Women and Depression

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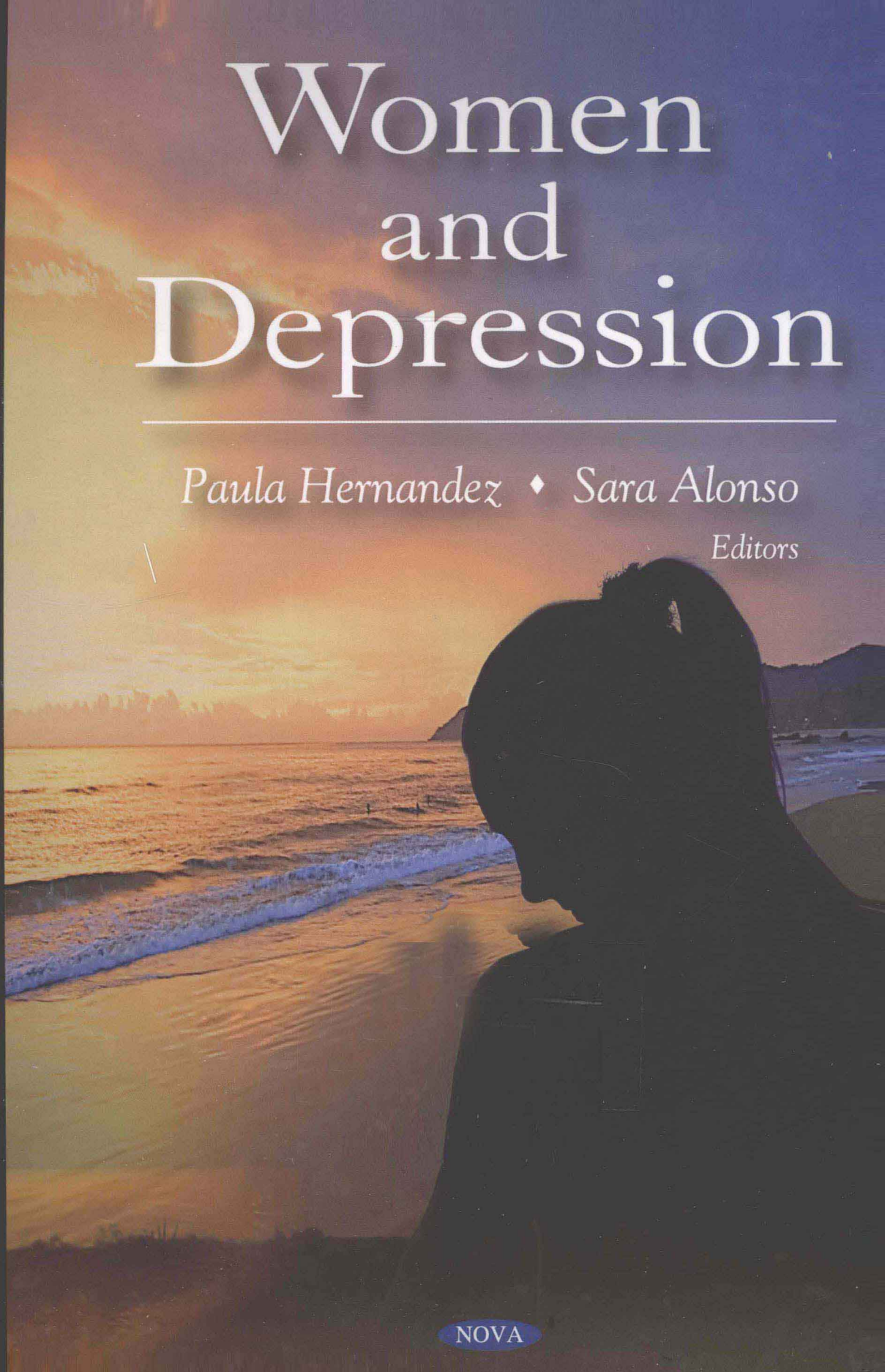
Editors



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WOMEN AND DEPRESSION

Preface

Depression is a serious medical illness affecting 5 to 8 percent of the adult population in a given year. Unlike normal emotional experiences of sadness, loss, or passing mood states, major depression is persistent and can significantly interfere with an individual's thoughts, behavior, mood, activity, and physical health. Among all medical illnesses, major depression is the leading cause of disability in the U.S. and many other developed countries.

Depression occurs twice as frequently in women as in men, for reasons that are not fully understood. More than half of those who experience a single episode of depression will continue to have episodes that occur as frequently as once or even twice a year. Without treatment, the frequency of depressive illness as well as the severity of symptoms tends to increase over time. Left untreated, depression can lead to suicide. This new book presents the latest research in the field.

Short Communication - *Background*: Smoking rates are elevated in psychiatric samples in general, rendering smoking a significant concern in this population. Moreover, women with psychiatric illness may be more likely to smoke cigarettes compared to men, in contrast with the higher rate of smoking for men in the general population. To extend our understanding of smoking in individuals with psychiatric illness, the authors studied a sample of patients seeking treatment, most of whom suffered from Major Depressive Disorder (MDD), assessing smoking history and, among current smokers, willingness to be contacted about a smoking cessation program.

