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Alexithymia, sense of coherence and dysregulation of biorhythms in fibromyalgia: implications for pain management and quality of life.

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per Anna,
e tutte le donne della mia famiglia.

‘‘Considering pain not as a marker of injury
but as a human experience
should not be an alternative or niche therapy,
but the very thing that unites us’’

Patrick Wall,
World Congress on Pain,
Vienna, Austria, 1999

Index

1. Background

1.1. Epidemiology and pathogenesis of Fibromyalgia

Fibromyalgia (FM) is a chronic syndrome, characterized by lasting and diffuse chronic musculoskeletal pain, that affects 0.4–8.8 % of the general population worldwide, with a global mean prevalence of 2.7 % (3.1 % in the Americas, 2.5 % in Europe, and 1.7 % in Asia), with women outnumber men by an average of 3:1 (Arnold et al, 2016; Wolf et al, 1995; McBeth et al, 2007; Jones et al, 2014; Queiroz, 2013; Vincent et al, 2013; Branco et al, 2010). FM is more prevalent also in people older than 50, with low education level, in those with low socioeconomic status and living in rural areas (Queiroz, 2013).

It is well known that FM is often co-morbid with other pathologic conditions such as headache, chronic fatigue syndrome, irritable bowel syndrome, difficulties with memory, concentration, mood and personality disorders, anxiety and psychological distress that strongly worse the quality of life of people affected (Queiroz et al, 2013; Carta et al, 2006; 2013a; Castelli et al, 2012; Malin&Littlejohn, 2012; Marcus&Deodhar, 2011; Mease, 2005).

Lacking an exact definition (Bennet, 2016), FM is commonly classified as "functional syndrome" because its etiology, pathogenesis and symptoms are not completely explained (Borchers & Gershwin, 2015), and as a "central sensitization syndrome" (Arnol et al, 2016; Adams et al, 2015; Cagnie et al, 2014; Nijs et al, 2011; Meus et al, 2007; Yunus, 2015, 2008, 2000; Meyer et al, 1995; McCarberg, 2012; Phillips et al, 2013), characterized by an increased sensitivity in the central nervous system to several stimuli (i.e.: pressure, light, medication, temperature) (Ngian et al, 2011; Arnold et al, 2016).

This hyperexcitability of the central nervous system in people with FM can be explained by, at least, three mechanisms (van Ittersum et al, 2013): 1) the extent of original nociception from damage or inflammation of peripheral tissue; 2) genetic factors; 3) psychological and behavioral factors that increased cerebral activation of limbic structures, the insula and large areas of the frontal, temporal and parietal cortices, resulted in a diminished inhibition of the descending pathways, crucial in the onset and maintenance of symptoms in patients with FM.

Glial cells activation by various stimuli also appears to play an important role in FM, when the release of pro-inflammatory cytokines, nitric oxide, prostaglandins and reactive oxygen are prolonged and stimulate the hyperexcitability of the spinal cord (Watkins et al, 2001).

Furthermore, various neurotransmitters also seem to be involved in the central sensitization. Serotonin, its precursor tryptophan and its metabolites are involved in pain, sleep and mood modulation and they appear lower in serum level and in the cerebrospinal fluid of people with FM, explaining its relation with mood disorders (Bellato et al, 2012). Other neurotransmitters also play a role, such as norepinephrine, dopamine, substance P, endorphins and metenkephalins. They belong to the endogenous opioid system that seem to be hyperactive but unable to modulate pain in people with FM (Bellato et al, 2012).

Finally, many authors insist on the role of stressful events in inducing a disruption of the hypothalamic-pituitary-adrenal (HPA) axis in people with FM: the exposure to prolonged stressful conditions can alter this axis functionality, with an increased production of the corticotrophin releasing factor and a potentially amplified pain perception (Burke et al, 2016; McBeth et al, 2005).

Since 90', meta-analyses (Herbert&Cohen, 1993; Zorrilla et al, 2001) have been shown mutual relations between central nervous, immune and

endocrinology systems in the stress response, mainly by the HPA axis and the Sympathetic Nervous System (SNS). Included studies in the meta-analyses above pointed out consistent stress-related increases in numbers of total white blood cells, as well as decreases in the numbers of helper T cells, suppressor T cells, cytotoxic T cells, B cells, and natural killer cells (NK). They also reported stress-related decreases in NK and T cell function, and T cell proliferative responses to phytohaemagglutinin (PHA) and concanavalin A (Con A).

Furthermore, HPA axis activity and cytokines are intrinsically intertwined: inflammatory cytokines stimulate adrenocorticotropic hormone (ACTH) and cortisol secretion, while, in turn, glucocorticoids (GC) suppress the synthesis of pro-inflammatory cytokines. In recent years the classic view that GC are universally anti-inflammatory has been challenged (Sorrels et al, 2009; Sorrels & Sapolsky, 2007). Under some circumstances, acute GC exposure could have pro-inflammatory effects on the peripheral immune response, as well as chronic exposure to GCs has been found to have pro-inflammatory effects on the specialized immune response to injury in the central nervous system (Sorrels & Sapolsky, 2007). Moreover, there are considerable individual differences in vulnerability to stress-related disease, including psychiatric disorders (Sorrels et al, 2009; Sapolsky, 2015).

These evidences may help to better understand that, after a long or severe overburdening due to stressful events, the dysregulation of stress-response system may play an important role in central sensitization process (Van Houdenhove & Luyten, 2009; Meus & Nijs, 2007). Hence, in vulnerable individuals, it may result in reduced effort tolerance and increased levels of pain and fatigue (Van Houdenhove & Luyten, 2009; Van Houdenhove & Egle, 2009; Fries et al, 2005).

In particular, increasing evidence supports a significant association not only between physical (Schwaller and Fitzgerald, 2014; Beggs, 2015) but also with psychological stress and trauma in early life and a great incidence of various types of chronic pain conditions (i.e.: FM) in later life (Burke et al, 2016). It seems that some key neurobiological substrates, including the hypothalamic-pituitary-adrenal axis, monoaminergic, opioidergic, endocannabinoid and immune systems, and epigenetic mechanisms play an important role in this association (Burke et al, 2016).

A recent meta-analysis (Afari et al, 2014) on the association between psychological trauma and Post Traumatic Stress Disorder (PTSD) with functional somatic syndromes, including FM, pointed out that people who reported exposure to trauma were 2.7 (95% CI = 2.27 – 3.10, $p<0.05$) times more likely to have a functional somatic syndrome.

Furthermore, some studies showed elevated levels of cortisol, mainly in the evening, associated with a dysregulation of circadian rhythms in FM and other chronic rheumatic conditions (Korszun , 2000, Ferraccioli et al, 1990; McCain &Tilbe, 1989). A recent study (Ucar et al, 2015), the only one in the field, specifically showed that disturbances of biological and social rhythms (sleep, eating, social and activity patterns) are marked in people with FM, with an association between this rhythms instability, pain severity and depressive symptoms.

1.2. Fibromyalgia and alexithymia

Negative emotions, psychological trauma, victimization, or serious emotional and relational conflicts are commonly experienced in people with FM and other central sensitization pain conditions and may amplify pain perception (Burger et al, 2016; Gatchel et al, 2007; Van Middendorp et al, 2008; 2010a, 2010b). This implies that how people with FM regulate

their emotions may be relevant for pain management, the adjustment to the impact of the syndrome and their quality of life (Geneen et al, 2012).

Alexithymia, literally "absence of words for emotions" (Sifneos, 1972), is a personality trait referred to a cognitive processing deficit in emotions regulation, characterized by difficulties in identifying and communicating feelings, distinguishing between feelings and the bodily sensations of emotional arousal and restricted imagination processes (i.e.: lacking of imagination, stimulus bounding, externally oriented cognitive style) (Taylor et al, 2016; 1997; Taylor & Bagby 2004; Taylor, 2000; 1984) . It is observed in many clinical conditions, especially in psychosomatic disorders (Taylor et al, 1997; Taylor, 2000), in which psychological factors, even if don't reach the threshold of a psychiatric disorder, may affect quality of life and entail pathophysiology and have therapeutic implications (Fava et al, 2016; Porcelli et al, 2015; Meloni et al, 2016; Carta et al, 2013b: Preti et al, 2013).

