CHAPTER 5

DISCUSSION

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A. DISCUSSION OF RESULTS

The experimental group for this study consisted of fibromyalgia patients who were on various pharmaceutical drugs and/or alternative treatments such as physiotherapy, non-allopathic treatments and exercise programs. Pharmaceutical drugs used by fibromyalgia patients in general often comprise a wide range of anti-depressive and analgesic medicines (refer to Chapter 4 – Appendix for a medication list for each of the participating patients in the present study). Because of the nature of these patients' therapies, great difficulties arose in the selection of patients and in attaining ethical clearance. Patients not receiving treatment were in the minority, making it impossible to put together a sample of satisfactory size. The alternative, expecting patients to refrain from taking the prescribed medication for the purpose of the study, would have been unethical, as these patients have to cope with unbearable pain daily. Finally, ethical clearance was granted on the condition that no alterations would be made to the patients' current medical treatment program for the purpose of the study.

Although the fact that the patients were not drug free could be considered a confounding factor, the purpose of this study was not to investigate the origin or nature of the disease (in which case it would be necessary to examine the factors without the influence of medication), but rather to study the status quo of their psychoneurology, that is., the state in which they exist within the context of their disease.

1. Sociodemographic results

The study group consisted of 16 patients (diagnosed according to the ACR diagnostic criteria for fibromyalgia) and 15 age- and sex-matched controls. The reason for the smaller control group is that during analysis of the results, it became clear that one of the control subjects met some of the exclusion criteria set up in the protocol for the study. The mean age of the patients was 43.94 years (SD 10.46) and 43.20 years (SD 11.19) for the control group. The youngest participants in the two study groups were both 21 years of age, the oldest patient 63 years, and the oldest control 60 years. Dividing the experimental subjects into age-interval classes, 6.25% fell into the 20 – 29 year range, 25% were between the ages of 30 to 39 years, 37.5% in the 40 – 49 year age interval class, 25% in the 50 – 59 year class, and 6.25% between the ages of 60 and 69 years. The patient group consisted of 14 females and 2 males, and the control group had 13 females and 2 males. In addition to age and sex (as selection criteria for the inclusion of controls), body mass index (BMI) was calculated for prospective controls to see to it that the BMI of the patient and control group did not differ significantly. The mean BMI was 25.84 (SD 4.53) for the patients and 24.64 (SD 3.18) for controls. Statistical differences between the patient and control group for age, gender and BMI were assessed by the Mann-Whitney test (used for small sample sizes) and found to be statistically non-significant.

Despite the small sample size and the random selection, the mean age of this group of fibromyalgia patients was very similar to that described in other publications. In 1994, Yunus reviewed studies with regard to the demographic characteristics of fibromyalgia (5). He combined the demographic outcomes of the studies and presented the following results for a combined sample of 524 participants: the mean age for the joint group was 44 years, exactly the same as in the present study. Four other studies on fibromyalgia calculated the mean age of patients to be 46 years (SD 10.5, n = 19) (1), 41.8 years (SD 6.5, n = 17) (2), 47 years (SD 7, n = 22) (3), and 38.6 years (SD 10.5, n = 30) (4). Furthermore, Yunus reported the most common age at presentation to be between 40 and 50 years (5). According to the descriptive statistics calculated for the age interval classes (in this study), the majority of patients were also in the 40 – 49 year age interval class.

However, not all published studies reflect the above distribution. In October 1997, the Fibromyalgia Network released information derived from fibromyalgia surveys done on 6240 participants. The average age of the fibromyalgia sufferers in this study was 52.6 years (6). A more recent epidemiological study in the United States also confirmed the prevalence of fibromyalgia to increase with age, but added that 1% of the general female population between the ages of 18 to 29 years, and 7% of woman who are 70 to 79 years of age were diagnosed with fibromyalgia (7), suggesting that most fibromyalgia sufferers are much older than what was observed in the present study. These findings are comparable to results obtained from a study on the prevalence and characteristics of fibromyalgia in the general population (8). These authors concluded that the prevalence of fibromyalgia is skewed towards the elderly between the ages of 60 and 79 years. It seems that the present study offered similar results to the studies with comparable sample sizes, but as soon as the study group size increased, the average age of fibromyalgia sufferers increased as well. Fibromyalgia is, however, not confined to middle and older age, but has also been reported among juveniles (5,7). The same was true for this study – although the study group did not comprise of any children, some of the participants reported onset of fibromyalgia symptoms as early as 14, 17 and 18 years of age (Chapter 4 - Appendix).

The female predominance among fibromyalgia sufferers, as reported by various authors (1,4,7), was also demonstrated in this study by the fact that only two males were available. According to the combined results by Yunus, 90% of fibromyalgia sufferers were female (5). The Fibromyalgia Network found 95% of the 6240 respondents in their study to be female (6). Moreover, studies exploring the difference in disease severity in female and male patients indicated that men with fibromyalgia had fewer symptoms, fewer symptom sites, and fewer tender points. Since this study group only had two male subjects, few conclusions could be made in this regard (9). One of the explanations offered for the phenomenon that most fibromyalgia sufferers are woman, involves sex differences in pain sensitivity. When the pain sensitivity of healthy woman and healthy men were compared in an experimental setting, woman had an increased sensitivity to pain, especially when mechanical pain was induced (10). In an attempt to identify the specific factors causing the higher pain sensitivity in woman, Sorensen *et al.* (1998) observed that muscle nociceptors show a higher sensitivity in woman (11). Therefore, it is possible that the tendency of (healthy) woman to be more responsive to pain may be the very factor that predisposes them to more pathological forms of mechanical hyperalgesia as observed in fibromyalgia.

A noteworthy difference was observed between patients and controls with regard to their marital status. 63% of patients and 86% of controls were married. Of the 37% single patients, 13% had never been married, 6% were divorced, 12% widowed, and another 6% separated. Only 14% of the controls were single, 7% had never been married and 7% were divorced. Noticing the difference between the number of married patients in comparison to married controls, it is tempting to assume that the reason for this difference is the strain put on the family and spouse living with someone suffering from fibromyalgia, which may cause the relationship to deteriorate. The functional disability and mood states associated with fibromyalgia causes physical, financial and emotional complications (especially when the patient is not able to work anymore and does not have either disability compensation or a medical scheme), aggravating the situation. The proportion of divorced and separated patients was double that of the controls, adding value to the speculation that marital problems in fibromyalgia originate, at least in part, from disability and negative mood states. The lower incidence of married individuals seen in this study is supported by the results obtained by other studies. A study that granted similar results reported 68.8% of the study group being married and 8.4% being divorced (12). Yet another study reported only 56.7% married patients (13). However, one study found no significant difference in marital status between the patients and controls (86% of fibromyalgia patients were married) (3).

The highest qualification obtained by the patients was a postgraduate degree (obtained by three out of the 16 patients). However, most of them (seven patients) only had a high school education. Four had a diploma and two a degree. Four out of 15 controls had a postgraduate qualification, one had a degree, six a diploma, and another four only a high school education. These findings are comparable with a study reporting 39.6% of the patients in their study group only having a primary school education, 25% with a secondary school, and 6.3% with a high school qualification (12), indicating that most of these patients did not have a qualification on tertiary level either. Another study published results showing patients having a lower level of education than control subjects (3). The possibility does however exist that in the present study, selection bias of the control group could have contributed to the difference between the patients and controls.

As expected, the employment status of the patients and the controls differed remarkably. The employment status of the experimental subjects was as follow: Only 31% of the patients were employed in contrast to 73% of the control group. 20% of the control group was not employed at the time of the study and 7% reported not ever occupying a paid job. Of the 69% of the unemployed patients, 13% had never been employed, probably indicating that there is no relation between the disability caused by fibromyalgia and their employment status. However, the other 55% indicated that they were unable to work because of their fibromyalgia complaints. 19% of the employed patients were only employed part time. This proportion of patients also reported that they were unable to maintain a full day's work because of chronic fatigue and pain caused by fibromyalgia-associated functional disability. The outcome in this study with regards to the employment status of the patients was verified by other studies' findings (3,12,13).

According to a study that assessed clinical care utilisation in fibromyalgia, 25% of the recruited subjects received disability assistance or were retired early because of fibromyalgia (13). Because of statistics such as these, physicians are advised to practise objectivity in diagnosing fibromyalgia and evaluating disability. They are warned against malingering – 'a conscious and voluntary fabrication of physical or psychological symptoms for personal gain' (14). In the present study, 19% of the patients received full disability compensation, 6% partial compensation and 75% no compensation at all. Since disability resources are limited in South Africa, it is unlikely that the patients in the present study exaggerated the degree of functional disability for financial gain.

Several studies exist on the sociodemographic features of fibromyalgia, and although there are many of similarities between those studies, as well as between those studies and the present one, there are also differences between results. The reason for the differences is mainly attributed to different methodologies such as vast differences in sample sizes and diverse study populations. An epidemiological study done by Neumann *et al.* (2003) demonstrated these differences by reviewing clinical features of fibromyalgia in different settings (7). These study groups ranged from patients in the general population to patients from clinics (rheumatology clinics and clinics treating associated conditions) as well as from hospitals and institutions. As expected, the demographic data varied from setting to setting. The sample in this study is representative of the fibromyalgia patients living in suburban areas in South Africa, treated by the same physician and attending the same clinic. Factors such as these could have an influence on the demographic data obtained in this study and could explain differences between this and other studies.

2. Diagnostic criteria and concomitant diseases

As already discussed in Chapter 1, a number of symptoms in fibromyalgia form part of conditions that are diagnostic entities themselves. A study investigating the overlapping features of 13 different syndromes marked by chronic multi-system illness (CMI), showed that fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome and non-ulcer dyspepsia often occur together (15). The same was observed in the present study's patient group. In this study only two of the patients did not fulfil the Fukuda diagnostic criteria for chronic fatigue syndrome in addition to their fibromyalgia diagnosis. Besides the presence of chronic fatigue syndrome features, the patients also presented with symptoms associated with irritable bowel syndrome (50.94% of patient group), premenstrual syndrome (18.75% of patient group) and thyroid problems (35.42% of patients). There was also a high prevalence of headaches (71.88%), anxiety (68.75%) and depression (87.50%) in the patient group evaluated. According to literature (5), these three symptoms have reached 'disease status'.