Methods. The authors conducted a retrospective study of 129 outpatients (88 women, 41 men). Seventy-eight percent of the sample was diagnosed as having MDD (53% with MDD only, 15% with comorbid MDD and anxiety disorder, and 10% with comorbid MDD and dysthymia). Fourteen percent were diagnosed with an anxiety disorder only, and the remainder had diagnoses such as Bipolar Disorder, Mood Disorder NOS, etc.

Results: Overall, 33% of our sample were current smokers and 12% were ex-smokers. Current smokers had completed significantly fewer years of formal education than the never smokers. Smoking rate was elevated in female patients (34%) compared to women in the community (16%), as well as a lesser increase in smoking rate in male patients (29%) compared to men in the community (20%). Seventeen percent of men and 10% of women were former smokers (ns), suggesting that nearly half of all psychiatric patients may smoke at one time or another and yielding a low quit ratio (percent of eversmokers who have quit) of

28%. Thirty-three percent of current smokers were willing to be contacted about a smoking cessation program, not differing by sex. Among current smokers, those willing to be contacted about a smoking cessation program had smoked more years, were older, had a higher Heaviness of Smoking Index, and had expressed a greater desire to quit when compared to current smokers who were unwilling to be contacted about a smoking cessation program.

Conclusions: Smoking poses a significant health risk, and the increased prevalence of smoking in psychiatric samples, combined with a decreased likelihood of quitting, results in even greater risks among those with psychiatric illness. A third of women in our sample were current smokers, placing this population at particular risk. The authors encourage endeavors to better understand differential mechanisms behind higher smoking rates in psychiatric samples, particularly in women, to develop more specific tools for smoking cessation programs. On a promising note, about 33% of those who currently smoke were willing to be contacted about a smoking cessation program, an ideal target group for such programs.

Chapter 1 - Dyslexia is a life-long condition (without a known cure), affecting approximately 10-15% of the population. It is medical in origin but educational in treatment. It affects the ability to communicate (e.g. writing, spelling), compute mathematical concepts (e.g. algebra) and other aspects of life which require using short-term memory and co-ordination.

Those with dyslexia who are not assessed/treated in early childhood are highly susceptible to emotional manifestations due to low self-esteem and low perceived ability caused by peers, parents and educators who misread their learning difficulties for laziness and lack of motivation. In fact ignoring or misreading a child's learning disability is a form of abuse which reaches far into today's educational systems. Gender has yet to be a major focus in the study of dyslexia, however there is growing evidence that it is an important factor in understanding why some dyslexics are resilient and others are affected emotionally.

There are three research projects included in this chapter. These aim to build personality profiles for dyslexic males and females according to the severity of their dyslexia. Depression and withdrawal emerge as key personality traits amongst these groups. A second study using this same data investigates profiles to successful (degree educated) dyslexics and how personality differences emerge amongst those who are diagnosed and undiagnosed. Diagnosis, gaining remedial help or support, meant that such individuals were more optimistic and did not doubt past events, compared to those who were undiagnosed and went through life thinking something was wrong but were unable to pinpoint the problem. It may also be the case that their coping strategies were successful enough to mean that their difficulties were not highlighted, however the emotional cost was great.

Lastly there was an interview study for dyslexics who were also diagnosed with clinical depression. Strong gender differences were identified with females using more withdrawal and self-blame than males who tend to use helplessness. Their life stories indicate neglect by teachers and parents which lead them to use perfectionism as a defence mechanism. Their difficulties led a number of them to contemplate suicide as there were no other perceived options available to them to deal with the anxiety from having an invisible learning disorder.

Chapter 2 - In the preceding chapter (Alexander-Passe, 2008) gave an understanding of what dyslexia is and how it affects both adults and children in settings from school to the

workplace. Both the empirical and the three research studies highlighted the emotional manifestations that come from having a learning disability, such as dyslexia. This chapter continues the investigation from first reviewing empirical evidence concerning stress, coping, avoidance and Defence mechanisms before suggesting a hypothetical model of 'Dyslexia Defence Mechanisms (DDMs)'. Such a model is based on the work of Vaillant (1992) Messiner (1980) but as dyslexics are a unique population, several aspects of normal Defence mechanisms are inappropriate. For example, the DDMs are split in Emotional and Behavioural, being predominately split by gender (Females-Emotional and Males-Behavioural). Avoidance of writing long words has been identified as a key coping strategy before DDMs are chosen, teachers, parents and practioneers should identify this as the start of a long negative path for children at school. Teachers are advised that when children fail in more tasks than they succeed in, such children will perceive learning and school as threats to their self-esteem and self-concept. They will seek out ways to protect themselves and Defence mechanisms may explain what mechanisms are chosen. Defence mechanisms have never been investigated with dyslexic populations, however reviewing empirical data they seem ideal candidates for such investigation.