Two recent systematic reviews (Di Tella&Castelli, 2016; 2013) showed that people with FM: 1) have higher prevalence of alexithymic trait (range 15-20%) compared to healthy controls, especially about difficulties in identifying and describing feelings, and 2) those with clear alexithymic trait present higher levels of pain when compared with subjects with low alexithymia, even if this association is often mediated by other psychological factors, especially depression.

1.3. Fibromyalgia and sense of coherence

If alexithymia worse the adaptation and pain management in FM, sense of coherence (SOC) refers to a more positive view of general health and derived from the salutogenic model of health promotion (Antonovsky, 1996). It concerns to the abilities of people to comprehend, manage and give meanings to life events, in order to maintain good health and well-

being (Lindstrom and Eriksson, 2006). Salutogenic model opens to the idea of well-being as something more positive than the absence of pain, suffering and need for medical care (Mittelmark&Bull, 2013).

Recently, it was pointed out the role of SOC in predicting improvement in psychological distress, overall general health, pain impact and quality of life in people with chronic pain (Lillefjell et al, 2015), reumathoid arthritis (Goulia et al, 2015), osteoarthritis (Benz et al, 2013). It was also shown the association between SOC and other psychological resistance resources (self-esteem, generalized self-efficacy, optimism, and social support) in older adult, and its role both as determinant of pain severity and as mediator between pain severity and such psychological resistance resources (Wiesmann et al, 2014). Moreover, SOC, together with pain severity and self-efficacy, were found to be significant determinants of life satisfaction in people with long-term musculoskeletal pain (Anke et al, 2013).

Just few studies have pointed out the association between SOC, well-being and adaptation to the illness in FM (Schrier et al, 2012; Govender et al, 2009; Söderberg et al, 1997). A study about the efficacy of ten-weeks physical therapy program on the impact of FM showed that pre-treatment perception of symptoms, well-being and SOC are predictors of the perception of general health at the follow-up (Hävermark&Langius-Eklöf, 2006).

Hence, if there are currently no known cures for FM, as well as for other chronic diseases, the necessity of a multidisciplinary approach to treatment for FM is clear and supported by international guidelines, with particular attention to psychotherapies, psychological and psycho-educational interventions for the assessment and treatment of pain (Castelnuovo et al, 2016a, 2016b; Arnold et al, 2016; Ablin et al, 2013;

Nijis et al, 2011). These interventions are usually aimed to focus on learning the origin of centralized pain and coping strategies to alleviate its severity, to improve somatic and emotional awareness, to cope with and manage residual symptoms of the illness and to maximize health-related quality of life despite symptoms of FM (Turk et al, 2016; Burger et al, 2016; Castelnuovo et al, 2016a, 2016b).

1.4. Aims and hypothesis of the study

The main aim of the present study was to verify the role of high alexithymia and low SOC as determinants (risk factors) for a severe FM impact, severe pain (current and in the last week), severe pain impact and poor QOL in a sample of 50 women with FM.

A secondary aim was to evaluate, in a sub-sample of 24 women with FM, the associations between the dysregulation of biological and social rhythms (eating, sleeping, daily life and social activities), FM impact, pain severity (current and in the last week), pain impact and QOL.

In the entire sample, it was hypothesized: 1) an association between SOC and FM impact, pain severity, pain impact and QOL, hence the higher SOC, the higher QOL, the lower FM impact, pain severity and pain impact; 2) an association between alexithymia and FM impact, pain severity, pain impact and QOL, hence the higher alexithymia, the lower QOL, the higher FM impact, pain severity and pain impact; 3) the significant role of high alexithymia and low SOC as determinants (risk factors) for severe FM impact, pain severity, pain impact and poor QOL.

In the sub-sample, it was hypothesized an association between the dysregulation of biological and social rhythms, FM impact, pain severity, pain impact and QOL, hence the higher the dysregulation, the higher the FM impact, pain severity, pain impact and the lower QOL.

2. Methods

2.1. Study sample, design and procedure

This correlational, case-control study was conducted among 50 consecutive women afferent to the Rheumatologic Service at the University-Hospital of Cagliari, Italy from November 2012 to October 2014, fulfilled the American College of Rheumatology Diagnostic Criteria for Fibromyalgia (Wolfe et al, 2010). Once recruited, all the patients were asked to answer to a clinical structured interview to assess psychiatric disorders and to fill a battery of self-report questionnaires to assess some psychosocial and behavioral factors, QOL, FM impact and pain severity.

2.2. Ethic Statements

All the evaluations of the study were conducted in accordance with the Declaration of Helsinki as part of the usual clinical practice. All the participants were verbally asked to give their informed consent to participate in the study.

2.3. Instruments

The Fibromyalgia Impact Questionnaire (FIQ) (Burckhardt et al, 1991; Bennet, 2005) in the Italian version (Sarzi-Puttini et al, 2003) was used to assess the impact of FM in the last week, in terms of physical functioning, feeling good, missing work, doing job, pain, fatigue, rest, stiffness, anxiety and depression. It is a self-report questionnaire composed by 20 item with Likert scales and visual analogical scales and its total score ranges from 0 to 100, with 100 marking the worst impact. Regarding the severity of the impact, a FIQ total score < 39 was found to represent a "mild" impact, ≥ 39 to < 59 "moderate", and ≥ 59 "severe" impact (Bennet et al, 2009).

The item “Pain” of the FIQ was used as an index of pain intensity in the last week. The score was obtained by its visual analogue scale, comprised of a horizontal line 10 centimeters in length, anchored by 2 verbal descriptors, one for each symptom extreme, ranging between 0= “no pain” to 10= “worst imaginable pain”. The respondent is asked to put a perpendicular sign to the line at the point that represents his/her pain intensity. Regarding the level of pain intensity, a score ≥7.5 was found to represent a “severe” pain (Boonstra et al, 2014).

Another Visual Analogue Scale (VAS) (Hawker et al, 2011) was used as a self-report single-item measure to assess the current pain intensity. A VAS score ≥7.5 was found to represent a “severe” pain […] (Boonstra et al, 2014).

The Short Form Health Survey (SF-12) (Ware et al, 1996) in the Italian version (Kodraliu et al, 2001) was used to measure quality of life (QOL). The SF-12 is a brief, valid, reliable and cross culturally applicable instrument, worldwide used. It consists of two domains: mental and physical health. The items can be rated by 3 or 5 points Likert scale. The total score ranges from 12 to 47, with higher scores indicating higher QOL in the last month.

The item “pain” of the SF-12 was used as an index of pain impact on daily work activities in the last month. The score ranges between 1= extremely to 5= not at all.

The Toronto Alexithymia Scale – 20 item (TAS-20) (Taylor et al, 2003; Parker et al, 2003) in the Italian version (Bressi et al, 1996) was used to

assess alexithymia and its three factors. It is a 20 item self-report questionnaire, with five-points Likert scales, that provides a total score and a score for each factor: "difficulty identifying feelings" (Factor 1), which measures the difficulty in distinguishing specific emotions and between emotions and bodily sensations of emotional arousal; "difficulty describing feelings" (Factor 2), which measures the difficulty in communicating by words one's emotions to the others; and "externally-oriented thinking" (Factor 3), which assesses the attitude to focus the attention externally and not on the inner emotional experience. The TAS-20 total score ranges from 20 to 100, with higher scores indicating higher levels of alexithymia. The cut-off scores are: $\leq$ 50 "low" alexithymia, 51-60 "mild" alexithymia, $\geq$ 61 "high" alexithymia.

The Sense of Coherence Scale 13- item (SOC) (Antonovsky et al, 1993) in the Italian version (Sardu et al, 2012) was used to measure the sense of coherence.

The SOC is a 13 item self-report questionnaire with 7-points Likert scales, that provides a total score and a score for each dimension: "comprehensibility" (C), which refers to the ability to perceive life events as consistent, structured and clear; "manageability" (Ma), which refers to the ability to perceive that available resources fit life's demands; and "meaningfulness" (Me), which refers to the feeling that life, emotionally, makes sense. The total score ranges from 13 to 91, with higher scores indicating a stronger SOC.

The Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN) (Giglio et al, 2009) in the Italian version (Moro et al, 2014) was used to measure the dysregulation of biorhythms, as the frequency of problems related to the maintenance of circadian rhythm regularity. It is

an interviewer-administered instrument including 21 items that evaluate five domains: “sleeping”, which refers to the capacity to maintain the regularity of the sleep patterns; “eating”, which refers to the capacity to maintain the regularity of diet patterns; “activities”, which refers to the capacity to maintain the regularity of the daily activities including household and work duties, physical activities, and sexual relationships; “social rhythms”, which refers to the capacity to maintain the regularity of the social activities and interpersonal relationships and “predominant rhythm”, which refers to the preference of work functioning or social functioning during day or night. All items were rated using a 4 points Likert scale scored 1 = not at all, 2 = seldom, 3 = sometimes, 4 = often, or in some items 1 = never, 2 = seldom, 3 = often, 4 = always, with higher scores indicating higher levels of dysregulation.

2.4. Statistical Analyses

Data were analyzed with the Statistical Package for Social Science (SPSS) for Windows (Chicago, Illinois60606, USA), version 21.

The descriptive statistics (N, %; mean ± sd) were used for nominal and continuous variables to point out the demographic characteristics of the samples (age; marital status; education level; occupation).

Pearson’ Correlations were performed to verify: 1) the associations between SOC, alexithymia, FM impact, pain severity, pain impact and QOL in the entire sample (N=50), and 2) the associations between dysregulation of biological and social rhythms, FM impact, pain severity, pain impact and QOL in the sub-sample (N=24).

Then, severe FM impact, severe pain, severe pain impact and poor QOL were assumed as outcomes for the case-control study design, on the basis of the FIQ cut-off scores ≥ 59 “severe” impact […] (Bennet et al, 2009),

the VAS for pain cut off ≥7.5 “severe pain”, the SF-12 “pain” and “total” scores ≤ 25°percentil “severe” impact of pain and “poor” QOL, the sample was five times divided into “cases” (FIQ total≥ 59; FIQ “pain” ≥7.5; VAS ≥7.5; SF12 “pain” ≤ 25°percentil; SF12 “total” ≤ 25°percentil) and “controls” (FIQ total< 59; FIQ “pain” <7.5; VAS <7.5; SF12 “pain” >25°percentil; SF12 “total” > 25°percentil).

A series of Chi-Square (nominal variables) and one-way ANOVA (continuous variables) were used to verify the homogeneity between “cases” and “controls”, in order to control for potential confounders factors (age, marital status, educational level, occupation).

Finally, the Odds Ratio association (univariate analysis) was calculated between each factor (high alexithymia; low sense of coherence) assumed as risks for each outcome (severe FM impact; severe actual pain; severe pain in the last week; severe pain impact; poor QOL) using the χ^2 test in 2 × 2 tables.

If high alexitymia is commonly defined by TAS-20 total score cut off ≥61(Parker et al, 2003) […], the categorization about high and low SOC is never defined by standardized cut offs (Helvik et al, 2014) […]. Even so, the categorization done in the present study using the 33.3° percentile to define the cut off for the levels of SOC is already performed by other authors (Helvik et al, 2014).

3. Results

3.1. Sociodemographic characteristics of the sample.

As shown in Table 3., in the overall sample (N=50) the mean age was 50±10.810 years old; about the educational level, N=6 had a degree, N=23 had a high school diploma, N=18 a primary school diploma, N=2 a secondary school diploma and N=1 did not report; about the marital

status, N=37 women were married, N=9 nubile, N=3 separated-divorced and N=1 was widow. Finally, about the occupation, N=18 were employed, N=18 housewifes, N=9 retired and N=10 were unemployed.

3.2. Associations between SOC, alexithymia, FM impact, pain severity, pain impact and QOL in the entire sample (N 50).

As shown in Table 1., in the entire sample (N=50) it was found statistically significant correlations between SOC, FM impact, pain severity in the last week and QOL, hence the higher the SOC scores:

- the lower the FM impact (FIQ total score/SOC total score: R= -0.495, p=0.000; FIQ total score/SOC "comprehensibility" score: R= -0.475, p=0.000; FIQ total score/SOC "manageability" score: R= -0.312, p=0.027; FIQ total score/SOC "meaningfulness" score: R= -0.503, p=0.000);
- the higher the QOL (SF12 total score/SOC total score: R= 0.645, p=0.000; SF12 total score/SOC "comprehensibility" score: R= 0.579, p=0.000; SF12 total score/SOC "manageability" score: R= 0.453, p=0.001; SF12 total score/SOC "meaningfulness" score: R= 0.648, p=0.000);
- except for the "manageability" dimension, the lower the pain severity in the last week (FIQ "pain"/SOC total score: R= -.366, p=0.009; FIQ "pain"/SOC "comprehensibility" score: R= -.348, p=0.013; FIQ "pain"/SOC "meaningfulness" score: R= -.389, p=0.005).

Regarding the pain impact in the last month (SF12 "pain"), there was a significant trend about the correlation with the SOC total score (R= -0.270, p=0.057) and statistically significant correlations with SOC "comprehensibility" score (R= -0.328, p=0.020) and SOC

"meaningfulness" (R= -0.282, p=0.047), hence the higher the sense of coherence scores the lower the pain impact.

It was not found any statistically significant correlation between SOC scores and current pain (VAS score), except for the SOC "comprehensibility" score (R= -0.280, p=0.049).

Alexithymia (total score and "f1 - difficulty identifying feelings") was significantly correlated with FM impact, pain severity and QOL, hence the higher the TAS-20 scores:

- the stronger the FM impact (FIQ total score /TAS-20 total score: R= 0.308, p=0.030; FIQ total score/TAS-20 "f1 - difficulty identifying feelings" score: R= 0.387, p=0.005);
- the higher pain severity in the last week (FIQ "pain"/TAS-20 total score: R= 0.340, p=0.016; FIQ "pain"/TAS-20 "f1 - difficulty identifying feelings" score: R= 0.369, p=0.008);
- the poorer QOL (SF12 total score/TAS-20 total score: R= -0.419, p=0.002; SF12 total score/TAS-20 "f1 - difficulty identifying feelings" score: R= -0.497, p=0.000).

It was not found any statistically significant correlation between alexithymia scores and pain impact in the last month (SF12 "pain") as well as between alexithymia scores and current pain (VAS score), except a significant trend for a correlation between TAS-20 "f1 - difficulty identifying feelings" and VAS score (R= -0.273, p=0.055).

3.3. Controlling for confounding factors in "Cases" and "Controls".

The mean scores about outcomes of interest (severe FM impact, severe pain, severe pain impact and poor QOL) of "Cases" and "Controls" are shown in Table 2.

As shown in Table 3., “Cases” and “Controls” did not show any statistically significant difference regarding age, marital status, education level, occupation, except about current pain severity as expressed by VAS: there were more employees and housewifes in “Controls” then in “Cases” (χ^2=14.672, df=4, p=0.005).

3.4. High alexithymia and low SOC as risk factors for a severe FM impact, severe pain and poor QOL.

Table 4. lists the frequencies, in “Cases” and “Controls” for each outcome, about factors considered as determinants. High alexithymia resulted being a risk factor for severe FM impact (χ^2= 4.372, p= 0.037; OR= 4.375, CI 95% 1.032-18.556), pain severity in the last week (χ^2= 5.109, p= 0.024; OR= 5.806, CI 95% 1.128-29.892) and poor QOL (χ^2= 5.937, p=0.019; OR= 4.978, CI 95% 1.295-19.130) (See also Figure 1., 2., 3.).

Also low SOC was a risk factor for severe FM impact (χ^2= 4.987, p=0.026; OR= 4.286, CI 95% 1.143-16.071), pain severity in the last week (χ^2= 7.414, p= 0.006; OR= 7.875, CI 95% 1.547-40.091) and poor QOL (χ^2= 8.517, p=0.005; OR= 6.429, CI 95% 1.735-23.819) (See also Figure 4., 5., 6.).