The overlapping nature of these diseases brings the diagnostic criteria of fibromyalgia (and all the other disorders in the CMI spectrum) into question. According to Dommerholt & Issa, the tender point count used in the diagnosis of fibromyalgia (American College of Rheumatology, 1990) is not specific enough for distinguishing it from the other disorders (16). Nevertheless, despite the fact that these syndromes all have their own diagnostic criteria and unique features distinguishing them from the rest, the possibility that we are dealing with different aspects of the same disease is undeniable. Naturally, the gaps in the diagnostic criteria of fibromyalgia (assuming it is in fact a distinct diagnostic entity) will have an influence on the psychoneurological profile composed from the results of this study.

3. Course and nature of fibromyalgia complaints

In this study the mean duration of the patients' complaints was 16.56 years (SD 11.03). The mean duration, as reported by other studies, varied from 6.6 (SD 6.4) (1) and 8.0 years (SD 8) (3) to 12.2 years for the Fibromyalgia Network study group (6). Certainly the duration of fibromyalgia in a specific patient (and a patient group) will be dependent on the age at which the complaints started as well as the age of that individual (or the mean age of the patient study group) at the time of the study. The differences in the mean duration between the studies were therefore probably due to variances in these two variables.

In the present study, the duration of complaints for each patient was also expressed as a percentage of his or her lifespan. This way it was possible to compare patients of different ages with one another. One of the patients has been suffering from fibromyalgia-related complaints for most of her life (74.5% of lifetime). Usually, in cases like these, the complaints started before 20 years of age. The duration of complaints (in terms of percentage of lifetime) for the rest of the study group was more than 50% for three of the patients, around 30 to 49% for 43.75% of the group and less than 30% of their lifetime for the rest of the study group.

The onset of fibromyalgia complaints ranged from 14 to 42 years of age for the present study. In this study, 18.75% of the patients' symptoms started to appear from the age of 10 to 19 years. The majority of the patients' complaints started during their twenty's and thirty's, with 43.75% of the patients reporting onset in the 20 to 29 year age interval range and 31.25% during the 30 – 39 year range. Only one patient reported fibromyalgia onset after 40 years of age. Other studies have confirmed fibromyalgia onset after 60 to be very rare (6).

It has been proposed that there is a link between trauma and the development of fibromyalgia. Data about a specific incident prior preceding the onset of the fibromyalgia complaints (as perceived by the patients) signified that 25% of the patients' complaints appeared following a major psychological stressor. In 12.5% of the patients the complaints seemed to be the consequence of a period of overexertion. An operation preceded complaints in 6.25% of the patients. Other events that occurred prior to the onset of complaints were serious illness and a car accident (6.25% respectively). In most of the cases (50%), fibromyalgia symptoms did not appear directly after a traumatic episode, but gradually. It is important to note that in the cases where symptoms worsened progressively, the symptoms were generally preceded by multiple or even a single life drama in the distant past. This phenomenon is clearly demonstrated by two patients in the present study (refer to Chapter 4 – Appendix). According to Patient 6's testimony, she was molested at the age of four. From 13 years of age she started to suffer from severe migraine headaches, for which she was hospitalised for the first time at 18 years of age. Early in her adult life the next traumatic happening took place when she had a miscarriage at the age of 22. At the time of the study (age 55), she had already undergone six surgical operations. Another patient, Patient 16, shared a similar life story. Her parents divorced when she was two years old, after which her grandparents brought her up. At the age of four, she also was molested. Patient 16 reported severe headaches starting at seven years of age. Apart from various illnesses, Patient 16 had already had five operations at the age of 52. Both these cases professed a link between trauma in the distant past and progressive development of fibromyalgia in adult life. In these two cases it started with headaches during childhood, but then circled out to other organ systems.

The results of the present study are in concordance with the outcome of the Fibromyalgia Network survey that showed that 41% of the respondents were not able to identify a specific trigger prior to onset. In the latter study, 39% of the 59% that were able to provide details regarding the foregoing happenings indicated that physical trauma activated their symptoms.

27% stated that their complaints started after a major emotional trauma. 15% reported an infection to have preceded fibromyalgia onset, 9% gave testimony of surgery and 5% of exposure to a chemical agent just before their symptoms began (6). In the light of these findings, as well as the findings obtained in the present study, it is impossible to ignore the role distressing events play in the development of fibromyalgia. The way in which these events are able to impair health and contribute to fibromyalgia symptoms was discussed in Chapter 1.

As far as the natural history of the symptoms is concerned, 37.5% of the patients reported that over the previous 12 months, their symptom status had improved. The same number of patients felt that their condition was worsening. 6.25% of these claimed to experience higher pain intensity, 18.75% more painful locations, and 12.5% had both more painful locations as well as higher pain intensity. 18.75% of the patients reported that no significant changes took place with regard to their symptoms and 6.25% did not have clarity on whether their condition had deteriorated or improved. Reviewing the literature, one study actually reported 0.2% of patients claiming to have recovered fully. 31% of the study group reported that their symptoms had improved, but 40% felt their health status were poorer than before. 20% of the patient group stated that the natural history of their symptoms were unchanged (6). These results were similar to the present study's findings, even though these results were an indication of the natural history of symptoms since diagnosis, and not the history over the previous 12 months like in the present study. The fact that there do not seem to be a difference in the natural history of fibromyalgia symptoms, whether it is assessed over the full duration of the syndrome or whether it is assessed over 12 months, might be indicative of the chronic nature of the disorder.

Although numerous factors influence fibromyalgia symptom status (the number and severity of symptoms), there are a limited number of publications identifying and examining these factors. The factors reported below, were issues mentioned by patients participating in this study during experimental sessions. The primary factor influencing on fibromyalgia symptom status was stress (reported by 100% of patients). 93.75% of patients regarded sleep to have a great influence on their fibromyalgia complaints: 18.8% perceived a full night's sleep as a worsening factor on their symptom status, while 75% reported that sleep actually caused their symptoms to diminish. Exercise was reported to affect 81.25% of the patients' symptoms. Exercise seems to be beneficial to some – 43.75% reported that their complaints were more controllable when following a light exercise program. However, 37.5% felt that exercise aggravates their symptoms. Cold and heat influenced 75% of the experimental group. These two factors were a major cause of distress in many patients. Cold worsened fibromyalgia symptoms in 68.8% of patients and heat in 56.3%. Only 6.3% benefit from cold, and only 18.8% stated that heat helps to relieve symptoms. Another factor reported to have a negative effect on fibromyalgia symptomology was humidity (this factor increased symptoms in 62.5% of patients). Interestingly, sunlight seemed to improve fibromyalgia symptom status in 25% of patients (12.5% felt that sunlight worsened their symptoms, though). Symptoms seemed to become worse at certain times of day in 56.3% of the patients. This also seemed to be the case with different seasons (37.5% of patients' symptoms increased with specific seasons or season changes). 12.5% of patients felt that changes in barometric pressure (height above sea level) worsened their symptoms, 6.25% felt that it improved symptom status. Alcohol and caffeine intensified complaints in 50% and 43.8% of the patient group respectively. 31.3% claimed that various foods, especially foods that have a high sugar and starch content, also have a negative effect on their symptoms. Eating fresh fruits and vegetables, however, were reported to relieve fibromyalgia complaints in 6.25% of the patient group. It is thus clear that various environmental factors are perceived to have different effects on the patients. There is not one single factor that benefits all the patients, and the only factor that had a negative effect on everyone was stress, a factor that influences healthy individuals as well.

Differences were seen with regard to the treatment programs selected for the patients. The treatment programs of the patients varied according to their current symptoms and complaints and with relation to their unique individual reaction to different therapies. All the patients (100%) made use of pharmaceutical medications to relieve their symptoms. Other treatments utilised by the patients (in addition to drugs) were physiotherapy (62.5%), exercise programs such as stretch exercises, swimming and walking (68.75%) and non-allopathic treatments such as acupuncture and meditation (56.25%). It is generally assumed that successful treatment of fibromyalgia does not exist without the combination of different treatment programs or what can be called an 'integrative treatment strategy'. Most of the patients in this patient group were on some sort of combined therapy for their symptoms: The combination of exercise, physiotherapy, and medication was mostly used by the patients (31.25 %). The second most prevalent combination therapy was the combination of non-allopathic treatment, physiotherapy and medication (18.75% of patients). 12.5% of the patients were using the combination of exercise and medication; another 12.5% used exercise, medication and non-allopathic treatment simultaneously; and yet another 12.5% made use of combined exercise, physiotherapy, non-allopathic treatment as well as medication. The combination of non-allopathic treatment and medication was used by 6.25 % of the patients. 6.25 % (one patient) only used pharmaceutical medications to treat fibromyalgia complaints.

In order to determine which of these therapies offered the most successful option in treating fibromyalgia, a calculation was done to determine whether the patient's condition improved or whether there was no change/ deterioration using a specific treatment program (Table 1.16, p. 4.19). According to this table not one of the therapies could confidently be associated with improvement of fibromyalgia. For instance: 25% showed improvement on pharmaceutical drugs, but 43.75% did not show any improvement at all. This does not necessarily mean that allopathic medicine does not work, but it confirms the complexity of the symptoms and that there is an altered functional interaction between various bodily systems in fibromyalgia. According to a study assessing different treatment strategies, 40.9% of patients that exercised showed improvement compared to 31.8% that did not. The percentage of patients that showed improvement with physiotherapy was similar to the number of patients that did not show any progress at all (37.5% and 31.5% respectively). Analgesic drugs failed to relieve pain in 46.3% of the patients in the study and only seemed to help 31.3% of the participants (17). These findings serve as a further motivation to use a combination of therapies in treating fibromyalgia. Therapies that offer positive results in conjunction with other therapies include methods helping sleeping patterns, thermal treatment, hydrotherapy, and antidepressant medication (6). Some of the patients in the present study also confirmed sleep medication and antidepressant drugs to improve symptom status. However, alternative therapies that have been shown to be quite successful on their own are cardiovascular fitness training, EMG-biofeedback, hypnotherapy, regional sympathetic blockade and cognitive behavioural therapy (17). Unfortunately, only a few of the subjects in this study used any of these therapies.

