élevée d'anxiété chez les PwMS qui souffrent de fatigue liée à la SEP. (Morrow, 2017). De fortes émotions négatives concernant leur maladie et leur relation interpersonnelle, un impact négatif sur le fonctionnement sexuel (Marita et al. 1996). Malheureusement, la SEP n'a pas seulement un effet sur le patient, mais elle est également source d'anxiété pour les membres de la famille. L'étude de Janssens et al. 2003, 2006 a montré que les partenaires des personnes atteintes de SP ont des niveaux élevés d'anxiété dans la période qui suit le diagnostic. Les résultats ont également montré que 40% des partenaires et 24% des partenaires .avaient des niveaux élevés d'anxiété

Dans l'effet supplémentaire de psychologique et biologique de la SEP, le patient atteint de la SEP éprouve le stress des événements de la vie plus, parce que la SEP est associée à un fardeau substantiel sur la société en raison du coût élevé des traitements disponibles et des perspectives d'emploi plus faibles et le maintien de

l'emploi pour les patients et leurs aidants (Filippi,2018). Des preuves étayant le concept selon lequel les événements de vie stressants peuvent jouer un rôle essentiel dans le déclenchement des poussées de SEP (Mitsonis et al. 2009, Mohr 2007, 2004). L'anxiété peut interférer avec la capacité d'une personne à gérer les maladies et d'autres aspects de la vie quotidienne (Kennedy 2012). En outre, cette situation peut exacerber l'anxiété.

Treatment

Selon Paul Tillich, " la thérapie peut mettre l'anxiété à la bonne place en raison de la structure de la finitude ", lorsque le patient vit avec une maladie chronique et invalidante, à chaque instant il est susceptible d'être confronté à l'anxiété de non-être, ainsi qu'à l'anxiété invalidante, que la source de l'anxiété n'est pas amovible. Nous devons alors nous concentrer sur la gestion de l'anxiété dans la maladie chronique.

Les modèles cognitifs standard se sont révélés efficaces et suffisants pour de nombreux patients souffrant de troubles anxieux. Cependant, un sous-groupe important peut souffrir d'anxiété chronique et de traitement pharmacologique. Ces patients peuvent ne pas progresser au cours de la thérapie cognitive en raison de problèmes liés aux schémas. Si la thérapie cognitivo-comportementale (TCC) est utile pour les troubles anxieux (Bandelow et al., 2015 ; Olatunji, Cisler, & Deacon, 2010), son efficacité est modeste, et la moitié des personnes souffrant d'anxiété répondent avec succès à la TCC. Hofmann, et al. (2018). les rechutes et les symptômes résiduels sont également fréquents (Martin et al. 2015). La pensée peut affecter nos émotions. Mais les changements dans les cognitions peuvent être affectés par les impulsions émotionnelles.

De même que l'évaluation cognitive d'un événement génère une réponse émotionnelle Ainsi, le changement de cognitions ne provoque pas nécessairement un changement d'émotion travaillant parce que les sentiments sont suscités par des processus neuronaux non conscients, et il effet sur les pensées. Les interventions cognitives enseignent le contrôle conscient de l'anxiété et la gestion des émotions sans prêter attention à la cause et à l'émotion en mettant l'accent sur la volonté et la technique de la pratique répétée, mais il semble que les sentiments inconscients et les émotions fondamentales déclenchent l'anxiété, sur la base de réponses conditionnées. Bien que l'anxiété puisse être régulée en se concentrant et en s'apaisant, elle continuera à être déclenchée lorsque des sentiments surgiront. Si l'on n'aide pas le patient à supporter

ces sentiments jusque-là refoulés, il ne pourra pas faire face à son anxiété. Selon le modèle de processus de Gross, toute émotion peut devenir dysrégulée lorsque le patient manque ou n'utilise pas une stratégie de régulation appropriée. (Grecucci et al. 2016).