High alexithymia nor low SOC did not show any significant association with severe current pain and severe pain impact.

3.5. Associations between dysregulation of biological and social rhythms, FM impact, pain severity, pain impact and QOL.

As shown in Table 5., in the sub-sample (N=24) it were found statistically significant correlations between dysregulation of biological and social rhythms, FM impact, pain severity and QOL, hence the higher the BRIAN

"total" score, the higher the FM impact (BRIAN total/FIQ total: R= 0.679, p=0.000), the pain severity in the last week (BRIAN tot/FIQ pain: R= 0.399, p= 0.05), the current pain severity (BRIAN total/VAS: R= 0.408, p=0.048), the pain impact (BRIAN total/SF-12 pain: R= -0.699, p= 0.000) and the poorer the QOL (BRIAN total/SF-12 total: R= -0.724, p=0.000).

Furthermore, the higher the BRIAN "activities" score, the higher the FM impact (BRIAN activities/FIQ total: R= 0.796, p=0.000), the pain severity in the last week (BRIAN activities/FIQ pain: R= 0.572, p=0.004), the current pain severity (BRIAN activities/VAS: R= 0.425, p=0.038), the pain impact (BRIAN activities/SF-12 pain: R= -0.650, p=0.001) and the poorer the QOL (BRIAN activities/SF-12 total: R= -0.787, p=0.000).

There were further significant correlations between BRIAN "social" score and the FM impact (BRIAN social/FIQ total: R= 0.425, p=0.039), pain impact (BRIAN social/SF-12 pain: R= -0.471, p=0.02) and QOL (BRIAN social/SF-12 total: R= -0.522, p=0.009); between BRIAN "sleeping" score, pain impact (BRIAN sleeping/SF-12 pain: R= -0.464, p=0.022) and QOL (BRIAN sleeping/SF-12 total: R= -0.397, p=0.05); between BRIAN "eating" and current pain severity (BRIAN eating/VAS: R= 0.407, p=0.048).

4. Discussion

This case-control study was aimed to point out the role of high alexithymia and low SOC as risk factors for a worse FM impact, related pain and QOL in a sample of women with this syndrome.

In the entire sample, it was found that the impact of FM, related pain and QOL were negatively correlated with SOC and positively with alexithymia. Specifically, high alexithymia and low SOC resulted as significant risk factors for a severe FM impact, severe pain and poor

QOL, after controlling for potential confounders such as age, marital status, education level, occupation.

These results are coherent with recent systematic reviews and recommendations about the FM management, that summarized the amount of studies that underlined the role of psychological factors in the genesis and maintenance of pain (Castelnuovo et al, 2016b), the importance to assess these factors to evaluate how emotions, cognition and behaviors influence the course of pain treatments (Castelnuovo et al, 2016b), and to tailor the best psychological support, within a multidisciplinary approach, to foster and reduce pain intensity in pain-related illness such as FM (Castelnuovo et al, 2016a; Macfarlane et al, 2016).

A recent extended report (Macfarlane et al, 2016) assessed evidences with a focus on systematic reviews and meta-analyses concerned with pharmacological/non-pharmacological FM management to revised European League Against Rheumatism (EULAR) recommendations. Concerning non-pharmacological treatments, authors expressed their agreement about Exercise as "strong for" recommendation; about Cognitive-Behavioral Therapies, Acupuncture, Hydrotherapy/Spa therapy, Meditative movement, Mindfulness/mind–body therapy and Multicomponent therapy (i.e.: educational or psychological therapies and exercise) as "weak for" recommendation; about Biofeedback, Capsaicin, Hypnotherapy, Massage and S-Adenosyl methionine as "weak against" any recommendation; Chiropractic and Other complementary and alternative therapies (i.e.: guided imagery, homeopathy) as "strong against" any recommendation.

A systematic review (Lami et al, 2013) analyzed the empirical studies about psychological treatment for FM that have been published over the last twenty years, pointing out that the most used intervention modality

was group treatment with a cognitive-behavioral approach, among intensive and remote treatments, multimodal therapy, hypnosis, cognitive-behavioral therapy for insomnia, behavioral therapies, mind-body-based techniques and biofeedback components. Authors highlighted that the efficacy of cognitive-behavioral therapy for FM did not concern the elimination of pain, but rather the training to enhance patients' skills to manage FM symptoms in order to learn to live with them.

Furthermore, the findings of the present study also contribute in providing the rationale for the development of psychological interventions specifically aimed at improve alexithymia and SOC in people with FM.

Alexithymia has been usually assumed to be a stable personality trait rather than a state-dependent phenomenon, hence both its absolute and relative stability are high, even over a long follow-up period (Wise et al, 1995; Luminet et al, 2001; Luminet et al, 2007). However, during a multimodal psychodynamic treatment, the symptoms load and alexithymia decreased in patients with various psychosomatic and psychiatric disorders (Stingl et al, 2008). A comprehensive, integrated group therapy program can improve alexithymia (Beresnevaite, 2000; Grabe et al, 2008; Rufer, 2010; Ogrodniczuk et al, 2011). The effect of rehabilitative interventions in subjects with alexithymia has been studied also in patients with somatic diseases (Mazzarella et al, 2010; Jackson and Emery, 2013; Wood and Doughty, 2013). Finally, a recent review on studies that have examined the effects of psychological interventions on alexithymia (Cameron et al, 2014) concluded that alexithymia is modifiable by those psychological interventions that directly targeted alexithymic features.

Many studies pointed out the high prevalence of alexithymia in people with FM (Avila et al, 2014; Di Tella&Castelli, 2016; 2013), and that it worse the perception and management of pain (Huber et al, 2009; Di

Tella&Castelli, 2016). Hence, in this population, it is very important to assess levels of alexithymia and target this cognitive deficit with appropriate psychological interventions.

It is known that people with high levels of alexithymia tend to misinterpret their emotional arousal as signs of physical disease because they have difficulties in identifying physical signals from the body such as the somatic manifestations (arousal) of emotions (Brewer et al, 2016; Lumley et al, 1996). In people with FM, this deficit could amplify pain perception, mainly its affective dimension (Huber et al, 2009; Di Tella & Castelli, 2016; Di Tella et al, 2017). Furthermore, alexithymia makes them susceptible to seeking medical care for symptoms for which no complete medical explanations can be found (Tuzer et al, 2011; Huber et al, 2009; Lumley et al, 2007).

Patients with FM account for 10–25% of rheumatology clinic populations, 2–6% of primary care clinic populations, and 8% of hospital populations (White et al, 2001).

FM is labeled, often with a negative connotation, as a part of a "somatization disorder", a "fashionable diagnosis", "idiopathic pain disorder", "non-disease", "psychosomatic syndrome", dismissing the true suffering of the patients (Kool et al, 2009; 2012; Yunus, 2008). In the absence of an univocal identified biological cause, subjective reports of symptoms by patients with FM are often viewed derogatorily and discredited as "psychogenic" (Adams & Turk, 2015).

Even if pain is recognized as a psychological experience with a deeply subjective dimension (Burke et al, 2015; Lumley et al, 2011) that requires to assume its affective component (Cahill et al, 2014; Veinante et al, 2013; Neugebauer et al, 2004), often disregulated in FM (Rossellò et al, 2015), labeling pain as "psychological" or "psychosomatic" is still alike to dismissing it as unreal (Oliveira et al, 2014).

FM is usually evaluated and treated by rheumatologists, even if it is characterized by a broad variety of clinical manifestations that involve many specialties (Borchers & Gershwin, 2015). Rheumatologists reported addressing mental health issues during some visits and are likely to prescribe antidepressants, refer to a psychiatrist, or return the patient to the primary care physician (Heiman et al, 2016). Due to its unknown etiology, the diagnosis often remain a challenge, both for patients and healthcare professionals, lasting more than two years, with an average of 3.7 consultations with different physicians (Macfarlane et al, 2016), adding up to 7.087 US $/year in direct and up to 10.001 US $/year in indirect medical costs, mainly associated with lack of a diagnosis (Bernik et al, 2013; Knight et al, 2013).