4. Current symptom presentation

The symptom presentation of the patients as reviewed by means of a questionnaire that included symptoms commonly associated with both fibromyalgia and chronic fatigue syndrome. The control group was screened for the same symptoms to serve as a comparative measure for the symptomology of fibromyalgia. All the symptoms were allocated to different symptom-categories (Table 2.2, p. 4.19). The means (for responses ranging from 0 = absent, to 3 = severe) for these categories were as follow: constitutional symptoms were 1.77 (SD 0.56) for patients, 0.13 (SD 0.3) for controls; symptoms relating to the skin were 0.89 (SD 0.52) for patients, 0.02 (SD 0.05) for controls; symptoms relating to the eyes were 0.99 (SD 0.63) for the patients, 0.08 (SD 0.21) for the controls; symptoms relating to the ears were 1.06 (SD 0.70) for the patients, 0.18 (SD 0.60) for the controls; symptoms associated with the nose and throat were 0.80 (SD 0.56) for patients and 0.02 (SD 0.06) for controls; symptoms of the mouth were 0.64 (SD 0.79) for the patient group, 0.02 (SD 0.06) for the controls; problems associated with the lymph nodes were 0.97 (SD 0.92) for patients and 0.03 (SD 0.13) for controls; problems with breasts were 0.48 (SD 0.66) for the patient group, 0.0 (SD 0.0) for the controls; respiratory symptoms were 0.92 (SD 0.57) for the patients and 0.03 (SD 0.06) for the controls; gastrointestinal symptoms were 0.94 (SD 0.56) for patients, 0.01 (SD 0.06) for controls; symptoms relating to muscle groups were 2.53 (SD 0.38) for the patients, 0.22 (SD 0.32) for the controls; symptoms of the joints were 1.52 (SD 0.77) for the patient group, 0.0 (SD 0.0) for the control group; symptoms associated with the genital-urinary tract were 0.41 (SD 0.46) for the patients, 0.01 (SD 0.04) for the control group; thyroid problems 0.71 (SD 0.75) for the patients and 0.0 (SD 0.0) for the controls; and neuropsychiatric symptoms were 0.99 (SD 0.52) for the patient group and 0.04 (SD 0.07) for the control group. The ANOVA test was used to calculate the statistical difference between the patient and control group. The p-values obtained for all the symptom-categories were highly significant ($p = 0.0001$). The mean total number of symptoms for the patient group was 51.69 (SD 23.29) with the minimum total number of symptoms 21, and the maximum total number of symptoms in a patient 95. The control group had a mean total number of symptoms of 4.33 (SD 5.33) with the minimum total number of symptoms nought, and the maximum number of total symptoms 15. A p-value was also calculated for the total number of symptoms for each study group ($p < 0.0001$). This data serves as additional evidence that fibromyalgia is characterised by multiple symptoms involving various organ systems.

A mean response (ranging from 0 – 3) was calculated for each of the individual symptoms as well. Symptoms that had a mean response of ≥ 2 were regarded as most severe in this particular fibromyalgia group and included fatigue, sleep abnormalities, tight or stiff muscles, neck pain, shoulder pain, upper and lower back pain and severe headaches. Figure 2.3 (p. 4.21) illustrates the responses to the questions enquiring about these symptoms for the patients and controls. The mean response for patients to 'fatigue' was 2.5 (SD 0.73), compared to the mean control response of 0.3 (SD 0.59). Patients responded to 'sleep abnormalities' with a mean of 2.4 (SD 0.89), and controls with a mean of 0.1 (SD 0.35). The mean patient response to symptoms relating to muscle pain and stiffness, was 2.9, SD 0.25 for tight/ stiff muscles (controls: 0.2, SD 0.41); 2.8, SD 0.4 for neck pain (controls: 0.3, SD 0.62); 2.8, SD 0.77 for shoulder pain (controls: 0.2, SD 0.56); 2.3, SD 1.2 for upper back pain (controls: 0.1, SD 0.26); 2.8, SD 0.45 for lower back pain (controls: 0.5, SD 0.83); and 2.1, SD 1.31 for severe headaches (controls: 0.0, SD 0.0). Since these mean responses were out of a total of three, it is clear that these symptoms were quite severe and are strongly related to fibromyalgia symptom status in this study group. In point of fact, according to Table 2.3 (p. 4.20) these symptoms were not only the most severe in this group but also the most common. The prevalence of these symptoms ranged from 75-100% in the patient group, with 100% of the experimental subjects presenting with general fatigue, tight or stiff muscles, and neck and lower back pain (this explains why fibromyalgia is described as a musculoskeletal disorder, even in the absence of evidence of anatomical abnormalities of the muscles). Sleep disturbances were present in 93.75% of patients. 0-40% of the controls also presented with some of these problems, as neck and low back pain were relatively common in the control group as well (26% and 40% of controls respectively). 20% of the control group also reported general fatigue and tight muscles to be a regular problem. These results for the control group are in accordance with a study (mentioned in the first chapter) which stated that a minimum of 75% of the population report at least one complaint (like fatigue, tiredness, dizziness and headaches) during a 30-day period (18). According to the data obtained in the present study, it seems that the symptoms that healthy individuals commonly present with was neck and low back pain, fatigue and tight muscles. Only when these minor symptoms are aggravated to a point where it becomes unbearable, as in the fibromyalgia patient group, will these symptoms reach 'syndrome' status.

Some work has been published on the connection between the presence of different types of allergies and muscle pain. To explore the matter, the patients and controls were asked to indicate whether they suffer from any type of allergy. In this study, 62.5% of the patient group reported to have some kind of allergy, a significant higher prevalence than in the control group (20.0%). In other words, 37.5% of the patients and 80% of the controls did not have any allergies at all. Despite the clear lower prevalence of allergies in the control group, the main difference between the patients and controls seemed to be in the number of allergies per person. The majority of subjects that reported to suffer from allergies had one allergy, i.e., 43.75% of the patient group and 13.3% of the control group. 12.5% of the patients and 0.07% of the controls suffered from two types of allergy. None of the controls had more than two allergies. In the patient group, however, one had three types if allergy. The mean number of allergies per patient was 0.88 (SD 0.8) and 0.27 (SD 0.59) for the controls. The statistical difference calculated for the two groups with the Mann-Whitney test, gave a statistical significant p-value of 0.0224 ($p \leq 0.05$). The higher prevalence of allergies in the patient group is significant because of the symptoms commonly associated with a systemic allergic manifestation: fatigue, muscle pain, joint pain, digestive symptoms, chest pain, mild depression, and racing pulse (19). The main culprits in the systemic allergic response are cytokines, regulatory proteins responsible for the intensity and duration of immune responses. Wallace *et al.* (2001) identified specific cytokines with relevance to fibromyalgia (20): IL-8, which intensifies pain, was shown to be twice normal levels in fibromyalgia. IL-1 receptor antagonist (IL-1ra) was also found to be double normal quantities. IL-1ra is known to increase the response to stress and counter-balance the effects of IL-8 (19). The most interesting finding made by Wallace *et al.* (2001), was that IL-6 (which increases pain, fatigue, alters mood and increases the response to stress) was produced at vastly increased levels when fibromyalgia patients' white blood cells were stimulated (20). This could explain why some individuals would develop fibromyalgia after an illness or infection.

Results from the Fibromyalgia Impact Questionnaire (FIQ) also provided useful information to set up a symptom-profile for the patients. The questionnaire comprised of ten scales (each scale ranged from 0 – 10) specifically associated with the symptoms causing distress in fibromyalgia patients. The scales were 'physical impairment' (mean patient score: 3.75 (SD 2.26), mean control score: 1.44 (SD 2.08)); 'do not feel good' (mean patient score: 6.79 (SD 2.36), mean control score: 0.45 (SD 1.29)); 'work missed' (mean patient score: 2.86 (SD 3.42), mean control score: 0.18 (SD 0.74)); 'could not do job' (mean patient score: 6.19 (SD 2.29), mean control score: 0.44 (SD 1.55)); 'pain' (mean patient score: 7.06 (SD 1.84), mean control score: 0.63 (SD 1.8)); 'fatigue' (mean patient score: 7.16 (SD 2.46), mean control score: 0.75 (SD 1.86)); 'not rested' (mean patient score: 7.88 (SD 2.0), mean control score: 0.31 (SD 0.72)); 'stiffness' (mean patient score: 6.69 (SD 1.7), mean control score: 0.19 (SD 0.77)); 'anxiety' (mean patient score: 5.25 (SD 2.93), mean control score: 0.13 (SD 0.35)); and 'depression' (mean patient score: 4.06 (SD 2.86), mean control score: 0.13 (SD 0.52)). The statistical difference between the patient and control group for each one of the ten individual scales was highly significant with $p < 0.0001$. The FIQ total score also differed significantly ($p < 0.0001$) between the groups with the mean total FIQ score 57.69 (SD 15.19) for the patients and 4.94 (SD 7.59) for the controls.

Another study also used the FIQ to assess disability in 180 participating fibromyalgia patients and found a mean total FIQ score of 57.74 (13), exactly the same as in this study. According to Burchardt *et al.* (1991), the authors that validated the FIQ, the average fibromyalgia patient scores about 50 on the FIQ, whilst severely afflicted patients obtain scores of 70 and higher (21). Four of the patients (Patient 2,3,6 and 7) in this study had scores higher than 70. Their FIQ scores corresponded to the outcome on their 'Review of current symptoms' – questionnaire, since these patients also presented with more symptoms and greater symptom severity (refer to Chapter 4 – Appendix).

As far as the subscales of the FIQ are concerned, the pain, fatigue, stiffness, sleep quality (assessed by 'not rested'-scale), anxiety and depression scales were of particular interest. A couple of studies granted similar type of information by assessing these important aspects of the FIQ on visual analogue scales out of ten (just as the FIQ does). A study done by Cohen, *et al.* (2000) indicated that the fibromyalgia patients had a mean score of 8.2 (SD 1.6) for pain and 7.9 (SD 1.9) for fatigue (3). These values are slightly higher than the values obtained in the present study. Another study recorded a lower value of 6.1 (SD 2.0) for pain and 7.5 (SD 2.2) for fatigue (4). Values documented for stiffness was 6.6, SD 2.7 (3); 5.7, SD 3.5 (4) and 4.7, SD 2.8 (1). It seems that the patient group in the present study gave the highest values for stiffness. Another aspect commonly assessed by other researchers, seems to be sleep disturbances or sleep quality. The FIQ evaluates this aspect by asking patients to indicate on a scale from zero (not rested at all) to ten (well rested), how rested they feel after a nights' sleep. Scores published by other authors are 5.8, SD 2.4 (4) and 6.2, SD 2.9 (1). These scores are lower than the scores obtained in this study, indicating a more severely afflicted patient group in the present study.