Un défaut de la TCC comme un traitement de puissance peut-être ne répond pas typiquement aux besoins universels (Rafaeli 2011). Aussi la tendance à "intellectualiser" l'expérience émotionnelle en adoptant une approche plus instructive, par opposition à une approche exploratoire. (Macka et al. 2002). Les schémas, en tant que structures cognitives profondes contenant les règles de base pour sélectionner, filtrer et coder l'information (Restrepo, 2007), peuvent être considérés comme l'une des sources sous-jacentes d'anxiété dans la TCC qui est ignorée. Le fait que les aspects émotionnels et cognitifs de l'expérience traumatique situés dans des systèmes cérébraux différents, peut expliquer pourquoi les schémas ne sont pas modifiables par des méthodes cognitives simples.(young,2013). Les recherches sur l'efficacité et l'efficience des techniques cognitives seules pour les troubles anxieux ont montré des résultats variables. (Kaczurkin,& Foa 2015). Si nous examinons la nature de l'anxiété, les réponses émotionnelles ayant une valeur de survie peuvent se produire sans la participation des systèmes de traitement supérieurs du cerveau - ceux qui sont impliqués dans la pensée, le raisonnement et la conscience. De plus, l'anxiété de trait et l'anxiété d'état sont cartographiées différemment dans le cerveau humain, alors le traitement de l'anxiété évoquée pour protéger l'organisme humain contre une .menace prédatrice doit être multidisciplinaire

Dans le cas d'une maladie chronique comme la SEP, où les sources d'anxiété sont multiples et liées à l'évolution de la maladie, la TCC n'est peut-être pas la meilleure indication pour le traitement de l'anxiété puisqu'elle se concentre sur l'anxiété aiguë et sur des cibles spécifiques qui suscitent l'anxiété. Cependant, dans certains cas comme le problème principal est une maladie chronique et avec la maladie qui menace leur avenir, et l'écart entre ici et maintenant jusqu'à remplissage futur vague souffrent des effets secondaires du médicament, méthode d'administration, pas de guérison définitive, stigmatisation. (cook et al. 2016) et problème co survenu anxiété de handicap et de non-être. Malheureusement, il existe peu de littérature sur les

traitements axés sur l'anxiété dans la SEP (Turner, 2016). Les efforts thérapeutiques peuvent être plus efficaces s'ils visent les mécanismes sous-jacents aux troubles anxieux. Dans cette recherche, l'effet de la thérapie des schémas sur l'anxiété chez un patient atteint de SEP en tant que modèle intégré de traitement a été étudié. Étant donné que les théories et les traitements qui en découlent ont été élaborés dans le monde ordinaire, il faut considérer que les patients atteints de la SEP ont un nouveau monde spécial lié à la maladie, avec des défis, des inquiétudes, des craintes et des espoirs. Par conséquent, aucun traitement spécifique ne peut être considéré comme fiable pour tous, en particulier pour les patients souffrant de cette maladie chronique. De plus, des recherches supplémentaires sont nécessaires pour trouver un traitement plus efficace pour tous. Selon Yalom (1931), comme le travail sur l'émotion n'est pas suffisant, l'intellectualisation et la logique dans le traitement n'est pas suffisante. Alors, peut-être le patient bénéficie de la thérapie des schémas en raison de l'avis à l'émotion et la cognition simultanément .

La méthode

Le traitement a consisté en un essai contrôlé randomisé à bras parallèles comparant un groupe recevant la thérapie par schéma plus la pratique habituelle actuelle avec un groupe recevant uniquement la pratique locale actuelle. L'essai a été réalisé à l'hôpital Kashani.

Nous avons recruté 106 patients ; 53 patients ont été affectés au groupe expérimental et 53 au groupe témoin. Les patients doivent avoir un diagnostic de SEP récurrente-rémittente confirmé cliniquement et une anxiété importante (score >26 à l'échelle BAI), un score à l'échelle Expanded Disability Status Scale < 6, aucune rechute en 3 mois, un âge ≥ 18 ans, un consentement éclairé écrit, la capacité de lire et d'écrire en persan, être capable de suivre le programme proposé, être non hospitalisé et ne pas avoir de problèmes de santé ou psychiatriques importants et de déficience cognitive .