Chapter 3 - The results from epidemiological studies suggest that adolescence is a critical period for understanding the development of depression for two reasons (Avenevoli, Knight, Kessler, & Merikangas, 2007). First, although during childhood, sex differences in depression are not reliably found, during the transition from early to middle adolescence (i.e., ages 12-15) sex differences emerge with girls reporting higher levels of both depressive symptoms (Angold, Erkanli, Silberg, Eaves, & Costello 2002; Twenge & Nolen-Hoeksema, 2002) and depressive disorders (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Hankin, Abramson, Moffitt, Silva, McGee, & Angell, 1998) than boys. Second, during the transition from middle to late adolescence, there is a dramatic, six-fold increase in depression rates (Hankin et al., 1998). Prevalence rates remain at similarly high levels throughout adulthood with adult depression typically being preceded by adolescent depression (Kim-Cohen, Caspi, & Moffitt, 2003). Although it is well established that both of these epidemiological shifts occur during adolescence, little research has examined the factors that underlie them. In the current chapter, the authors will examine both the emergence of sex differences in depression and the surge in depression rates in adolescence from the perspective of cognitive vulnerability-stress theories of depression.

Chapter 4 - *Background*: Differences in emotion processing during Major Depressive Disorder (MDD) have not been well explored as a potential explanation for age and gender disparities in rates of depression and depressive symptoms. Early studies by our group demonstrated that those with MDD underperform in emotion processing of faces, although recently the authors showed a selective decrement in younger women with MDD. The authors now extend this study of gender differences in facial emotion processing during MDD to the full age spectrum. The authors assessed emotion processing performance using posed facial emotional expressions in those with early (age 18- 35) and middle/ late (age 36-73) MDD as well as in women and men to determine if there was differential impact of MDD in these four groups. The authors hypothesized that knowledge about gender, age, and emotion processing performance differences might increase understanding of risk for and expression of MDD in women and in those with later onset MDD.

Methods: Participants included 161 individuals in younger age groups (YA; 123 women, 38 men) and 150 individuals in middle/ elder age groups (MEA; 100 women, 50 men) diagnosed with MDD, as well as 97 healthy control YAs (60 women, 37 men) and 35 healthy controls MEAs (24 women, 11 men). A conservative age classification $\leq$ age 35 was used to separate YAs from MEAs in order to be to be confident that potential causes of middle-late onset MDD (e.g., cardiovascular) were less likely to be present in the younger MDD groups.

Results: There was an interaction between age, gender, and MDD status for response time, with slower response times in YA MDD patients compared to their age-matched control groups. This effect of slower response time was not detected in the comparisons between MEAs with and without MDD. MEA women, YA women, and MEA men with MDD made significantly more errors than did their same-age, same-gender control counterparts ($ps < .05$), whereas YA men with MDD performed similarly to same-age control men ($p > .26$). Further, although MEA women and men with MDD performed more poorly in facial perception relative to same age control cohorts, MEA men with late onset MDD performed worse than MEA men with early onset MDD, in contrast to no difference between performance of MEA women with late and early onset MDD.

Conclusions: These findings suggest that YA men with MDD may have a different neurobiological etiology of depression compared to YA women. In contrast, MEA men and all women with MDD appear to have similar difficulties with emotion processing, suggesting overlap in brain regions affected, albeit likely through different mechanisms. Notably, MEA men with late onset MDD appear to have a greater burden of emotion processing decrement compared to other depressed groups.

Chapter 5- Literature on psychiatric comorbidities in neurologic diseases (including stroke, multiple sclerosis, Parkinson disease, Alzheimer dementia) are generally consistent about the prevalence of female gender in depression in most of these illnesses. These data are in agreement with those of functional depression, in which female preponderance in depression rates appears to be a consistent finding. In the literature, several possible explanations have been suggested and investigated, such as biological, social and psychological factors. However, existing data on the role of gender in depression in neurological comorbidities is, to our knowledge, only exhaustive for post-stroke depression (PSD) and less exhaustive for other diseases.

Chapter 6- The Latino/Hispanic population is the fastest growing ethnic group in the United States. The proportion of Latino/Hispanics in the population grew by 14.2% in fourteen years, from 6.4% in 1980 (14.6 million) to an estimated 12.5% (35.5 million) in 2001(with a 58% increase during the 90's). These numbers do not include illegal migrants, a number that is difficult to establish. It is well known that most of the migrating populations that arrive in the USA are of Latino/Hispanic origin, being Mexican Americans the largest subgroup, Puerto Ricans the second, and Cuban Americans the third largest subgroup. Some of them leave their country of origin to pursue the "American dream", which for many of them is synonymous to having freedom, better educational and economic opportunities, and prosperity. Others have to do so because of threats or political issues.