Note that, in the present study, the patient scores for depression and anxiety were lower (4.06 and 5.25 out of ten respectively) than the scores obtained for pain, fatigue, sleep disturbances and stiffness. This also seemed to be true for Cohen's study, which recorded a score of 4.9, SD 3.2 for anxiety and 3.4, SD 3.4 for depression, much lower than the scores for pain and fatigue mentioned previously (3). Firstly, this could simply be an indication that anxiety and depression are not one of the major symptoms associated with fibromyalgia. On the other hand, the lower depression and anxiety scores are more likely to be due to the use of anti-depressive medications by the patients in the present study. Contradicting this possibility is the fact that similar results were obtained in Cohen's study, where patients refrained from taking their anti-depressant drugs for the purpose of the study (3).

An alternative way to evaluate anxiety and depression in the patients was to look at prevalence rather than the severity of these two conditions within the patient group. 68.75% of the present patient group reported self-assessed global anxiety whereas 87.50% had self-assessed global depression. A study that found similar values for the prevalence of anxiety in their patient group reported 63% of the patients to have anxiety (4) as opposed to another study that reported a prevalence of 31% (1). Interestingly, a study that compared the lifetime prevalence of anxiety disorders in fibromyalgia, rheumatoid arthritis and major depression patients, found that 26% of the fibromyalgia group had anxiety disorders such as panic disorder and/or agoraphobia. None of the rheumatoid arthritis patients reported the presence of an anxiety disorder at any stage in their lifetime (22).

The prevalence of self-assessed global depression in the present study's patient group was 87.50%, which provides a different picture on depression in fibromyalgia than the severity score of 4.06 out of ten. The reported measures of the prevalence of depression show great variation from study to study. The most obvious reason for these differences is probably that the prevalence-measures of depression differ when patients report self-assessed depression as opposed to studies where patients were evaluated by a qualified psychiatrist for clinical major depression according to the criteria set out in the Diagnostic and Statistical Manual of Mental Disorders (DSM). Examples of these differences were demonstrated by two studies that found the frequency of major depression (assessed according to criteria set out by the American Psychiatric Association) in the fibromyalgia patient group to be 43% (23) and 20% (24) respectively. These were significantly higher than the control groups in these studies that comprised of patients with other pain conditions.

Accordingly it can be said that depression and anxiety in fibromyalgia do not present a problem of the same magnitude as the pain, stiffness, fatigue and sleeping problems associated with the condition, but definitely forms part of a profile for fibromyalgia. This profile is distinctly higher than that of other pain conditions such as rheumatoid arthritis (22,23). In fact, depression and anxiety play such an important role in conditions characterised by medically unexplained symptoms, that recommendations had been made to remove the category somatoform disorders in the DSM-V since depression and anxiety characterises patients with medically unexplained symptoms better (25). In the latter study they found that 44.7% of the 206 patients with unexplained symptoms had full anxiety diagnoses, 45.6% had either full of minor depression diagnoses and only 4.4% had a full DSM-IV somatoform diagnosis or abridged somatisation disorder (18.9%) (25).

Another study evaluated the prevalence and predictors of psychiatric disorders in fibromyalgia specifically (26). In this specific study, 115 fibromyalgia patients were evaluated with the Structured Clinical Interview for DSM-IV after they were grouped into one of three psychosocial subgroups (dysfunctional, interpersonally distressed and adaptive copers). Axis I diagnoses were present in 74.8% of the participants, with the 'dysfunctional' subgroup mainly reporting anxiety, and the 'interpersonally distressed' subgroup, mainly mood disorders. Axis II diagnosis were present only in 8.7% of the participants. The authors concluded that fibromyalgia is not a homogeneous diagnosis, but has varying proportions of comorbid anxiety and depression depending on of the psychosocial features of the patients (26).

5. Hypothalamic-pituitary-adrenal (HPA)-axis function

The malfunctioning of the HPA-axis has been linked with depressive illnesses and chronic pain as part of a physiological stress response that generates a loss of affective and cognitive flexibility, anxiety, sleep disturbances and activates the autonomic nervous system (27). Reviewing previous publications exploring HPA-axis function in fibromyalgia (Chapter 1, p. 1.41-1.42), conflicting results have been published. As a result, there is a lack of agreement as to the overall state of HPA-axis activity in fibromyalgia. Findings from studies assessing HPA-axis function in fibromyalgia point in the direction of altered activation at both the pituitary and adrenal level. Fibromyalgia seems to be associated with a hyperactive HPA-axis function during restful conditions (evident in elevated basal cortisol levels), an exaggerated reaction of the pituitary gland to stress (evident in higher than normal ACTH levels in response to CRH), accompanied by reduced sensitivity of the adrenal gland to ACTH (28). It is hypothesised that the inability of the adrenal glands to respond to elevated ACTH levels might be an adaptive mechanism of the adrenal cortex to chronic stress (29).

In the present study, HPA-axis function was evaluated by analysis of the salivary cortisol by means of ELISA. Patients showed elevated cortisol levels in comparison to control subjects. The patients had a mean salivary cortisol level of 9.59 ng/ml (SD 2.79), statistically significantly higher that the control mean cortisol level of 5.60 ng/ml (SD 2.3). A p-value of 0.0003 was obtained with the Mann-Whitney test for the statistical difference between the two study groups. The pattern of elevated cortisol levels, together with symptoms of fatigue and cognitive impairment, is similar to that observed in burnout syndrome, which is believed to be the result of ineffective coping with enduring stress (30). In point of fact, HPA-axis activity has directly been correlated with passive coping where CRH – ACTH – cortisol levels increase when feelings of hopelessness arise (31). What is more, elevated CRH levels have been linked with anxiety (32), and could be the pathophysiological mechanism underlying the high prevalence of anxiety disorders amongst fibromyalgia sufferers.

Hemispheric laterality is said to play a major role in the stress-induced activation of the HPA-axis, with the right prefrontal cortex predominantly exerting stimulatory effects and the left prefrontal cortex inhibitory effects (33). In other words, cortisol secretion is predominantly controlled by the right hemisphere in healthy individuals (31). When the right hemisphere is unable to perform this task, it is possible that the left hemisphere could adopt this function. However, left hemisphere driven cortisol regulation (as seen in PSTD patients), is said to be associated with a significantly higher incidence of physical complaints, recurrent illness, affective and behavioural abnormalities (just as observed in fibromyalgia) (31). The question that arises is whether cortisol function could, as a result of early life trauma to the right brain, be regulated by the left hemisphere in fibromyalgia. This possibility is explored further in the discussion on hemisphere dominance.

6. Autonomic nervous system function

In this study, autonomic nervous system function was assessed by exposing the experimental subjects to both a physical and a psychological stressor. To access the response of the autonomic nervous system to physical stress, an orthostatic test was performed during which subjects were expected to lie in the supine bodily position for 10 minutes, sit upright for 10 minutes and then stand against a wall for 10 minutes. The heart rate variability recordings obtained during each of these bodily positions were analysed in 5-minute segments, so that the first five minutes of each section (bodily position) could be used as an indication of how the autonomic nervous system compensates to the new bodily position, and the second five minutes for the description of the status of the autonomic nervous system in that specific position. To access the effect of a psychological stressor on the autonomic nervous system, a baseline recording was performed in the sitting position, after which heart rate variability was recorded while the subjects were filling out the Experiences in Close Relationships-questionnaire (ECR-R).

As discussed in Chapter 3, a wide variety of analytical techniques are available for analysis of heart rate variability, the most common measures being descriptive statistical and frequency domain measures. In the analysis of the present study's data, the only statistical measure utilized is the mean heart rate, since the other statistical measures have limited application in basic psychophysiological research (34). Analysing the heart rate variability results obtained, both similarities and differences were noticed between the patients and controls. There was a tendency towards faster heart rate in the subjects with fibromyalgia during supine (patients – 75.48 bpm, SD 11.19; controls – 65.12 bpm, SD 12.59), sitting (patients – 77.76 bpm, SD 10.84; controls – 69.01 bpm, SD 12.38), and standing (patients – 93.29 bpm, SD 14.65; controls – 82.53 bpm, SD 13.79). These differences between the patients' and the controls' mean heart rate was significant for the supine position (supine: $p = 0.0299$; sitting: $p = 0.0594$; standing: $p = 0.0630$). Both groups showed notable increases in heart rate upon sitting up from supine (patients: $p = 0.0113$; controls: $p = 0.0597$) as well as on standing from sitting (patients: $p = 0.0002$; controls: $p = 0.0060$). However, with each manoeuvre, the patients' mean heart rate showed greater increases (the difference in change between the patients and the controls was not significant). Since a racing pulse is associated with anxiety and allergies (19), the increased heart rate in the patient group is noteworthy.

Power spectral density analysis provided the basic information on how variance (in terms of power) distributes as a function of frequency and allows the study of the frequency specific oscillations that correspond to the influences of the sympathetic and parasympathetic branches of the autonomic nervous system respectively (35). By means of this technique it was also possible to instantaneously detect alteration of the autonomic tone in response to changes in posture (during the orthostatic test) or psychological stress. In the frequency domain, the power spectral density of the low frequency band (0.05 - 0.15 Hz) describes the activity of the sympathetic nervous system function, whereas the power spectral density of the high frequencies (0.15 - 0.35 Hz) is indicative of vagal (parasympathetic) activity. Autonomic tone (sympathetic-parasympathetic balance) is described by the ratio between these two frequency bands (LF/HF), indicating which branch of the autonomic nervous system is dominant with physiological compensation, or during a specific bodily position. The amount of variability is demonstrated by the total power in the frequency domain (the sum of the very low, low and high frequency components).