Furthermore, people with FM often reported dismissive attitudes from others, such as disbelief, stigmatization, lack of acceptance by their relatives, friends, coworkers and the health care system, that consider them as "lazy" or "attention seeking" people, with "all in their head" (Kool et al, 2009; Arnold et al, 2008). Such dismissiveness can have substantial negative impact on patients, who are already distressed (Lobo et al, 2014; Kool et al, 2012) and also in the degree of their pain (Lobo et al, 2014). On the other hand, validation of the FM experience by a clinician increases the patient's overall QOL (Lobo et al, 2014).

Moving from the "Explaining Pain" model of Moseley and Butler (Moseley & Butler, 2015), a recent pilot study (Burger et al, 2016) pointed out the efficacy on pain severity and alexithymia of a psychological intervention aimed to help people with chronic musculoskeletal pain to learn that their pain is influenced primarily by a central nervous system processes and to enhance their awareness and expression of emotions, eventually related to psychological trauma or conflict. Authors tested a novel psychological attribution and emotional

awareness and expression therapy with 72 patients with chronic musculoskeletal pain by a baseline, post-treatment, and 6-month follow-up assessment without a control group. They found significant improvements in hypothesized change processes: psychological attributions for pain, emotional awareness, emotional approach coping, and alexithymia. Pain, interference, depression, and distress showed large effect size improvements at post-treatment, which were maintained or even enhanced at 6 months. Approximately 2/3 of the patients improved at least 30% in pain and 1/3 of them improved 70%. Furthermore, changes in attribution and emotional processes predicted outcomes. Finally, a study (Pepe et al, 2014) aimed to investigate the effects of written emotional disclosure as an adjunct to physiotherapy in 40 patients with musculoskeletal pain found that, although both the writing and control groups displayed lower pain scores after 10 sessions of Mézières physiotherapy, the difference was stronger in the writing group. Pain scores continued to decrease six months after physiotherapy in the writing group alone. The postural evaluation revealed a greater improvement in the writing group than in the control group, while the alexithymia and psychological problems/symptoms decreased in the writing group alone. These results indicate that written emotional disclosure is an effective adjunct to physiotherapy to improve physical and psychological health in people with musculoskeletal pain.

If alexithymia refers to a deficit in affects regulation that worse pain perception and management, SOC may be considered and treated as a protective factor able to strengthen resilience and sustain positive subjective state of health and wellbeing, also in people suffering from a pain-related illness as FM. This is a crucial point for improving the effects of treatments of these patients, since there is a connection between

psychological factors and FM impact and related pain, as shown in the present study.

Even if also SOC is generally considered a relatively stable trait (Schnyder et al, 2000), mainly in people with high levels (Nilsson et al, 2003), it is reasonable to assume that interventions improving psychological adjustment could enhance also the SOC.

Concerning psychotherapy, among neurotic patients treated for 10 weeks, it was found an increase in SOC level specifically in patients with a low level at the beginning of the treatment (Szymona, 2005). Another recent study (Lövheim et al, 2013) aimed to describe the changes in SOC in old age in a 5-year follow up in relation with negative life events including severe physical and mental diseases, pointed out a significant correlation between accumulation of negative life events and decrease in SOC and underlined the usefulness of psychological interventions to maintaining and strengthening SOC.

Furthermore, SOC predicted improvement in psychological distress and health related quality of life over time in people with FM after a program including information about the syndrome, pain and muscle physiology, training in warm water, stretching, body awareness therapy and relaxation in groups of 15 patients twice weekly, 2 hours during 10 weeks (Hävermark et al, 2006).

SOC improved also after an accredited motivational intervention for women of correctional institutions, including homework exercises, relaxation exercises and group work, aimed to encourage to identify something meaningful to engage in (Höjdahl et al, 2015). A recent randomized trial (Knekt et al, 2015) on the effectiveness of long- and short-term psychotherapy on psychosocial functioning and QOL of people with mood or anxiety disorder during a 5-year follow-up showed that, at

the follow-up, SOC significantly more improvement in long-term than in the short-term therapy groups.

Another study on the impact of early intervention on SOC among adults with first-episode of depression (Valtonen et al, 2015) showed that both rehabilitation and conventional depression treatment may enhance SOC and that rehabilitation itself enhances SOC more effectively among those with less severe depression or those whose depressive symptoms had further decreased at the 1-year follow-up.

Another promising finding of the present study, even if really preliminary, refers to the dysregulation of biorhythms that resulted significantly associated with worse FM impact, pain severity and impact, poor QOL, especially about "activities" and "social rhythms" dimensions. Interestingly, when the overall sample was been divided into "cases" and "controls" on the basis of current pain severity (outcome), there were significantly more employed and housewifes in "controls" than in "cases". Furthermore, on the basis of findings about the association between dysregulation of biological and social rhythms and pain in FM, it could be supposed a circular relation: the higher current pain severity the stronger the difficulties in work/household and social activities, as completing and performing them in the time scheduled, keeping usual rhythm of physical activity, communicating and having interpersonal relationships with significant others and give them attention.

Actually just few studies investigated the association between the dysregulation of biological and social rhythms and FM, even if the relative high prevalence of mood disorders in FM (Ucar et al, 2015; Carta et al, 2006; 2013). Regarding eating habits of women with FM, a recent study (Dias Batista et al, 2015) pointed out that they showed a lower qualitatively and quantitatively food intake in comparison with healthy

women, that vitamin E is negatively correlated with FM impact and that the percentage of protein is positively correlated with pain threshold.

As alexithymia and SOC, biological and social rhythms' regulation might be an important target for psychological and/or psychoeducational interventions to treat symptoms, prevent relapses and improve behaviors related to lifestyle regularity to decrees FM impact and improve QOL (Ucar et al, 2015). The stabilization of biological and social rhythms in people with mood disorders by above mentioned interventions is regarded as an important goal in preventing illness recurrence (Frank et al, 2000; 2005). Hence, further studies are needed to evaluate the efficacy of those interventions on FM impact and symptoms of people affected when there is a dysregulation of biological and social rhythms in people affected.

5. Conclusion

The present study pointed out that FM impact, related pain and QOL were negatively correlated with SOC and positively with alexithymia.

Furthermore, high alexithymia and low SOC resulted as significant risk factors for a severe FM impact, severe pain and poor QOL, after controlling for potential confounders such as age, marital status, education level, occupation.

Finally, it was preliminary observed that the dysregulation of biorhythms was significantly associated with a worse FM impact, severe pain and a poor QOL.

Further studies are needed to point out the implications of psychological factors in pain management and in QOL improvement of people with FM.

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7. Appendix

Table 1. Pearson's correlations between SOC, alexithymia, FM impact, pain severity, pain impact and QOL.

	FIQ tot	FIQ pain	VAS	SF12 tot	SF12 pain	TAS20 tot	TAS20 f1	TAS20 f2	TAS20 f3	SOC tot	SOC c	SOC ma	SOC me
FIQ tot	1												
FIQ pain	,776(**)	1											
	,000												
VAS	,455(**)	,293(*)	1										
	,001	,039											
SF12 tot	-,782(**)	-,514(**)	-,395(**)	1									
	,000	,000	,004										
SF12 pain	,495(**)	,346(*)	,426(**)	-,611(**)	1								
	,000	,014	,002	,000									
TAS20 tot	**,308(*)**	**,340(*)**	,234	**-,419(**)**	,088	1							
	,030	,016	,101	,002	,542								
TAS20 f1	**,387(**)**	**,369(**)**	,273	**-,497(**)**	,150	,869(**)	1						
	,005	,008	,055	,000	,300	,000							
TAS20 f2	,161	,237	,135	-,251	-,075	,825(**)	,603(**)	1					
	,263	,097	,350	,078	,602	,000	,000						
TAS20 f3	,111	,129	,121	-,147	,052	,582(**)	,255	,312(*)	1				
	,444	,371	,403	,307	,719	,000	,074	,027					
SOC tot	**-,495(**)**	**-,366(**)**	-,244	**,645(**)**	-,270	-,688(**)	-,720(**)	-,487(**)	-,323(*)	1			
	,000	,009	,087	,000	,057	,000	,000	,000	,022				
SOC c	**-,475(**)**	**-,348(*)**	**-,280(*)**	**,579(**)**	**-,328(*)**	-,578(**)	-,556(**)	-,501(**)	-,298(*)	,891(**)	1		
	,000	,013	,049	,000	,020	,000	,000	,000	,035	,000			
SOC ma	**-,312(*)**	-,219	-,242	**,453(**)**	-,087	-,585(**)	-,639(**)	-,354(*)	-,256	,862(**)	,660(**)	1	
	,027	,126	,091	,001	,546	,000	,000	,012	,072	,000	,000		
SOC me	**-,503(**)**	**-,389(**)**	-,103	**,648(**)**	**-,282(*)**	-,630(**)	-,684(**)	-,399(**)	-,290(*)	,849(**)	,637(**)	,591(**)	1
	,000	,005	,476	,000	,047	,000	,000	,004	,041	,000	,000	,000	