A recent trend is the fact that more women have been entering the migration stream, which had been primarily male. Latino/Hispanic women, especially migrants, have been identified to be at a higher risk for mental health problems due to the myriad of acculturation

issues and economic hardships they may suffer with the migration process. Frequently, Latino/Hispanics are identified as a high-risk group for serious physical and mental health conditions, particularly depression, anxiety, substance abuse, cardiovascular disease and diabetes. These problems tend to be more prevalent among women. Furthermore, research has demonstrated that Latino/Hispanic ethnicity emerged as a risk factor for depressive symptoms, mainly among disadvantaged subgroups experiencing serious hardship (i.e., higher poverty) in the context of their historical, political, and societal reality. Given that by 2020 depression is expected to be the second largest health care problem after heart disease worldwide, the scope of this problem will be enormous among Latino/Hispanic women.

There is a need for continued research of the various factors associated with the depression phenomena in Latino/Hispanic women. Given that Latino/Hispanic women are not a homogenous group, the design and development of linguistically and culturally sensitive and effective interventions that may serve for the prevention of depression in that group needs to be considered in a more specific manner.

It is crucial to pay attention to the significant differences between the Latino/Hispanic subpopulations. Programs intended to reduce feelings of isolation, lack of support, power, language barriers and economic hardship need to be developed by private and public agencies. This can include activities to enhance assertiveness and communication skills, empowerment, and financial independence in order to diminish risk factors for the development of depression in Latino/Hispanic women.

For being effective, interventions need to have a grassroots origin. Interventions that address issues in a more sensitive way, taking into consideration cultural factors, will be more readily accepted by Latino/Hispanic women and will reduce the resistance these women may have and will give them a higher probability of improving their quality of life and adaptation to the host society.

Chapter 7 - *Background:* There is large evidence that major depressive disorder (MDD) has prevalence rates almost twice as high in females as in men. However, few studies have investigated in MDD the regional cerebral blood flow (rCBF) differences between genders. The aim of the study was to identify the influence of gender on the rCBF distribution in a group of depressed patients. This was performed by means of Volume of Interest (VOI) analysis and Principal Component Analysis (PCA), this latter exploring functional brain connectivity and transforming a number of correlated variables by clustering them into functionally uncorrelated factors

Methods: A group of 76 major depressed patients (36 males and 40 females) were investigated by ^{99m}Tc-HMPAO and SPECT. Analysis of covariance (ANCOVA) and PCA were performed on 54 VOIs. Neuropsychiatric tests (MADRS, SCID, CFQ, KSP) were also carried out to assess disease severity without finding any gender differences.

Results: VOIs analysis identified in females as compared to males a significantly higher rCBF distribution ($F(1,73)=10.875$; $p=0.002$). A significant VOI*Gender interaction was also found ($F(26,1898)=2.180$; $p=0.001$) revealing that 10 regions belonging to the frontal, temporal, parietal and occipital cortex were particularly involved in gender differences. An overall effect of gender was also found for PCA ($F(1,73)=8.814$; $p=0.004$). The significant PCs*Gender interaction ($F(12,876)=3.258$; $p<0.000$) revealed lower rCBF distribution in males as compared to females in 6 PCs. Such PCs, grouped brain regions belonging to

parietal-limbic cortex (PC3; p=0.033), parieto-temporo-occipital cortex (PCs 8 and 9; p=0.001), fronto-parietal cortex (PC10; p=0.017), fronto-temporal cortex (PC12; p=0.001) and hippocampi (PC 13; p=0.017). Age related hippocampal differences were found in PC13 in female only.

Conclusion: PC8 grouped two areas involved in linguistic processing, the angular and the supramarginal gyrus of the left hemispheres for which gender differences are widely accepted. PC9 with the right angular gyrus was also likely to show rCBF differences since females are known to be more bilaterally organized. Gender differences in hippocampi confirmed previous findings. However, medial prefrontal cortex (anterior cingulate) bilaterally and right dorsolateral prefrontal cortex, regions known from the existing literature to be implicated in MDD, were grouped by PCA into different PCs (PC1 and PC4, respectively) but did not show any sex difference speaking against specific gender related rCBF changes in major depression.

PCA grouping functionally connected brain regions increased the depth of the analysis yielding more information on the processes underlying perfusion distribution measurements in MDD.

Chapter 8 - Depression is the most common psychiatric disorder worldwide. No single antidepressant has been shown to be more effective than any other in lifting depression, and the effectiveness of any particular antidepressant in an individual is difficult to predict. Thus, doctors must prescribe antidepressants based on trial and error. Single nucleotide polymorphisms (SNPs) can be used in clinical association studies to determine the contribution of genes to drug efficacy. In addition, some findings suggest that women respond differently to antidepressant treatment than men. In this chapter, the authors review gender differences, pharmacogenomics, and gene-gender interactions with the drug efficacy of antidepressants in depression. First, the authors survey the SNPs and genes identified as genetic markers that are correlated and associated with the drug efficacy of antidepressants. Evidence is accumulating to suggest that the efficacy of antidepressants results from the combined effects of a number of genetic variants, such as SNPs. Although there are not enough data currently available to prove this hypothesis, more and more genetic variants associated with antidepressant response are being discovered. Secondly, the authors investigate the recent reports that antidepressants may work somewhat differently in men and women. Some theoretical reasons have been suggested for suspecting that gender differences in antidepressant response exist. Thirdly, the authors study gender-specific SNP and gene contributions to antidepressant treatment response and demonstrate pattern recognition approaches to evaluate the epistasis among genes and gender. These techniques may provide tools for clinical association studies and help find genes and SNPs involved in responses to therapeutic drugs or adverse drug reactions.