While power spectral densities did not differ significantly between the patients and controls in the supine and sitting positions, there was a significant difference ($p = 0.0188$) in both the low and the high frequencies in the standing position (patients - LF (n.u.): 72.61 (SD 17.96), HF (n.u.): 27.39 (SD 17.96); controls - LF (n.u.): 86.12 (SD 8.97), HF (n.u.): 13.88 (SD 8.97). Patients exhibited lower sympathetic and higher parasympathetic activity in comparison to controls while standing. Chronic corticosterone treatment is one of the factors known to reduce the low frequency component of HRV (36). One can therefore expect high psychological or physiological stress induced cortisol levels to have a similar effect on the sympathetic nervous system. The lower sympathetic activity in the patient group can therefore possibly be contributed to the elevated cortisol levels observed in this group. These differences in parasympathetic and sympathetic activity between the patients and controls were also demonstrated by the sympathetic-parasympathetic balance in the standing position: the LF/HF ratio of the controls was double that of the patients (patients: 5.42, SD 5.36; controls: 10.98, SD 10.11; $p = 0.1046$). This implies that although the sympathetic nervous system is dominant in the standing position in the patients (as seen in the healthy controls), the relative amount of vagal activity in relation to sympathetic activity is higher than in the controls. The lower LF/HF ratio in the patients is also caused by lower than normal sympathetic activity in the standing bodily position.

As far as the physiological compensation to the new bodily position is concerned, notable differences were observed between the patients and controls in the delta value (change from supine to sitting and from sitting to standing) of the spectral densities (Figure 5.1.3., p. 4.26). First of all, the delta values for the change within a group were noteworthy for both the low and high frequency component, but these changes were not all statistically significant because of the great standard deviation calculated for the means. For the change from supine to sitting, the delta value for the low frequency component in the patient group was much smaller than the value for the control group (patients: Δ = 5.81 ms^2, SD 312.6); controls: Δ = 246.01 ms^2, SD 369.31; $p = 0.0739$). Conversely, the delta value for the high frequency component was greater in the patient group (patients: Δ = - 196.15 ms^2, SD 540.54); controls: Δ = - 6.92 ms^2, SD 63.19; $p = 0.1848$). These results imply that upon sitting upright from the supine position, the patients' autonomic nervous system did compensate by increasing sympathetic activity (as expected), but to a much smaller extent than the controls. In addition to the relative lack of sympathetic activity in response to postural change, the parasympathetic nervous system seems to overcompensate by reacting much more strongly to the postural change than did the parasympathetic nervous system of the controls. For the change from sitting to standing, the delta value for the low frequency component in the patient group was similar to that of the control group (patients: Δ = 103.65 ms^2, SD 353.97); controls: Δ = 125.61 ms^2, SD 439.21; $p = 0.8867$). But, the delta value for the high frequency component was significantly lower in the patient group (patients: Δ = -5.19 ms^2, SD 259.89; controls: Δ = - 264.12 ms^2, SD 352.60; $p = 0.0374$). These results imply that upon standing from the sitting position, the patients' autonomic nervous system did compensate by increasing sympathetic activity, almost as happened with the healthy controls. However, it seems as if the parasympathetic nervous system of the patients is unable to compensate for the standing position as happened with the controls. The p-values calculated for the difference in change (delta values) between the two groups was non-significant for both the spectral components (LF and HF).

The patient group also had diminished variability in heart rate (in all three bodily positions), as evident in the lowered total power in the frequency domain. The difference in total power between the patients and controls was significant for the sitting and standing positions ($p = 0.0355$ and $p = 0.0437$ respectively). Although the overall suppression of the autonomic nervous system is probably partially the consequence of the anti-depressive drugs the patients use (as seen in Chapter 3, p.3.38.), lowered heart rate variability still forms part of the status quo of their neurological profile. As far as the physiological compensation to postural change is concerned, the patients and controls seem to respond oppositely from each other in terms of total power. Upon sitting from supine, the total power (heart rate variability) of the patients decreased while that of the controls increased significantly (patients: Δ = - 189.21 ms², SD 763.92; controls: Δ = 273.68 ms², SD 389.66; p = 0.0666). Upon standing up from the sitting position, the total power (heart rate variability) of the patients increased while that of the controls decreased (patients: Δ = 106.05 ms², SD 506.44; controls: Δ = - 143.59 ms², SD 541.33; p = 0.2285). The p-values calculated for the difference in change (delta values) between the two groups was non-significant.

An interesting difference was observed between the patients and controls in response to the psychological stressor. First of all, the patients' mean heart rate increased significantly (p = 0.0005) while filling out the ECR-questionnaire, while the control's heart rate remained the same. In addition, the patients' autonomic nervous system did not seem to respond to the psychological stressor with a decrease in heart rate variability as expected. Figure 5.2.2 (p. 4.28) shows how the total power of the controls decreased while they filled out the ECR-R questionnaire, while the total power of the patients remained the same (patients: Δ = 10.87 ms², SD 113.07; controls: Δ = 259.11 ms², SD 492.82; p = 0.1307). As far as the autonomic balance is concerned, both groups showed sympathetic dominance during the baseline (patients: 2.13, SD 2.47; controls: 2.92, SD 2.4) and stressor recording (patients: 3.16, SD 3.06; controls: 1.89, SD 0.9). However, according to the LF/HF ratio, the patients' autonomic nervous system compensated for the psychological stressor with increased dominance of the sympathetic nervous system (through diminished parasympathetic activity). The controls' autonomic condition shifted to a state of decreased sympathetic dominance by mainly decreasing the sympathetic activity (Figure 5.2.1.B, p. 4.27). Interestingly, a study exploring the relationship between depressed mood and parasympathetic control of heart rate during psychological stress (challenging speech tasks), found depressive mood to be correlated with a greater decrease in vagal activity during stress (37). The patients' depressed mood state could therefore have a relationship with their decrease in parasympathetic activity when exposed to a psychological stressor.

In summary it can be said that, in this study, the fibromyalgia patients' autonomic nervous system activity during a stabilised bodily position was marked by faster mean heart rates, lower sympathetic and higher parasympathetic activity in the standing position (in comparison to controls), a weakened shift towards sympathetic dominance during the standing position and lowered overall heart rate variability. Upon compensation for a new bodily position, their mean heart rates showed greater increase than in the control group. During the second change from sitting to standing, the patients' sympathetic and parasympathetic nervous system showed a similar response to what was observed during the controls' physiological compensation to the first change from supine to sitting. This observation was also made for the total power (amount of heart rate variability). When exposed to the psychological stressor, the patients' autonomic nervous system failed to respond with lowered heart rate variability as seen in the healthy controls. These findings suggest that the patients' autonomic nervous system is reluctant to respond to both physical and psychological stress. It has been shown that an inability to activate the sympathetic nervous system during stress may be a feature of avoidant attachments (38). What is more, the sympathetic nervous system contributes to positive emotions (38). The lowered sympathetic activity of the fibromyalgia patients in comparison to controls might therefore have a relationship with their psychological profile in terms of their mood state and attachment styles. The autonomic perturbations in fibromyalgia may also contribute to the pain experienced by patients (54). Cortelli & Pierangeli (2003) proposed that, since the nociceptive and the autonomic nervous system interact at the levels of the periphery, spinal cord, brainstem and forebrain; it is possible that brainstem pain modulating systems forming part of the central autonomic network may play an important role in the pathophysiology of chronic pain (54).

7. Hemisphere dominance

In this study, the Herrmann Brain Dominance Instrument (HBDI) was used to assess lateralisation in the patient group. The control group was not evaluated for hemisphere dominance because of insufficient funds, but a bank of normal values is available against which findings can be compared. Although Ned Herrmann, the founder of the instrument, claims to have based it on physiology (the instrument was validated against EEG recordings), there are some concerns pertaining to the instrument's division of the brain into limbic and cerebral (cortical) structures as well as the interpretation of the results in neurophysiological terms. For instance, according to the HBDI, a person who tends to be emotional and enjoys being in the company of others, probably shows right limbic thinking.

In neurological terms this is inaccurate, since the limbic structures cannot 'think' but only influence decision making in the frontal cerebral structures. Moreover, it is important to recognise that though referred to as hemispheric dominance, the HBDI in fact measures an individual's preferred way of thinking or 'thinking style'. Despite the criticism of the HBDI, several doctoral degrees were conducted using the instrument. Owing to a lack of alternative affordable methods (and other reasons mentioned in Chapter 2) the instrument was included in the study with the understanding that it was developed from a psychological point of view (regardless of what the founder may claim). For the purpose of this study the focus will thus be on preferred way of thinking as a psychological phenomenon and although HBDI analytical terms are, it is not presumed that thinking is performed by specific quadrants.

Thinking styles is in the context of HBDI terminology named after so-called brain quadrants, e.g. the *cerebral left* (quadrant A), which is associated with mathematical, logical and analytical thinking, as well as a preference towards autonomy; *limbic left* (quadrant B), associated with the need to be in control (leadership), structured tasks and attention to detail; the *cerebral right* (quadrant D), responsible for the ability to take risks, selling ideas, integrating and inventing solutions; and the *limbic right* (quadrant C), involved in working with people, building relationships, teaching, and intuition about other people's intentions and emotional states.

For the purpose of this study, the results obtained by the HBDI were displayed in different ways, each way providing information in a unique manner. First of all, the brain profiles of the patients were plotted onto the two-dimensional graph set out by Herrmann in 'The Creative Brain' (39), called the 'group composite graph' (Figure 6.1.1., p. 4.28). However, it is rather difficult to distinguish the different patient profiles on this graph. For this reason the generic codes for each one of the patients were plotted on another (similar) graph, displaying the generic code of each patient in the quadrant dominant for that specific patient ('generic code' refers to the 27 different types of profiles described by the HBDI, p.2.19; 'dominance' are defined as the quadrant in which peak scores were obtained). In this graph (Figure 6.3.1., p. 4.30) 12 of the 16 patients' generic codes fell in the C quadrant, suggesting that 75% of the patient group is dominant for the limbic right brain quadrant. In other words, the majority of the patients show thinking patterns influenced by input from the right limbic structures in the brain. As a result these patients are very emotional. Two patients' generic codes fell in the B quadrant, showing dominance in the limbic left quadrant. Therefore, during decision-making processes, these individuals will be punctual, organised, and would like to be in control of each situation (the drawback to the need to be in control is that a much anxiety can arise when the person feels that the situation is beyond control). Only one patient's generic code fell into each of the remaining cerebral quadrants (A and D). Although these two patients seem to be an exception to the rest of the patients, their generic codes were still presented very close to the dividing margin between the cerebral and limbic quadrants on the two-dimensional graph. Since the HBDI does not intent to classify subjects into distinct classes, and aims to present the results on this specific graph on a continuum from left to right, and limbic to cerebral, these two patients' thinking styles also seem to have relatively strong influence from the limbic brain structures.