The squares contain the correlation coefficient above the *p*-value
**Correlation is significant at the 0.01 level (2-tailed)
*Correlation is significant at the 0.05 level (2-tailed)

FIQ: Fibromyalgia Impact Questionnaire; VAS: Visual Analogue Scale; SF12: Short Form Health Survey; TAS 20: Toronto Alexithymia Scale – 20 item; f1: difficulty identifying feelings; f2: difficulty communicating feelings; f3: externally oriented thought; SOC: Sense of Coherence Scale; c: comprehensibility; ma: manageability; me: meaningfulness; tot: total; FM: Fibromyalgia; QOL: Quality of Life.

Table 2. Cases and Controls: mean scores about outcomes

		N	%	mean ± sd
Outcome: FM impact				**FIQ total score**
cases	Severe (FIQ ≥59)	26	52	72.48 ± 9.029
controls	Mild-Moderate (FIQ <59)	24	48	45.55 ± 13.059
total		50	100	
Outcome: pain severity in the last week				**FIQ pain score**
cases	yes (FIQ "pain" ≥7.5)	27	54	8.84 ± 0.865
controls	no (FIQ "pain" <7.5)	23	46	4.7 ± 2.303
total		50	100	
Outcome: current pain severity				**VAS score**
cases	yes (VAS ≥7.5)	14	28	8.64 ± 0.892
controls	no (VAS <7.5)	36	72	3.97 ± 1.982
total		50	100	
Outcome: severe pain impact in the last month				**SF-12 pain score**
cases	yes (SF-12 pain ≤2*)	15	30	1.67 ± 0.488
controls	no (SF-12 pain >2*)	35	70	3.37 ± 0.490
total		50	100	
Outcome: poor QOL				**SF-12 total score**
cases	yes (SF-12 ≤24*)	17	34	21.47 ± 3.184
controls	no (SF-12 >24*)	33	66	30.58 ± 4.730
total		50	100	

*25 percentile

FM: fibromyalgia; FIQ: Fibromyalgia Impact Questionnaire; VAS: Visual Analogue Scale; SF-12: Short Form Health Survey - 12 item; QOL: Quality of Life.

Table 3. Socio-demographic and psychosocial characteristics of the sample as potential confounders.

		OUTCOMES									
		FM impact		pain severity in the last week		current pain severity		severe pain impact in the last month		poor QOL	
	Entire sample	Cases Severe (FIQ ≥59)	Controls Mild-Moderate (FIQ <59)	Cases yes (FIQ pain ≥7.5)	Controls no (FIQ pain <7.5)	Cases yes (VAS ≥7.5)	Controls no (VAS <7.5)	Cases yes (SF-12 pain ≤2*)	Controls no (SF-12 pain >2*)	Cases yes (SF-12 ≤24*)	Controls no (SF-12 >24*)
	N 50	N 26	N 24	N 30	N 20	N 14	N 36	N 15	N 35	N 17	N 33
AGE											
	50,54 ±10,810	52,54 ±11,154	48,38 ±10,214	52,00 ±11,136	48,35 ±10,184	51,86 ±10,826	50,06 ±10,914	51,67 ±10,452	50,06 ±11,074	50.12 ±10,804	50,76 ±10,974
homogeneity		F=1,885, df=1;49, p=0.176		F=1,379, df=1;49, p=0.246		F=0,284, df=1;49, p=0,596		F=0,229, df=1;49, p=0,634		F=0,039, df=1;49, p=0,845	
EDUCATION											
nr	1	0	1	0	1	1	0	0	1	0	1
degree	6	3	3	2	4	1	5	3	3	2	4
high school	23	10	13	12	11	6	17	6	17	8	15
primary school	18	12	6	14	4	0	2	0	2	1	1
secondary school	2	1	1	2	0	6	12	6	12	6	12
homogeneity		χ^2= 3.317, df =4, p=0.506		χ^2=7.568, df =4, p=0.109		χ^2=4.027, df=4, p=0.402		χ^2=2.692, df=4, p=0.611		χ^2=0.754, df=4, p=0.944	
MARITAL STATUS											
married	37	20	17	23	14	9	28	11	26	14	23
nubile	9	3	6	4	5	3	6	3	6	2	7
separated/divorced	3	2	1	2	1	1	2	1	2	1	2
widow	1	1	0	1	0	1	0	0	1	0	1
homogeneity		χ^2= 2.501, df =3, p=0.475		χ^2=1.702, df =3, p=0.637		χ^2=2.989, df =3, p=0.393		χ^2=0.493, df =3, p=0.920		χ^2=1.315, df =3, p=0.726	
OCCUPATION											
nr	1	0	1	0	1	1	0	0	1	0	1
employed	18	8	10	8	10	4	14	6	12	5	13
housewife	18	8	10	13	5	1	17	4	14	7	11
retired	3	3	0	3	0	2	1	1	2	0	3
unemployed	10	7	3	6	4	6	4	4	6	5	5
homogeneity		χ^2= 5.974, df =4, p=0.201		χ^2=6.435, df=4, p=0.169		χ^2=14.672, df=4, **p=0.005**		χ^2=1.534, df=4, p=0.821		χ^2=3.704, df=4, p=0.448	

*25 percentile.

FM: fibromyalgia; FIQ: Fibromyalgia Impact Questionnaire; VAS: Visual Analogue Scale; SF-12: Short Form Health Survey - 12 item; QOL: Quality of Life; nr: not responded.

Table 4. High alexithymia and low SOC as risk factors for severe FM impact, severe pain, severe pain impact, poor QOL.

FACTORS	OUTCOMES	N (%) In Cases	N (%) In Controls	N (%) in the overall sample	χ^2	p	OR	CI 95%
High alexithymia (TAS-20 total score ≥61)	**Severe FM impact** (FIQ total score ≥59)	10 (77%)	3 (23%)	13/50 (26%)	4.372	**0.037**	4.375	1.032-18.556
Low sense of coherence (SOC total score ≤54.95*)		12 (75%)	4 (25%)	16/50 (32%)	4.987	**0.026**	4.286	1.143-16.071
High alexithymia (TAS-20 total score ≥61)	**Pain severity in the last week** (FIQ pain score ≥7.5)	11 (85%)	2 (15%)	13/50 (26%)	5.109	**0.024**	5.806	1.128-29.892
Low sense of coherence (SOC total score ≤54.95*)		14 (87.5%)	2 (12.5%)	16/50 (32%)	7.414	**0.006**	7.875	1.547-40.091
High alexithymia (TAS-20 total score ≥61)	**Current pain severity** (VAS score ≥7.5)	6 (46%)	7 (54%)	13/50 (26%)	2.872	0.093	3.107	0.812-11.893
Low sense of coherence (SOC total score ≤54.95*)		6 (37.5%)	10 (62.5%)	16/50 (32%)	1.053	0.243	1.950	0.539-7.052
High alexithymia (TAS-20 total score ≥61)	**Severity of pain impact in the last month** (SF12 pain score ≤2**)	4 (31%)	9 (69%)	13/50 (26%)	0.005	0.602	1.051	0.266-4.145
Low sense of coherence (SOC total score ≤54.95*)		6 (37.5%)	10 (62.5%)	16/50 (26%)	0.630	0.318	1.667	0.470-5.916
High alexithymia (TAS-20 total score ≥61)	**Poor QOL** (SF12 total score ≤24**)	8 (61.5%)	5 (38.5%)	13/50 (26%)	5.937	**0.019**	4.978	1.295-19.130
Low sense of coherence (SOC total score ≤54.95*)		10 (62.5%)	6 (37.5%)	16/50 (26%)	8.517	**0.005**	6.429	1.735-23.819

*33.3 percentile
** 25 percentile

FM= Fibromyalgia; FIQ: fibromyalgia Impact Questionnaire; TAS-20= Toronto Alexithymia Scale-20 item; SOC= Sense of Coherence Scale; VAS: Visual Analogue Scale; SF-12: Short Form Health Survey – 12 item; QOL: Quality of Life.