Chapter 9 - High rates of depression are often reported among women with HIV (Cook et al. 2002). Factors contributing to depression among persons with HIV have been identified as greater, age, physical symptoms, comorbid health conditions, loneliness, substance abuse, stigma, and other stressors (Jones et al., 2003; Heckman et al., 2001; Oursler et al, 2006; Rabkin et al., 2004; Riley et al., 2003; Vance, 2006). Factors mitigating depression in this population include effective coping strategies, social support, and spirituality (Coleman et al., 2006; Heckman et al., 2001; Heckman et al., 2002). However, despite the growing aging

population living with HIV, the impact of depression on older women with HIV has received limited attention in the research literature. The success of antiretroviral therapy has moved HIV into the category of chronic disease. In New York City, the epicenter of HIV in the United States, 33% of the 100,000 people living with this virus are now over the age of 50 (New York City Department of Health and Mental Hygiene, 2007). This pattern is seen throughout the United States, where it is expected that one-half of those with HIV will be 50 years or older by 2015. This graying population of persons with HIV will confront the challenges of physical and mental health comorbidities, coupled with the panoply of psychosocial challenges that are associated with aging. The present study is one of the first to examine the effects of stressors on depressive symptoms among a large sample of women 50 years and older living with HIV.

The sample consisted of 264 women, 50 to 76 years old (*M* age = 55 years). Approximately one-third had post-high school educations, 58% were Black, 34% were Hispanic, and 5% were White. To examine the impact of health-related and psychosocial stressors, the conceptual model employed for analysis was a modified Stress and Coping Model (Folkman and Lazarus, 1984). The multivariate model explained 48% of the variance in depressive symptoms. The number of comorbid conditions and the need for assistance as a result of HIV infection were positively related to greater depressive symptoms, as were both loneliness and stigma. Higher cognitive functioning and spirituality were significantly related to lower levels of depression. These findings support the need for interventions to address depression, health, and psychosocial stressors among older women with HIV. In addition, programs to increase access to spiritual resources for older women with HIV may help to ameliorate depression in this population.

Chapter 10 - Between 11 and 30% of older people worldwide suffer from depressive symptoms, and approximately 17 to 35% of depressed patients suffer cognitive loss. Community samples show a doubling of comorbid mood disorder and cognitive deficits every 5 years after the age of 70 until by age 85, approximately 25% of older individuals demonstrate both conditions. Women have almost double the risk of men for suffering these comorbid conditions before the age of 80.

Research on the biological and physiological changes associated with unipolar major depression center on the prefrontal lobes and the fronto-striatal neural loops that are associated with emotional responsiveness, cognition, and behavior. With the advent of new advances in neuroimaging techniques, researchers can explore the anatomical, biochemical and physiological substrates of late-life depression. Imaging studies report that some regions within the prefrontal cortex are selectively reduced in volume during late-life depression. Stable relationships between cognition and brain biochemicals that are seen in healthy elderly are disturbed in depressed individuals, and myelination of white matter tracts appears compromised. This chapter will discuss the 1) diagnosis of late-life depression and how late-onset differs from early-onset depression, 2) medical context in which late-life depression often occurs, 3) neurocognitive profiles of depressed patients, 4) associated anatomic and physiologic brain abnormalities, 5) putative links between late-life depression and the emergence of dementing syndromes, and 6) effects of pharmacological and psychotherapeutic intervention. Knowledge about the characteristics of late-life depression and successful

interventions can mitigate and sometimes reverse the onset of a downward spiral in functioning and physical health that frequently accompanies late-life mood disorders.

Chapter 11 - Diabetes and depression are both significant public health concerns for women. Depression is a risk factor for incident type 2 diabetes, and it also increases risk for poor diabetes outcomes. Research linking depression to health risks is limited in several important ways, particularly by common practices employed to measure depression. In this chapter the authors review evidence linking depression and diabetes in women, and describe limitations of the extant literature. The authors then review our own work that begins to address these limitations. The authors conclude with a review of the treatment literature and recommendations for addressing depression in women with diabetes.

Chapter 12 - The psychological and physical challenges associated with cancer often result in considerable distress and symptoms of depression. Major Depression is a significant mental health concern among patients with cancer, as it affects 20 – 25% of all patients diagnosed with cancer. This chapter examines the factors that both increase and decrease the risk of developing depression following a cancer diagnosis. Cancer related variables including the type of cancer, stage of disease, and level of pain and physical impairment are examined as they relate to depression in women with cancer. Other risk factors including age, prior history of depression, and coping style are also examined. In addition, spirituality and religiosity, as well as level and quality of social support are discussed as buffering factors against the negative effects of a cancer diagnosis. Knowledge and understanding of these factors are imperative for appropriate assessment and diagnosis of depression in oncology patients, and the implications and limitations of this body of research are briefly examined.