The second way in which the patients' brain profiles were described, were by means of profile code-classes (Figure 6.3.2. A and B, p. 4.31). These classes are groupings of generic codes with common characteristics. Generic codes (e.g. 2-1-3-1, 2-1-1-1 or 3-2-1-1) describe unique combinations representative of the four HBDI quadrants in the following arrangement: A-B-C-D. In these combinations, a '1' indicates a primary (very strong) preference, '2' a secondary preference (intermediate), and '3' a tertiary (low) preference. Therefore, the generic code 3-2-1-1 actually means: cerebral left quadrant A (low preference) – limbic left quadrant B (intermediate preference) – limbic right quadrant C (very strong preference) – cerebral right quadrant D (very strong preference).

In the present study, the patients' brain profiles corresponded to the following profile code-classes:

2-1-1-1: This profile is a triple dominant profile with the three most preferred quadrants being both the cerebral and limbic right quadrants as well as the limbic left quadrant. The highest percentage (43.75%) of the patient group showed this generic code to be their preference as far as thinking styles is concerned. The dominance in three different quadrants is associated with a reasonable amount of integration between organised and structured processing from the left hemisphere (limbic left quadrant), and holistic, synthesising and creative modes of thinking from the right hemisphere. This multi-dominant array of preferences is said to be characterised by a 'generalised' nature, able to utilise most of the brain structures in problem solving. A subgroup of the 2-1-1-1 generic code, is the 3-1-1-1 code. Individuals with this profile function in a similar manner as the 2-

1-1-1 individuals, just more to the extreme. 12.5% of the patients had the 3-1-1-1 profile. What may be problematic about this type of thinking processes (both the 2-1-1-1 and 3-1-1-1 codes) is the lack of preference (or even avoidance in the case of the 3-1-1-1 generic code) of logical, rational and analytical thinking of the left cerebral quadrant. The avoidance of the mode of thinking of this quadrant tends to reinforce the use of the dominant structures, in this case, making the use of the dominant structure more visible (40).

2-2-1-1: The 25% of patients showing this generic profile were mainly right brain orientated (with primaries in both the right hemisphere quadrants). This profile is thus associated with a strong preference for so-called right brain thinking, i.e. visualising, creativity, communication, working with people and being emotional and intuitive. Though all the left-brain functions are available to the individual in problem solving, using the left hemisphere is a secondary preference. One of the patients had the 3-2-1-1 profile (a subgroup of the 2-2-1-1 profile code). To this individual, the use of the cerebral left quadrant is a tertiary preference. As with the 2-1-1-1 profile, it is possible that the functions of the left cerebral quadrant is in point of fact avoided in problem solving (especially in the case of the 3-2-1-1 generic profile).

2-1-1-2: 12.5% of the patients had 2-1-1-2 generic profiles. This profile shows dominance in thought processes influenced by the limbic structures, with two primaries, the limbic left as well as the limbic right quadrant. This profile is characterised by strong preferences towards conservative thinking and controlled behaviour, with a need for organization and structure as well as detail and accuracy. These desires and preferences are due to influence from the limbic left brain structures and cause the individual with primary dominance in this quadrant to worry about details. In addition to, and opposing these thought processes are the emotional and interpersonal preferences from the limbic right quadrant. A primary dominance in this quadrant is associated with high emotionality, intuitive ‘feelings’, an interest in music and a sense of spirituality. These diverse qualities of the two limbic quadrants can lead to internal conflict since both these thinking styles are primary within the same individual (40).

The last three patients did not seem to show similar thinking patterns to the rest of the patient group. Their thinking style preferences were as follows: **1-2-1-1:** This profile is also an example of a triple dominant profile, exhibiting primaries in both the right hemisphere quadrants as well as in the cerebral left quadrant. This individual will be more experimental than organised and more emotional than controlled. **1-1-3-3:** This profile is double dominant in the left hemisphere (cerebral and limbic left quadrants). This profile clearly exhibits an avoidance of the right hemisphere thinking processes. The left-brain characteristics would therefore be even more profound in this profile as it is reinforced by the extreme lack of right-brain thinking. **1-1-1-2:** One of the patients showed this triple dominant profile. Characteristic of this profile is dominant features of both the left hemisphere quadrants and the limbic right quadrant. What was interesting about these patients, was that they were three of the five patients that did not have insecure attachment styles. This may be indicative of the relationship between early life experiences and the development of preference for the utilisation of specific brain quadrants in thinking.

Figure 6.3.2 C (p. 4.31) demonstrated the dominance in the respective HBDI quadrants in yet another way. In this bar graph, the number of patients that showed primary preference in the thinking style associated with each respective quadrant were displayed. (Primary preference is indicated by a score higher than 67 for the quadrant). Only 18.75% of the patients primarily preferred cerebral left quadrant (quadrant A) thinking. The limbic left and cerebral right quadrant styles (B and D) were primarily preferred by 68.75% and 75% of the patients, respectively. The vast majority of the patients (93.75%) showed that the limbic right structure thinking style (quadrant C) was their primary choice in thinking style. In other words, these patients show relatively strong preferences for all the brain quadrants except for the cerebral left quadrant, which is associated with mathematical, logical and rational thinking. The findings summarised on this graph accentuate the avoidance of the cerebral left quadrant in thinking styles as already indicated by the profile code-classes.

Figure 6.1.2. (p. 4.29) illustrates the mean profile for the patients evaluated in this study. In other words, the mean score for each one of the individual quadrants was calculated from the patient scores, and illustrated on a graph to show the ‘average’ fibromyalgia patient’s brain profile for this study. The mean score for the cerebral left quadrant was 54.46 (SD 26.87), 80.69 (SD 18.5) for the limbic left quadrant, 90.94 (SD 22.92) for the limbic right quadrant and 72.56 (SD 22.29) for the cerebral right quadrant. Combining these quadrant scores over the two brain halves, a mean score of 54.38 (SD 11.99) was obtained for the right hemisphere and 45.63 (SD 11.99) for the left hemisphere. The mean score for the cerebral structures was 42.63 (7.46) as opposed to 57.4 (SD 7.46) for the so-called limbic

structures. From this graph, and the data presented in the previous paragraphs, it is thus clear that that there is a strong preference for thinking styles associated with activity in the right brain structures as well as the limbic structures. Most of the patients seem to be very emotional, a characteristic of the quadrant where the limbic and right brain structures overlap (limbic right quadrant).

The HBDI has an interesting and valuable feature in that it, at a certain stage, forces the subject to choose between self-descriptive adjective pairs. Apparently the adjective pair score reveals the thinking style preference that is most instinctive to that person. Therefore, the quadrant with the highest adjective pair score (among the four quadrants) is the thinking style preference that is favoured in stressful situations (39). In the present study, the limbic right quadrant's mean score was notably higher than all the other quadrants (8.63, SD 2.25). This implies that during problem solving activities in stressful situations, most of the patients in this group will exhibit thinking patterns strongly influenced by emotionality. The limbic left quadrant had the second highest score with 6.19, SD 2.26. The mean adjective pair scores for the two cerebral quadrants (left and right) were rather similar with 4.63 (SD 2.5) and 4.56 (SD 2.0) respectively. According to these results, the patients strongly prefer the emotional right limbic quadrant and the organising (or sequential) left limbic quadrant to the two cerebral quadrants in thought processes during stress. Comparing the mean profile scores (which is an indication of thinking styles exhibited in every day life) to the mean adjective pair scores, an interesting shift was observed in the preference of one quadrant to another. Figure 6.2 (p. 4.30) illustrates the mean profile scores in relation to the mean adjective pair scores. There were no remarkable shifts in the scores in the left hemisphere quadrants. Conversely, the mean adjective pair scores for the right limbic quadrant increased notably. Furthermore, the mean adjective pair score for the cerebral right quadrant were noticeably decreased (in relation to the profile score). Thus, in addition to the strong preference for right limbic structure thinking during restful conditions, thinking style preferences for most of the patients in this study group will shift even more to this quadrant during stressful situations. This implies that, during stress, these patients are predisposed to use emotional coping mechanisms, probably because of the loss of the ability to utilise so-called cortical processing for problem solving.

In summary it can be said that the majority of the fibromyalgia patients evaluated in this study appear to use right-brain processing in daily functioning, together with decision making processes strongly influenced by the limbic structures. In HBDI terminology, this type of thinking is characteristic of the 2-1-1-1 generic profile code. According to population studies, the 2-1-1-1-profile code is the most common brain profile, with 16% of the population displaying this generic profile. Moreover, there is a clear female predominance in this profile, with 24% of the female population exhibiting this pattern of thinking processes (40). The second most common generic profile in this present study group, the 2-2-1-1-profile, is the third most common profile in the population (14%) with relatively small differences in the male and female population (11% and 17% respectively). Thus it seems that these profiles are not specific to the fibromyalgia patients, but are representative of the general (healthy) female population. The implication of these findings is perhaps that these specific profiles codes, may not be the cause of firomyalgia symptoms, but rather a predisposing factor in the development of fibromyalgia, explaining the higher prevalence of fibromyalgia among woman. However, there has been no indication that the emotional reaction to stress (as indicated by the adjective pairs in this study) is unique to the 2-1-1-1 and 2-2-1-1-profile. Therefore, emotional coping seems to be typical to this specific fibromyalgia patient group.

In spite of the criticism of the interpretation of the results obtained by the HBDI (especially the strange neurological terminology) there are cerebral perfusion studies confirming the HBDI results mentioned above (41,42,43). Regional blood flow abnormalities detected in fibromyalgia included a decreased flow in the frontal, temporal and parietal areas (cortical structures). In some cases, this hypoperfusion was restricted to the left hemisphere (41). Another study found an 8% reduction in the total cortex perfusion of fibromyalgia patients (42). Therefore, the HBDI results indicating a lower preference for cerebral thinking, especially that of the cerebral left quadrant, are verified by cerebral perfusion results. As far as the strong preference for the right hemisphere is concerned, research has shown that relative greater right frontal EEG activation in adults may be a marker for negative affect, dysphoric mood state, and depression (43). Additionally, greater right frontal EEG activity (influenced by the right amygdala) has been noted in infants and young children with behaviours marked by fearfulness (anxiety) (44). Right brain dominance has also been associated with heightened HPA responsitivity (45). According to these findings, the anxiety, depression and hypercortisolism of fibromyalgia could perhaps be associated with their right hemisphere dominance. This would insinuate that cortisol function could not be regulated by the left hemisphere as speculated at the end of Section 5 (p. 5.17).