Table 5. Pearson's correlations between biological and social rhythms, FM impact, pain severity, pain impact and QOL.

	BRIAN total	BRIAN eating	BRIAN sleeping	BRIAN activities	BRIAN social	FIQ total	FIQ pain	VAS	SF12 pain	SF12 total
BRIAN total	1									
BRIAN eating	,555(**) ,005	1								
BRIAN sleeping	,694(**) ,000	,147 ,494	1							
BRIAN activities	,841(**) ,000	,303 ,150	,433(*) ,035	1						
BRIAN social	,656(**) ,001	,134 ,534	,326 ,120	,576(**) ,003	1					
FIQ total	**,679(**)** **,000**	,278 ,188	,321 ,126	**,796(**)** **,000**	**,425(*)** **,039**	1				
FIQ pain	**,399** **,053**	,221 ,299	,062 ,772	**,572(**)** **,004**	,068 ,751	,792(**) ,000	1			
VAS	**,408(*)** **,048**	**,407(*)** **,048**	,094 ,661	**,425(*)** **,038**	,151 ,481	,667(**) ,000	,598(**) ,002	1		
SF12 pain	**-,699(**)** **,000**	-,296 ,160	**-,464(*)** **,022**	**-,650(**)** **,001**	**-,471(*)** **,020**	-,738(**) ,000	-,466(*) ,022	-,691(**) ,000	1	
SF12 total	**-,724(**)** **,000**	-,332 ,113	**-,397** **,055**	**-,787(**)** **,000**	**-,522(**)** **,009**	-,815(**) ,000	-,498(*) ,013	-,624(**) ,001	,790(**) ,000	1

The squares contain the correlation coefficient above the *p*-value
**Correlation is significant at the 0.01 level (2-tailed)
*Correlation is significant at the 0.05 level (2-tailed)

BRIAN: Biological Rhythms Interview of Assesment in Neuropsychiatry; FIQ: Fibromyalgia Impact Questionnaire; VAS: Visual Analogue Scale; SF12: Short Form Health Survey; FM: Fibromyalgia; QOL: Quality of Life.