Les individus présentant des déficits cognitifs et des antécédents de troubles psychotiques tels qu'ils ne seraient pas en mesure de s'engager et de bénéficier de ce programme en groupe ont été exclus de l'étude. En effet, si les individus présentaient des déficits cognitifs importants, la plupart du contenu du programme de gestion de l'anxiété ne serait pas approprié. Ont également été exclues de l'étude les personnes ayant eu une rechute au cours des trois derniers mois, car une rechute pourrait entraîner une augmentation temporaire de l'anxiété, les personnes ayant commencé

un traitement par un médicament modificateur de la maladie ou un antidépresseur au cours des trois derniers mois, car l'un des premiers effets secondaires possibles de ces médicaments est l'anxiété, et enfin, les personnes souffrant de troubles psychiatriques .

Les participants ont été identifiés et recrutés par les neurologues des hôpitaux impliqués dans le programme en tant que co-chercheur, lorsqu'ils se sont présentés pour un examen médical .

Après avoir donné leur consentement éclairé, les patients ont été inscrits dans la base de données de l'essai et ont été répartis au hasard entre la thérapie par le schéma et le contrôle à l'aide du logiciel attribué .

L'intervention dans la thérapie des schémas était axée sur la gestion de l'anxiété basée sur l'auto-efficacité et l'autogestion. Elle comprenait 20 séances hebdomadaires de 90 minutes (avec une pause de 15 minutes), avec des activités de devoirs entre les séances. Il était conçu pour des groupes de 8 personnes et était dispensé par deux psychologues. Le programme était standardisé : Des présentations PowerPoint soutenaient chaque session et un manuel détaillé du thérapeute ainsi qu'un cahier d'exercices pour les patients accompagnaient le programme .

Pour le groupe ST, une évaluation a été réalisée sous la forme d'un pré-test, d'un post-test immédiat et d'un post-test différé 6 mois après la fin du programme de thérapie par les schémas et aux mêmes moments pour les personnes du groupe témoin. Les informations sociodémographiques relatives à l'âge, au sexe, au niveau d'éducation, à l'état civil, au nombre d'enfants et au statut professionnel ainsi que les données médicales comprenant la date du diagnostic, le type de maladie, le niveau de handicap (EDSS, Kurtzke, 1983) et les informations sur les rechutes et les traitements ont été évaluées. Le critère principal était l'impact de la thérapie par schéma sur l'anxiété évaluée par le BAI et le niveau de cortisol 12 mois après le début du programme. Les critères secondaires comprenaient l'impact sur les dimensions psychologiques évaluées par l'Hospital Anxiety and Depression Scale (HADS), l'intensité de la fatigue évaluée par la Fatigue Severity Scale (FSS), la qualité du sommeil évaluée par le Pittsburgh Sleep Quality Index (PSI 1.0), la dépression mesurée par le BDI et la qualité de vie évaluée par le MSIS29.

Le critère de mesure principal utilisé dans cette étude était l'échelle d'anxiété de l'hôpital et de dépression d'anxiété (HADS-A) et l'IAB (inventaire d'anxiété de Beck). Les objectifs secondaires ont été mesurés par l'IDB (inventaire de dépression de Beck), l'échelle d'impact de la sclérose en plaques - 29 (MSIS), l'échelle de la gravité de la fatigue (FSS), l'indice de la qualité du sommeil de Pittsburg (IQPS) et l'EDSS.

Les résultats:

Les statistiques descriptives comprenant la moyenne et l'écart-type pour les variables numériques ainsi que le nombre (pourcentage) pour les variables de classe sont présentées dans le tableau 1. Selon les résultats, les femmes et les hommes représentaient respectivement 76,4% et 23,6% de la population de l'échantillon. L'âge moyen des participants était de 36,22 ans. La classification des participants en fonction de leur niveau d'éducation était la suivante : 9,4 % avaient un diplôme, 75,5 % une licence, 14,2 % une maîtrise et 0,9 % un doctorat. Parmi les participants, 17,9 % étaient célibataires et 82,1 % étaient mariés. Le score EDSS moyen était de 1,35.