Chapter 13 - Converging evidence suggests that patients affected by epilepsy show a considerably higher incidence of depression than the average population (about 65% versus 25%). Since women are twice as likely as men to suffer from depression, female gender could be considered a major risk factor to develop this condition, although gender-related epidemiological data are somewhat controversial. Overall, it is recommended that clinicians pay particular attention, when dealing with women with epilepsy, to examine for early signs of depression. With regards to the neurobiological and psychological underpinnings of these conditions, the key elements to be considered are the partial overlapping in neuro-chemical mechanisms involved both in depression and epilepsy, and the large number of interlinked psychosocial determinants, including clinical features of epilepsy such as seizure type, frequency, and cortical focus. Moreover, sex hormones are important, since they are known to contribute remodelling the hippocampus, a structure which plays a pivotal role in both epilepsy and depression. In women, as opposed to men, the levels of sex hormones are more relevant because of their physiological cyclic fluctuations. Estrogens, rather than other ovarian hormones, show an effect similar to antidepressant drugs by stimulating hippocampal synaptogenesis. With regards to epilepsy, a decrease in estrogen levels is linked to a significant increase in seizures frequency. The exact relationship between epilepsy and depression is not fully understood. However, an emerging picture may suggest potential therapeutic strategies to improve the clinical management of women with epilepsy: first and foremost, an optimal control of seizures can be obtained by using an appropriate pharmacological regimen or neurophysiological devices, such as vagus nerve stimulation. The choice of the antiepileptic drug should take into due account the behavioral profile of the

medication, as some of them (e.g. lamotrigine, carbamazepine) can have a positive effect on mood. Selective serotonin reuptake inhibitors and dual-action antidepressant medications are also considered first-line therapy. Finally, electroconvulsive therapy and vagus nerve stimulation can prove useful in selected cases.

Chapter 14 - Temporomandibular disorders (TMD) are characterized as a heterogeneous set of clinical problems involving the masticatory musculature and/or the temporomandibular joint (TMJ). TMD are considered to be one of the musculoskeletal disorders, and are usually subclassified as myogenous, arthrogenous or combined disorders. The symptoms and clinical signs of TMD include joint sounds, TMJ and masticatory muscle pain and restricted mandibular movements.

Several population-based studies indicate that women experience more TMD-related pain than men, usually at a ratio of two to one. The most prominent sex differences have been found at the age of 20-40 years. Altogether, there seem to be both local and central factors involved in the aetiology of TMD. Epidemiological and clinical studies have shown that besides local pain, facial pain is related to pain condition in different parts of the body. It has also been shown that psychological factors are related to TMD, especially those involving muscular problems.

It has been shown that chronic pain conditions and depressive disorders have some pathophysiologic characteristics in common. Additionally, an association between depression and TMD-related pain has been found in several studies, both in clinical and epidemiological ones. It has been suggested that especially TMD pain as part of a generalised pain condition is connected with depression. The comorbidity has been found to be stronger among women than men.

The diagnosis and treatment of TMD pain may be complicated, especially when the condition is linked with psychological problems. Depression may have an effect on the outcome of the treatment of TMD. Especially when TMD are related to chronic pain conditions, a multidisciplinary approach is needed, besides conservative treatment of TMD. Dentists can provide an important contribution to health care by identifying depression in patients and referring them for treatment.

Chapter 15 - Patients and methods. In a prospective study the authors observed which female patients developed depression following an acute and painful vertebral fracture. On the day of diagnosing the vertebral fracture the patients filled the questionnaires 1 and 2. The depression developed in some patients was diagnosed by means of the DSM – IV questionnaire. For the statistical evaluation of questionnaires the authors chose randomly 32 patients with depression (out of 33 patients) aged 51-73, and 32 patients without depression (out of 44 patients) aged 52-70.

The aim of the study: To verify the hypothesis that the patients with more traumatic experience in the anamnesis (Questionnaire No. 1) are more depression prone following the osteoporotic vertebrae fractures and their character features are typical for subjects with higher emotional vulnerability (Questionnaire No. 2).

Statistical analysis: 1. Questionnaires 1 and 2 were evaluated by two statistical methods: a) automatization of mathematical and statistical estimates and tests based on binomial distribution; b) ADALINE Programme.

2. Assessment of relative risk for developing depression.

Results: Questionnaire No. 1 completed by depressed patients contained statistically significant higher number of positive answers to questions defining experienced stress situations (differences in values of weights of questionnaire parameters expressed in percentages within linear combination of the whole group).

Questionnaire No. 2 completed by depressed patients contained statistically significant higher number of positive answers by more depression prone subjects in comparison with non-depressed patients (differences in values of weights of questionnaire parameters.

Patients lapsed into depression most often on the 32nd day following the vertebra fracture.

Proposed questionnaires are according to validity criteria (sensitivity, specificity, prediction value of positive test, prediction values of negative test, test effectiveness) indicated for identification of persons risking the onset of depression following the osteoporotic fracture of vertebrae.