Nevertheless, whether the natural emotion-based style of thinking predisposes to the development of fibromyalgia, or whether early life experiences with the development of insecure attachment predisposes to both emotion-based thinking and the development of fibromyalgia, is yet to be investigated by future studies.

8. Attachment

Attachment is an inborn characteristic that motivates an infant to seek proximity to parents and establish communication with them. This system essentially evolves in response to early childhood experiences. The attachment system organises motivational, emotional and memory processes with respect to the mother (or significant caregiving figures) (46). Repeated interpersonal experiences will therefore become encoded in implicit memory as expectations, which will be transformed to mental working models of attachment on what to expect from the caregiver in times of need. In adult life, when confronted with a stress situation, the cognitive schema that predicted the likely behaviour of the attachment figure in threatening circumstances during infancy will allocate appropriate behavioural actions during adulthood (47). The attachment system/ style developed during childhood will thus manifest throughout the lifespan of the individual (48). During times of stress, the adult is likely to seek 'attachment figures' as sources of comfort. For adults, such figures may be close friends or, as assessed in this study, romantic partners (46).

In this discussion, the attachment patterns of the patients and controls are described by Bartholomew's two-dimensional, four-category conceptual scheme of individual differences in adult attachment (refer to Chapter 2, p.2.7). The two dimensions are labeled 'model of self' (relating to anxiety) and 'model of others' (relating to avoidance) (49). Bartholomew's illustration enables researchers to view the subject's attachment styles on a continuum, but defines the diverse ends of the continuum, simplifying the interpretation of results. The four categories described are *securely* attached individuals, who are comfortable with intimacy and autonomy; *preoccupied* individuals, constantly worried about their relationships; *fearful* people, who are fearful of intimacy and socially avoidant; and *dismissing* people, who dismiss intimacy and prefer to be independent (49,50).

The four attachment categories are described in terms of anxiety and avoidance. In this study, the mean anxiety score was 3.45 (SD 1.46) for the patient group and 1.62 (SD 0.49) for the control group. Mean avoidance scores were 3.59 (SD 1.57) for patients and 1.95 (SD 0.88) for controls. The statistical difference (calculated with ANOVA) between the two study groups was highly significant with p = 0.0001 for anxiety and p = 0.0015 for avoidance. The anxiety and avoidance score of each subject was plotted onto Bartholomew's two-dimensional graph, organising all the subjects into the four attachment classes (Figure 7.1., p.4.32).

Reviewing Bartholomew's graph of the subjects in this study, clear differences in the attachment styles of patients and controls can be observed. According to Figure 7.1 and Table 7.1. (p. 4.32.), all the control subjects (100 %) had secure attachment styles (low anxiety and low avoidance). Secure people tend to have relatively enduring and satisfying relationships marked by mutual sharing and a collaborative give-and-take between the members (46). They are comfortable expressing their emotions (50), and tend not to suffer from depression and other psychological/ psychosomatic disorders. The patients, on the other hand, were scattered among all the attachment classes. Only 31.25 % of the patients were secure in their adult romantic relationships. The other 68.75 % of the patient group had insecure attachment styles. 18.75 % showed preoccupied attachment (high anxiety, low avoidance): In general these people tend to have highly conflictual relationships (46). Although they are comfortable expressing their emotions, preoccupied individuals often experience a lot of negative emotions, which can often interfere with their relationships. These individuals can be preoccupied with the past, struggling to forget distressing experiences (46). Another 18.75 % of the patients had fearful-avoidant attachment (high anxiety, high avoidance): Fearful people tend to have much difficulty in their relationships. They tend to avoid becoming emotionally attached to others, and, when they do enter a committed relationship, the relationship may be characterized by mistrust or a lack of confidence (50). Dismissing attachment (low anxiety, high avoidance) was present in yet another 18.75 % of the patient group: Generally, people in this quadrant tend to prefer their own autonomy – oftentimes at the expense of their close relationships. Although these people often have high self-confidence, they sometimes come across as hostile or competitive by others, and this interferes with their close relationships (50). One of the patients (6.25 %) was right between the dismissing-avoidant and secure quadrant. Note that these groupings are general patterns, and that a given individual may reveal elements of more than one attachment classification (46). Additionally, it should be remembered that the grouping of subjects on the two-dimensional graph is not a strict classification of attachment classes, but should be viewed as a continuum ranging from low anxiety and avoidance to high anxiety and avoidance (49).

The question to be asked is: what is the cause of the high anxiety and avoidance amongst the fibromyalgia patient group? Although previous studies on fibromyalgia and attachment could not be found, other studies may throw some light on the question. According to a basic survey with 280 participants diagnosed with fibromyalgia, 62% of the patients reported physical and/ or emotional trauma before fibromyalgia onset (6). In the present study, the patients' medical and psychological pasts with regards to specific traumatic incidents (whether it was previous hospitalisations, surgeries or accidents, or a major psychological distressing happening) were reviewed. It was notable that these patients' histories were often marked by one trauma after the other. The mean number of traumatic events that occurred in the patient group (throughout their lives) was 5.5 events (SD 4.44). Two of the patients reported a total of 14 events that they felt were particularly distressing. In contrast to the patients, the control subjects experienced a mean total number of traumatic events of 2.07 events (SD 0.96) with the highest number of events in the group being four. The statistical difference calculated for the two groups (by means of the Mann-Whitney test) were highly significant ($p = 0.0071$). Further studies are necessary to ascertain whether differences in perception of trauma between normal and fibromyalgia individuals may contribute to the higher incidence of traumatic events reported in the patient group.

Despite the possibility that the testimonies of trauma by the patient group could be exaggerated, ample research findings have confirmed the effect trauma has on the development of the attachment system of an individual (refer to Chapter 1, Section 3.1.). It has already been discussed how interactive experience during early life (transmitted to the infant through its relationship with its primary caregiver) is of prime importance in the maturation of the infant brain. The significance of this relationship explains why relational trauma such as abuse and neglect during early life can have permanent effects on personality organization (51). In this study, patients reported sexual abuse, parental divorce, alcoholic parents, the loss of one or both parents and stressful family environments as early childhood trauma (refer to Chapter 4 – Appendix). When a traumatic event is experienced and the caregiver provides a sense of security, the child is helped to cope by a process called 'interactive repair'. Conversely, with abusive, inattentive or absent parents, extreme levels of stimulation and arousal are induced (or not removed through interactive repair), leaving the child in an extremely disturbed psychobiological state that is beyond his/her immature coping mechanisms (52). Because the attachment system is instinctive to humans, infants will become attached to the primary caregiver, even if the caregiver is psychologically or physically abusive (46). In such cases, insecure attachment is likely to develop, marked by a representational working model of distrust of others (avoidance) and self-doubt (anxiety) (53). If the child experiences 'fright without solution', he will most likely resort to a state of dissociation in order to survive the overwhelming levels of distress (51).

According to Maunder and Hunter (2001) attachment subtypes tend to persist over an individual's lifespan (47). In order to see if age-dependent differences exists in attachment over the lifecycle, statistical correlations were calculated between age and attachment-related anxiety and avoidance. Although no correlations were statistically significant, the direction of the correlations yielded interesting indications and a larger study population may show a more significant trend. The correlation between age and anxiety in the patients was – 0. 12 ($p = 0.6686$), and – 0.24 ($p = 0.3785$) for avoidance. In the control group the correlation between age and anxiety was – 0.46 ($p = 0.0952$) and – 0.25 ($p = 0.3867$) for avoidance. Although the following speculation is not really warranted by the results, it is tempting to argue along the following lines. Firstly, both anxiety and avoidance is negatively related (although non-significant) to age, which means that the patients' as well as the controls' attachment styles seem to become more secure over time. Secondly, in the control group, the r-value (correlation) between age and anxiety was almost twice the r-value for the patient group, signifying that although patient anxiety also decreases with advancing age, the healthy subjects seem to be twice as secure as far as anxiety is concerned as they age. This leads to the speculation that in the fibromyalgia study group, there is resistance to change (becoming more secure in adult relationships), and that attachment behaviour is more likely to stay the same through their lifecycle. Insecurely attached individuals tend to have long-lasting, less complex autoregulatory modes because of underdeveloped subcortical-limbic connections (51). For the purpose of a larger follow-up study it can therefore be hypothesised that, because of the more primitive strategies for survival, these patients lack the ability to incorporate new, positive experiences into their working model of attachment in order to become more secure in romantic relationships as healthy individuals are able to do. However, research is needed on the proposed rigid nature of fibromyalgia patients' attachment styles in comparison to controls. A much larger, longitudinal study might yield interesting results.

In summary, it can be said that the attachment style that developed during childhood is likely to manifest in adult relationships. In this study, the majority of patients were shown to be insecurely attached with higher anxiety and avoidance scores than observed in the control group. According to Bowlby's theory, secure attachment is an "inner resource" that may help the individual to cope successfully with life adversities (55). These individuals deal with distress by acknowledging it, endorsing constructive actions, and turning to others for emotional and instrumental support (56). Without this "secure base", anxious individuals tend to deal with stressful events by relying on passive, ruminative, emotion-focused strategies (56). An anxious attachment style could therefore be associated with the high emotionality of the patients under stress, as indicated by the adjective pairs of the HBDI (refer to Section 7, p. 5.29). Avoidant individuals, on the other hand, might deal with distress by relying on distancing withdrawal strategies (56). The exaggerated activity of the parasympathetic nervous system during stress in this patient group (Section 6, p. 5.19) could have a relationship with the tendency of avoidant individuals to withdraw from stressful situations. The higher incidence of adverse traumatic events during the patients' early lives might be a contributing factor in the development of the insecure attachment styles of the patients.