Les résultats de l'analyse à mesures répétées (ANOVA) ont mis en évidence des différences significatives dans l'anxiété et la dépression après la thérapie du schéma. De plus, il n'y avait pas de relation significative entre la thérapie du schéma et la qualité de vie, la qualité du sommeil et la fatigue. Cependant, l'absence de changement dans l'EDSS peut être considérée comme un bon résultat.

Discussion

L'objectif de cette étude est d'examiner les effets de la thérapie par les schémas sur l'anxiété chez les patients atteints de SEP. Les résultats ont montré l'effet significatif de la thérapie des schémas sur l'anxiété, la dépression et la modification de certains schémas. Peut-être que la thérapie par les schémas guérit en quelque sorte l'anxiété découlant du stade de développement, comme l'anxiété de se fragmenter parce que les besoins ne sont pas satisfaits, l'échec amoureux, la peur de perdre un objet aimé, le manque d'approbation ou le sentiment de culpabilité. Il semble que l'estompement des schémas d'assujettissement et d'abnégation modifie le locus de contrôle et la relation interpersonnelle et entraîne une diminution de l'anxiété. Le patient apprend à ne pas inhiber ses sentiments et à transformer une relation unilatérale en une relation

souhaitable en réduisant sa responsabilité envers les autres et en accordant plus d'attention à ses propres besoins, et à surmonter les sentiments de solitude et d'impuissance, que Fromm considérait comme la principale source d'anxiété. De plus, les résultats n'ont montré aucun effet significatif sur la fatigue, la qualité de vie et la qualité du sommeil. D'autres recherches menées ont montré que d'autres traitements avaient une influence sur l'anxiété. Les facteurs associés à la SEP tels que la dysfonction sexuelle avec une prévalence estimée de 40% à 80% chez les femmes et de 50% à 90% chez les hommes (Domingo et al., 2018), la douleur (avec une prévalence de 50-86%, (Murphy et al. 2017), la dysfonction vésicale chez 75% des patients (Das Gupta et al. 2003) sont un facteur important qui affecte le sommeil, la qualité de vie, et la fatigue de façon dramatique. De même, les événements mineurs indésirables, les tracas et le stress quotidien majeur prédisent de manière significative les symptômes psychologiques et ont un effet réciproque sur la psychothérapie. Cependant, lorsqu'une personne a une phobie des chiens, nous pouvons l'interpréter en nous basant sur toutes les théories. Le traitement d'une personne ayant une phobie du chien par des théories psychologiques est une chose, l'anxiété et la peur chez un patient qui souffre d'une maladie chronique avec des caractéristiques invalidantes est un cheval de couleur différente. Il semble que dans les maladies chroniques comme la SEP, qui présente un potentiel de récurrence et de rechute, en raison de l'évolution imprévisible de la SEP et des rechutes, les patients atteints de la SEP rémittente (RRMS) souffrent du stress de l'anticipation de la rechute et de ses conséquences imprévisibles. Ils ne disposent d'aucune information concernant le moment, la gravité et les conséquences de leur prochaine poussée. Ce handicap est directement lié au niveau d'incertitude concernant les événements futurs, et il propulse ces patients vers la peur chronique ou, comme on pourrait l'appeler, la peur de la progression ainsi que l'anxiété en réduisant leur possibilité de se préparer efficacement pour l'avenir (Khatibi, 2020). Par conséquent, le patient atteint de SEP ressent simultanément la peur et l'anxiété. Les patients ressentent différents niveaux d'anxiété au niveau cognitif et émotionnel. En expliquant les raisons des comportements et des événements, des émotions et de la formation de la cognition, la thérapie des schémas change certains rôles dans la vie des patients. Bien que les patients ne puissent pas supprimer la source de l'anxiété, ils peuvent la contrôler. La thérapie par les schémas avec la conscience de soi est une occasion d'identifier les schémas, de les surmonter et, finalement, d'être responsable de soi. Selon l'existentialisme, la prise de conscience