Relative risk (RR) for developing depression in patients with osteoporotic fracture, which answered in Questionnaire No. 1 eight and more questions positive is *7,0 time* higher than in patiens with osteoporotic fracture, which answered in Questionnaire No. 1 less than eight guestions positive. For Questionnaire No. 2 it is *8,5 time* higher.

Conclusion: The authors recommend using questionnaires No. 1 and 2 in female patients with acute painful vertebrae fractures to select patients with the risk of depression development. These patients should be followed more frequently as outpatients and in case of first clinical symptoms of depression should be recommended for special psychiatric care. Early therapy of depression enables to accelerate the mobilisation, rehabilitation and resocialisation of patients, to improve the quality of their lives and to reduce the costs of analgetic treatment of pain, sedatives and rehabilitation.

Chapter 16 - Depression is more prevalent in adult women than men; the etiology of this difference is elusive. Differences in the hormonal milieu of the sexes may play a role, but societal factors may also take their toll. Women physicians and nurses are no exception regarding depression. In the USA although the lifetime prevalence of depression is 12-13% for male and 18-20% for female physicians (the latter being equal to that of the general population), their completed suicide rate is 1.4-2.3 times higher than that of the general population.

Greek society is characterized by close-knit relationships that may also provide a more supportive environment. In the same country the healthcare sector is profoundly iatrocentric and the number of nurses compared to that of physicians is disproportionately low.

Bearing these Greek particularities in mind, the authors have assessed depression and anxiety in medical and nursing personnel and found no overall differences among subjects. However, age and depression scores were positively correlated in female nurses only. Furthermore, in other studies, the authors noted that smoking behavior of physicians (regardless of gender) was more anxiety- than depression-driven. In another study the authors discovered that in nurses their degree of sense of coherence renders them either resistant or vulnerable to depression and burnout.

In conclusion, stress management interventions should be sought in the healthcare workplace, but they should be equally focused on medical and nursing personnel, and particularly women.

Chapter 17 - This study aimed to identify the profile of students from two Nursing courses (Bachelor - diurnal and Teaching Diploma – afternoon) verifying signs of depression and self-esteem levels, comparing these variables. A total of 114 students, properly informed, from the diurnal and afternoon courses at the College of Nursing at Ribeirão Preto participated in the study. The data search was obtained on known, valid and largely used instruments: Brazilian Economic Classification Criteria – CEB; Beck's Depression Inventory –BDI; Janis and Field's Self-Esteem Scale. The data were submitted to analysis of correlation with significance level at 5%. The results show prevalence of 94 women (82,4%), 63% between 20 and 24 years old; 32.06% (Teaching Diploma) are older than 25 years and 32% (Bachelor) are younger than 20 years old; 69.6% (Bachelor) do not work, and 86.1% belong to classes A2 and B; 75.8% (Teaching Diploma) work and 67.4% from the total belong to classes B2 and C. The data show 15.4% (Bachelor) and 28.6% (Teaching Diploma) with signs indicative of depression (three severe cases in the afternoon courses). The self-esteem levels were classified in 97.4% as medium and high. None of the cases indicative of moderate and severe depression presented low self-esteem. The conclusion is that there are significant differences between the profiles of the two groups of subjects especially the higher incidence of depression among the Teaching Diploma students. It is possible that the prestige perceived in the academic context is a resilient factor, positively influencing the students' self evaluation.

Chapter 18 - Compared to men, women are disproportionately subject to both depression and certain adverse cardiovascular outcomes. In this chapter, the authors review a large body of data on women, depression, and cardiovascular disease (CVD). First, the authors highlight epidemiologic data related to women's higher prevalence of depression, and discuss possible explanations thereof. Second, the authors explore findings on the nature and scope of CVD among women. Next, the authors summarize data regarding the status of depression as a risk factor for future CVD and a prognostic indicator for established CVD, emphasizing findings pertinent to women. The authors then examine possible mechanisms underlying the depression-CVD relationship and conclude by exploring a host of treatment issues. Throughout the chapter, the authors offer a variety of recommendations and directions for future research. The present chapter, in its integration of large and diverse research literatures, should serve as a useful resource for professionals interested in the links between women, depression, and CVD.

Chapter 19 - Depression patients characterized by chronobiologic alterations as diminution of locomotor activity, altered sleep architecture, changes in the cyclic pattern of cortisol, growth, and thyroid hormones secretion, all governed by the Suprachiasmatic Nuclei in the hypothalamus. Several previous studies in animals confirmed anatomical and functional relationships between Suprachiasmatic Nuclei and Vestibular Nuclei through Raphe Nuclei in the brain stem. In our research the authors demonstrated that vestibular activity is diminished at the right side in Major Depression and Bipolar Disease patients during the Depression phase of the illness. It is hypothesized that the right Vestibular hypo activity is induced by ipsilateral dysfunction of Raphe Nuclei or Suprachiasmatic Nuclei, two

neuronal nuclei that modulate vestibular function. To support this idea the authors analyze, in this chapter, the multiple evidences of anatomical and functional alterations of the serotoninergic Raphe Nuclei and of chronobiologic-suprachiasmatic disturbances in depressed patients, and the authors discuss the importance of studying the right–left asymmetry of activity of both nuclei in the future. The study of the bilateral distribution of cortisol, leptin, orexin and estrogen receptors in Raphe Nuclei is also proposed in order to investigate the possible contribution of those depression-associated hormones in right-left asymmetric Raphe Nuclei activity. In summary, the possibility of an asymmetric modulating effect of Raphe Nuclei on Suprachiasmatic Nuclei could contribute to the development of chronobiologic symptoms including depressed mood, and on the other side, Raphe Nuclei modulating effects on Vestibular Nuclei, could explain the asymmetric vestibular response.