B. CORRELATIONS

The question to be asked is whether a specific psychoneurological profile could be discerned in the limited group of fibromyalgia patients investigated in this study. This question is answered by reviewing the results discussed in Section A of this chapter in the light of correlations (Pearson coefficients) and predictive relationships (model R-square) calculated through regression analysis (Figure 1). When interpreting these associations, it is to be remembered that the independent variables are possible predictors of fibromyalgia disease status. The dependent variables represent the descriptors of fibromyalgia disease status. When a specific independent variable is the only significant predictor of a dependent variable, their relationship is expressed in model R-squares (reported as r^2 or a percentage). When there is more than one significant predictor, the relationship with the dependent variable is expressed as partial R-squares (reported as r^2 or a percentage). The relationships within the independent variable group and within the dependent variable group were calculated as correlations (only significant r-values are cited).

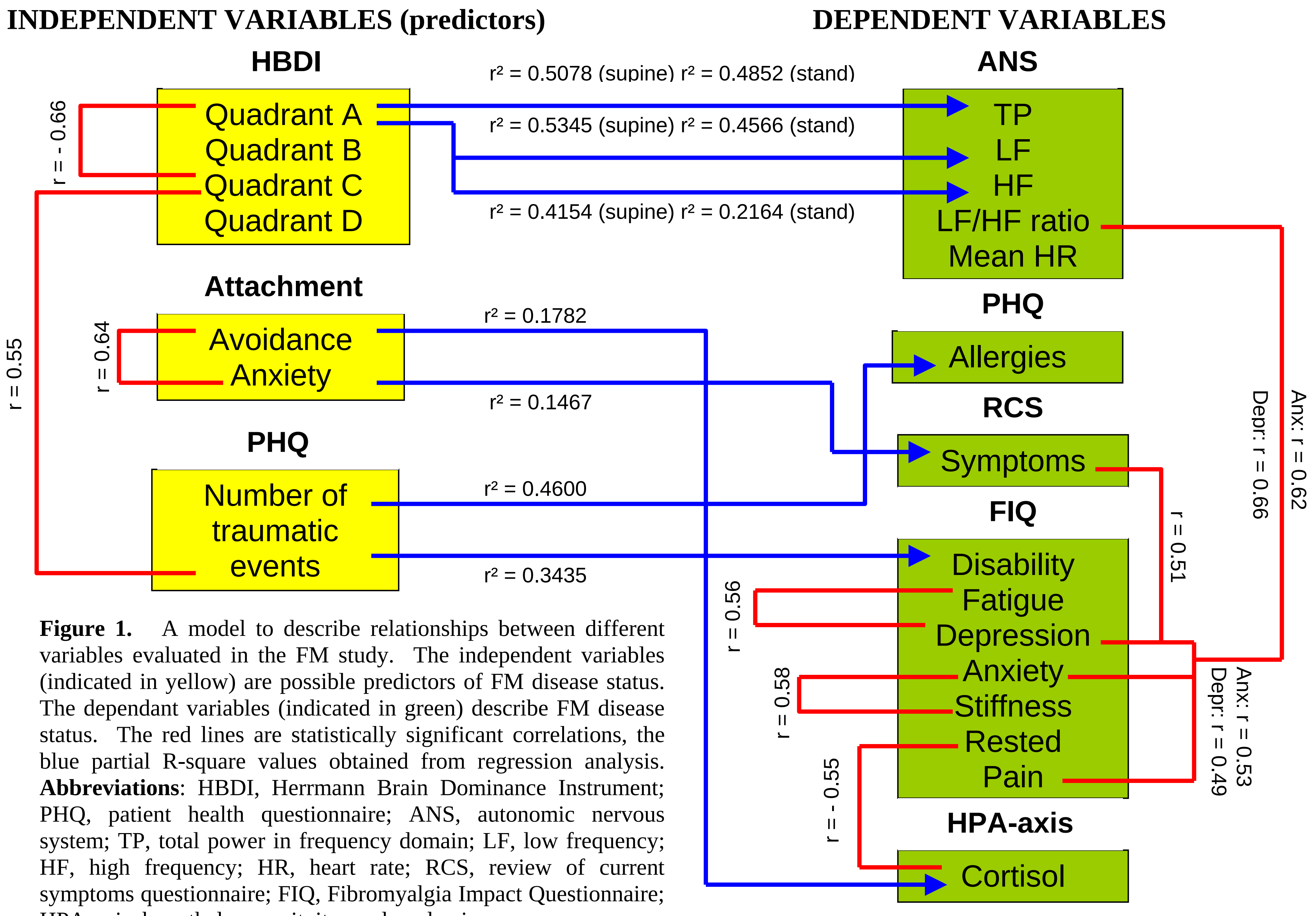

Figure 1. A model to describe relationships between different variables evaluated in the FM study. The independent variables (indicated in yellow) are possible predictors of FM disease status. The dependant variables (indicated in green) describe FM disease status. The red lines are statistically significant correlations, the blue partial R-square values obtained from regression analysis. **Abbreviations**: HBDI, Herrmann Brain Dominance Instrument; PHQ, patient health questionnaire; ANS, autonomic nervous system; TP, total power in frequency domain; LF, low frequency; HF, high frequency; HR, heart rate; RCS, review of current symptoms questionnaire; FIQ, Fibromyalgia Impact Questionnaire; HPA-axis, hypothalamus-pituitary-adrenal axis.

There can be no doubt that the patient group fully met the diagnostic criteria for fibromyalgia (set out by the American College of Rheumatology) and that their reported pain and physical discomfort levels (as seen from the FIQ) were significantly higher than normal (<0.0001). The patients also presented with a significantly higher number of symptoms (<0.0001). Regression analysis showed anxiety to be the best predictive factor in the number of symptoms a patient developed (model R-square = 14.67%). As would be expected, anxiety and depressive symptoms correlated positively with their degree of pain ($r = 0.53$, $p = 0.0429$ and $r = 0.49$, $p = 0.0607$ respectively). Anxiety also correlated with muscle stiffness ($r = 0.58$, $p = 0.0240$), confirming the 'pain-anxiety-muscle tension hypothesis' (discussed in Chapter 1, p.1.8) which states that the anxious individual creates a cycle whereby his chronic anticipation leads to increased muscle tension, causing muscle tightening, which eventually becomes a source of pain leading to additional anxiety, reinforcing the cycle. Depression had a positive correlation with the total number of symptoms the patients presented with ($r = 0.51$, $p = 0.0507$). It was also seen that most (87.5%) of the patients met the diagnostic requirements for chronic fatigue syndrome. In this study, fatigue did not correlate significantly with the degree of pain experienced by the patient group, though ($r = 0.37$, $p = 0.1744$). Nevertheless, fatigue did seem to have a relatively strong relationship with depression ($r = 0.56$, $p = 0.0312$).

When attachment styles were considered, the majority of patients showed insecure attachment styles. The two dimensions of attachment, i.e. anxiety and avoidance, had a strong positive correlation ($r = 0.64$, $p = 0.0099$), indicating that a high score in the one dimension is usually associated with a high score in the other. In contrast to the control group, the older portion of the patients did not seem to be any more secure than the younger group, illustrating the inflexible nature of their attachment styles. As attachment style is considered dependent on early life experiences, especially the interaction with primary caregivers, it was considered useful to evaluate both experimental groups for the prevalence of traumatic events during childhood. Of interest is the fact that the perceived or rather reported prevalence of significant adverse events in the patients' adult lives were also significantly higher (than that of the control group) and may show these events as contributing factors to the development of their symptoms. Another point of interest is that according to the partial R-square calculated through regression analysis, the number of adverse events that occurred throughout the individual's lifetime accounts for 34.35% of fibromyalgia impairment and 46.0% of the number of allergies the individual suffer from.

According to the HBDI results, the majority of patients exhibit thinking patterns strongly influenced by the right limbic brain structures, a tendency which seems to be exacerbated under stress. The strong emotionality of their preferred way of thinking correlated significantly with the number of adverse events ($r = 0.55$, $p = 0.0351$). The model R-square indicated that the preference for left cerebral thinking predicts 50.78% of the of heart rate variability at rest and 48.52% during physical stress. It also accounted for 53.45% of the sympathetic activity during rest and 45.66% of the sympathetic activity during physical stress. The partial R-square for the relationship between vagal activity during rest and analytical thinking patterns was 0.4154. The implication is that their avoidance of logical, rational thinking accounts (at least in part) for the overall lowered heart rate variability observed in the patient group.

Some deviations from the norm were noted in their neuroendocrine profile. Firstly, the cortisol levels were significantly higher than normal ($p = 0.0003$). 17.82% of the cortisol level seems to be predicted by attachment-related avoidance ($r^2 = 0.1782$). The elevated cortisol levels in the patient group were negatively correlated ($r = -0.55$, $p = 0.0354$) with how rested the patients felt following a night's sleep. In other words, the higher the cortisol level, the less the patients could maintain a full night's sleep, and the less they felt rested in the morning. What is of great importance is the fact that the heart rate variability of these patients, which is a reflection of the autonomic nervous system function, was significantly lower than normal ($p = 0.0437$). Decreased heart rate variability during rest is generally seen as an indication of physical and psychological illness, which confirms that fibromyalgia disease state is accompanied by psychological and physiological abnormalities. The patients' autonomic nervous systems were also reluctant to respond to both physical and psychological stress. In the standing position, patients seemed to have lower sympathetic and higher parasympathetic activity. With regard to sympathetic-parasympathetic balance, they exhibited a weakened shift towards sympathetic dominance upon physical stress. The autonomic balance of the patients correlated with depression ($r = 0.66$, $p = 0.0079$) and anxiety ($r = 0.62$, $p = 0.0130$) as determined by the FIQ.

C. PSYCHONEUROLOGICAL PROFILE OF FIBROMYALGIA PATIENTS ACCORDING TO RESULTS FROM THIS STUDY

It can be said that the patient group in this study were characterised by a high prevalence of adverse events, insecure attachment styles, thinking styles marked by high emotionality in the absence of rationality, multiple somatic symptoms (apart from chronic pain), and altered stress-axes activity reflected in low heart rate variability, poor autonomic responses to acute stressors and elevated basal cortisol levels. In most cases, these results differed significantly from the age- and sex-matched control group. Therefore it can be concluded with confidence that this specific group of fibromyalgia patients have a distinct psychoneurological profile.

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