de la raison du comportement entraîne un sentiment de contrôle et de domination et peut réduire l'anxiété et la peur de la mort. Le sentiment de pouvoir et de contrôle qui découle de la prise de conscience est efficace, même dans la situation existante. Le ST augmente la perspicacité et la conscience et crée un sentiment de contrôle, mais il est très important de créer une perspective de vie et un sens à la vie. Comme le dit Pole Tillich, "la seule chose que nous pouvons faire contre l'anxiété est de la mettre à la bonne place. Nous pouvons mettre l'anxiété à la bonne place et encourager les patients à avoir le courage d'être dans leur vie. Le Courage d'Être est le pouvoir de l'homme de s'affirmer en dépit des anxiétés dominantes qu'il rencontre dans son .(existence contemporaine, et de gagner le pouvoir de la vie" (Tillich, 1952

Dans l'ensemble, cette recherche comporte des points forts, mais aussi des points faibles et des limites. Selon les critères d'Ingram présentés par Hayes et Scott (2000), la stabilité et l'acceptabilité sont les points forts de la recherche. Dans la présente étude, la réduction de l'anxiété et de la dépression a été maintenue après six mois. En outre, le taux d'attrition de 10 % montre que les patients étaient intéressés par le traitement. L'absence de sécurité était l'une des faiblesses car elle entraînait des débats et des conflits au sein de la famille. Une autre que je peux évoquer est le manque de généralité du changement. Le peu de temps et la tendance des patients à traiter l'assujettissement et l'abnégation ne laissent pas assez de temps pour d'autres schémas. Un autre point à prendre en compte est que chez les personnes souffrant d'affections médicales, il est souvent difficile de différencier clairement les symptômes psychologiques de ceux attribuables au physique. Il existe peu de recherches sur la thérapie par les schémas dans les maladies chroniques .

Ces dernières années, quelques études intéressantes ont été menées. Compte tenu des limites de la présente étude, les résultats suggèrent un certain nombre de directions pour les recherches futures. Tout d'abord, la formation des groupes de traitement n'a pas été faite de manière aléatoire et les patients ont choisi leur groupe en fonction du temps, de l'âge et de l'état civil, et la relation stable entre les membres des groupes peut avoir affecté les résultats de l'étude. L'intérêt pour le type de traitement et la disponibilité du thérapeute pendant le suivi doivent être considérés comme une source de soutien qui peut affecter les résultats. Deuxièmement, la durée du suivi a été prolongée dans les deux groupes, surtout dans le groupe témoin.

Troisièmement, jusqu'à présent, il n'y a pas eu de recherche sur la thérapie par les schémas pour les patients atteints de SEP. Par conséquent, l'accès à la littérature était limité. Quatrièmement, pendant les périodes de suivi, des facteurs de confusion peuvent avoir menacé la validité de nos estimations de l'effet à long terme en raison des variables intervenantes. Par exemple, pendant que cette recherche était menée, les gens vivaient une crise sociale, économique et politique en Iran. En outre, en plus de toutes ces questions sociales, les patients avaient des problèmes liés à la maladie, notamment l'approvisionnement en médicaments pour le traitement et, parfois, ils avaient des problèmes d'accès aux médicaments contre la SEP. Il est clair que "les problèmes de santé mentale sont liés aux privations, à la pauvreté, aux inégalités et à d'autres déterminants sociaux et économiques de la santé. Les crises économiques sont donc des périodes à haut risque pour le bien-être mental de la population, des personnes touchées et de leurs familles" (OMS, 2007). Cependant, au niveau clinique, les patients peuvent bénéficier de la thérapie des schémas pour réduire l'anxiété et la dépression. Le traitement est susceptible d'avoir des résultats différents dans les communautés dont le niveau de bien-être économique et social est plus élevé. Il est donc nécessaire de mener d'autres études sur des symptômes importants comme la douleur, la vessie et les dysfonctionnements sexuels dans d'autres cultures. Par ailleurs, il est préférable d'ajouter les psychothérapies existentielles à la thérapie des schémas et de considérer et étudier l'anxiété liée au handicap comme un concept distinct.