Chapter 20 - The study of depression as a possible risk factor in the incidence of coronary heart disease (CHD) and for recurring coronary episodes or death in previously ill people has a certain tradition in the literature, but publications on this possible relation increased greatly after the appearance of a meta-analysis by Booth-Kewley and Friedman (1987). These authors reviewed 87 studies on the relationship between psychosocial risk factors, especially Type A Behavior (TAB) and its components, and cardiac disease (CD). Among their results referring to the relation between these factors and all types of CD is that greater effect size is produced on analysis of results from studies using TAB measured by the Structured Interview, with depression as a risk factor of considerable weight. Booth-Kewley and Friedman noted that although depression seemed to be reliably associated with CD, it had largely been underestimated. As from the 1980s, and particularly during the 1990s, the number of publications on this as a possible risk factor for CD increased, with a corresponding decline in the number of studies on TAB. Thus Scheidt (2000), in his editorial for a special edition of the Journal of Psychosomatic Research devoted to research on psychosocial factors implicated in cardiovascular diseases, expressed surprise about the absence of contributions to the special edition on TAB as a risk factor for CD.

The importance of depression is particularly great if the authors consider the results of the meta-analysis by Booth-Kewley and Friedman (1987) who found an effect size expressed in **z** score of 6.44 for the relationship between depression and all types of CD. Effect size was 5.24 for the relationship between depression and myocardial infarction (MI) and 4.29 for the relationship between depression and angina pectoris as an indicator of CHD. Thus it was not unexpected when Lespérance and Frasure-Smith (2000) suggested that it was time to replace TAB with depression as a psychological priority for cardiologists because depression: a) is the fourth most frequent cause of mortality and early invalidity and the second in industrialized countries, only preceded by CHD; b) clearly plays a large part in medical prescription non-adherence and failure to follow recommendations on life-style changes; c) may interfere with and reduce the efficacy of other treatment aimed at ensuring that cardiovascular patients lead active and productive lives. Further weight is added to this issue by the fact that the rate of CHD has increased more rapidly in women than in men since 1984. In addition, estimated mortality for the period 1990-2020 indicates that ischemic cardiopathy and depression are leading factors contributing to world wide mortality (Murray and Lopez, 1997a; 1997b). Thus the authors are dealing with a major health issue, albeit controversial; in spite of the evidence in favor of its association with CHD, depression is not

considered a risk factor, as became clear at the annual meeting of the American College of Cardiology held in Bethesda, 2002. The final report listed ten risk factors for CHD, and depression was not included.

From the available etiologic meta-analyses, it may be affirmed that there is a significant association between depression and CHD in the general population. The authors could also affirm a significant association between depression and CHD in women if the authors focus on the crude results of our meta-analysis performed with data obtained from women only. The evidence provided by prognostic studies about the relationship between depression and CHD in the general population is similar to that of etiologic studies, although the data for women only are scarce. The considerable reduction of RR values found using results adjusted for other factors means that the possible effect of depression is closely related with other risk factors for CHD. It is therefore necessary to determine the weight of each of these risk factors and the risk associated to their combination, as well as the type of association and the pathways whereby depression may contribute to the manifestation of CHD. Conclusions based on the results of meta-analyses should, however, be made with reservations due to the limitations of the prospective studies included in them and to the limitations of the meta-analyses themselves. The prevalence of depression after a CHD event seems higher in women than in men, although systematic studies are lacking in this respect. The authors believe that the correct evaluation of all these results is not to negate the possible role of depression in the incidence and recurrence of CHD, but rather to strive for more and better research into this topic.

Chapter 21 - During the last few years our knowledge about disturbed brain function in major depression has been increased mainly due to new possibilities offered by neuroimaging methods like functional Magnetic Resonance Imaging (fMRI). Several key structures were identified to play an important role in major depression, such as the rostral and subgenual parts of the anterior cingulate cortex (ACC), the orbitofrontal cortex (OFC) and the dorsolateral prefrontal cortex (DLPFC). Subcortical regions like the amygdala, the thalamus and the nucleus accumbens also seem to play an important role. In comparison to the large number of studies investigating major depression with neuroimaging methods in general, only a few studies have directly addressed the question of gender-specific differences so far although there are hints that gender specific differences may exist. This review summarizes the most important findings related to neurobiological correlates of gender differences, neural responses in depression and particularly neuroimaging findings for depression in women suggesting new lines of research in this field.