Figure 1. High Alexithymia as risk factor for Severe FM impact

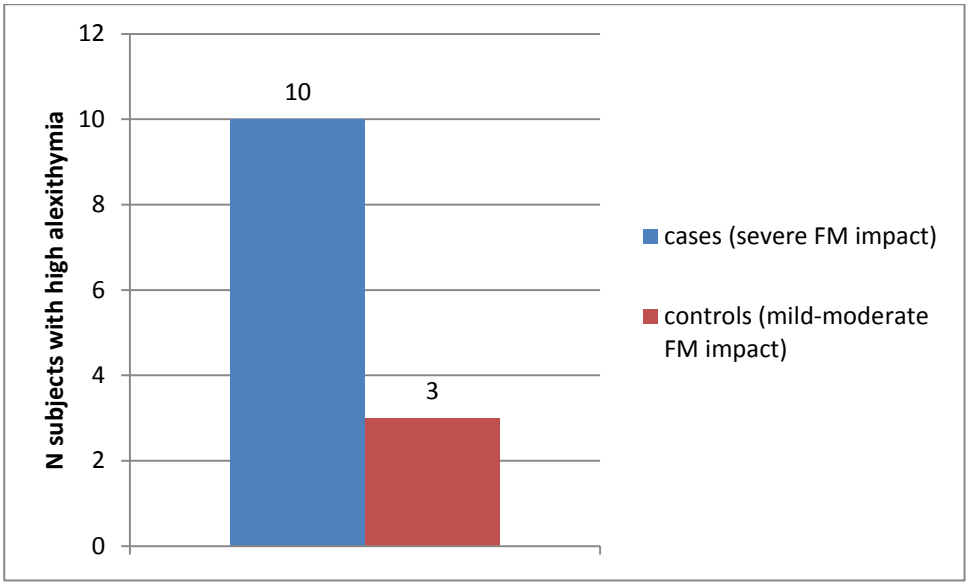


Figure 2. High Alexithymia as risk factor for severe pain in the last week

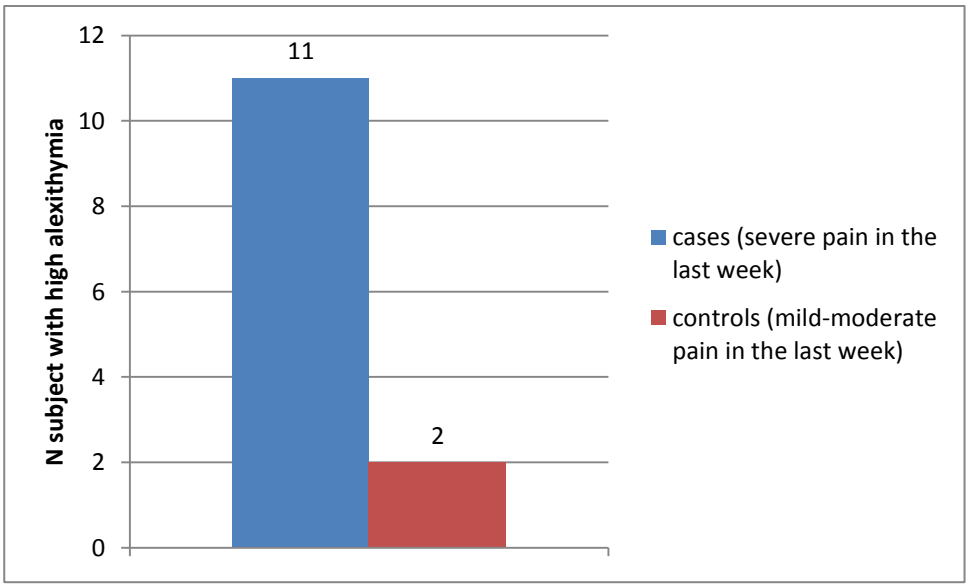


Figure 3. High Alexithymia as risk factor for poor QOL

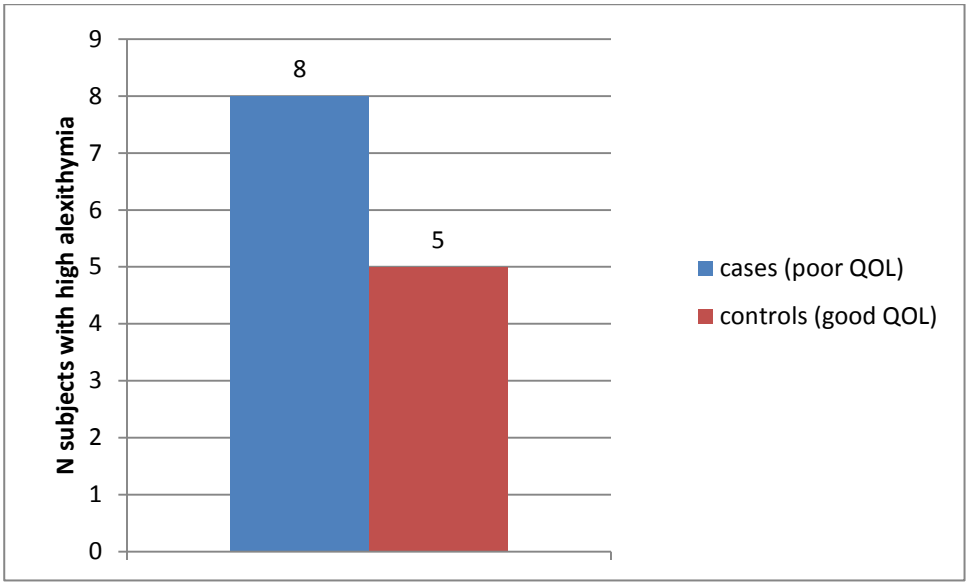


Figure 4. Low Sense of Coherence as risk factor for Severe FM impact

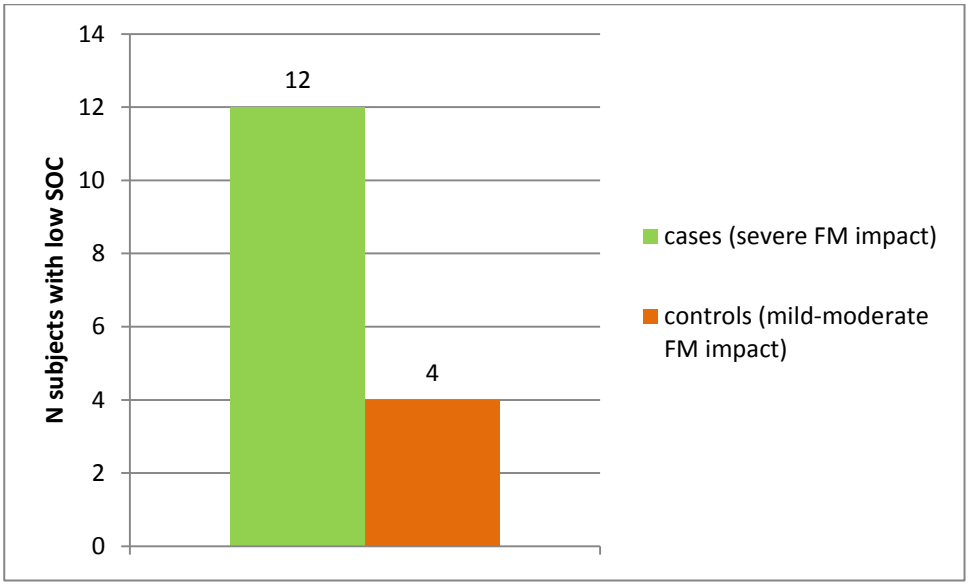


Figure 5. Low Sense of Coerence as risk factor for Severe pain in the last week

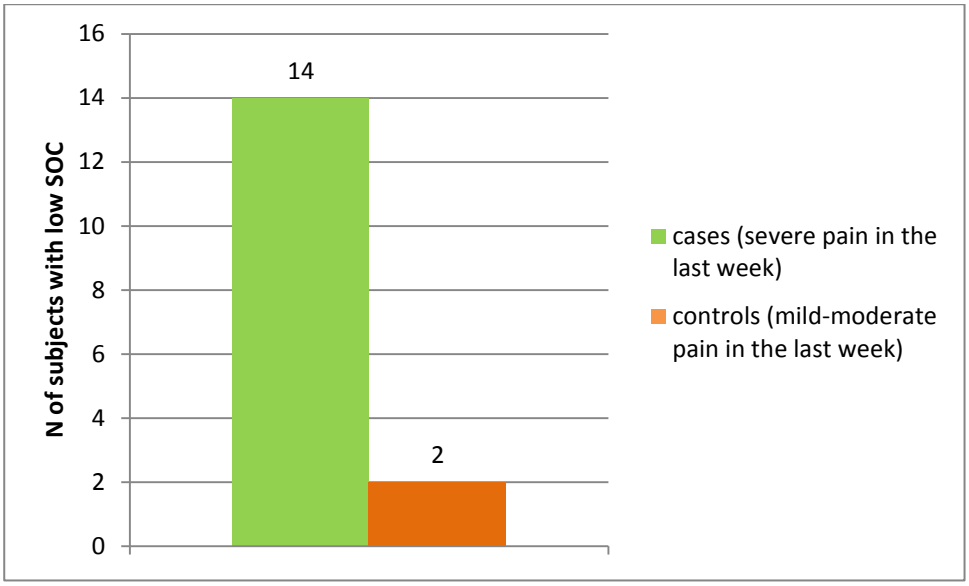
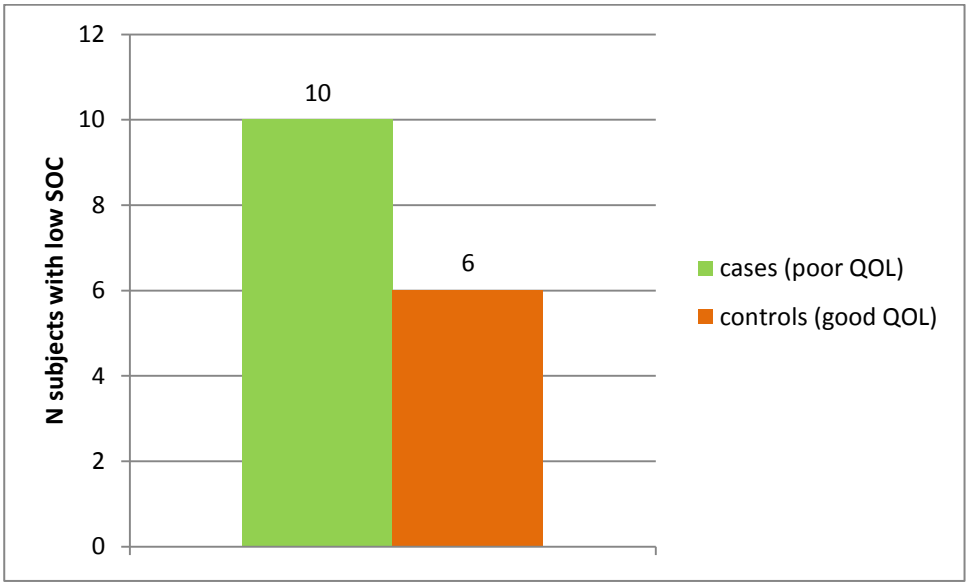


Figure 6. Low Sense of Coherence as risk factor for poor QOL



SCALA VAS

VALUTAZIONE DEL DOLORE DA PARTE DEL PAZIENTE

NESSUN DOLORE _____ MASSIMO DOLORE POSSIBILE

FIBROMYALGIA IMPACT QUESTIONNARIE

FIQ

ISTRUZIONI: nelle domande dal numero 1 al numero 11 del questionario che segue, verranno poste delle domande riguardo alle attività che si è stati in grado di svolgere nell'ultima settimana.

Rispondere a ciascuna domanda, mettendo una crocetta nella casella corrispondente (solo una risposta per ciascuna domanda).

Se normalmente non si svolge l'attività cui la domandasi riferisce, barrare le casella 4.

NEL CORSO DELL'ULTIMA SETTIMANA E' STATO IN GRADO DI	SEMPRE 0	QUASI SEMPRE 1	QUALCHE VOLTA 2	MAI 3	ATTIVITA' NON SVOLTA ATTUALMENTE
1) ANDARE A FARE LA SPESA	0	1	2	3	4
2) FARE IL BUCATO (LAVATRICE)	0	1	2	3	4
3) PREPARARE I PASTI	0	1	2	3	4
4) LAVARE I PIATTI	0	1	2	3	4
5) PASSARE L'ASPIRAPOLVERE	0	1	2	3	4
6) RIFARE I LETTI	0	1	2	3	4
7) CAMMINARE PER QUALCHE ISOLATO	0	1	2	3	4
8) ANDARE A FAR VISITA A PARENTI O AMICI	0	1	2	3	4
9) FARE LAVORI DI GIARDINAGGIO – ORTO	0	1	2	3	4
10) GUIDARE L'AUTO	0	1	2	3	4
11) SALIRE LE SCALE	0	1	2	3	4

12) QUANTI GIORNI SU 7 DELL'ULTIMA SETTIMANA SI E' SENTITA BENE?

0	1	2	3	4	5	6	7

13) QUANTI GIORNI SU 7 DELL'ULTIMA SETTIMANA NON E' ANDATA A LAVORO O NON HA POTUTO FARE LAVORI DOMESTICI A CAUSA DELLA FIBROMIALGIA?

0	1	2	3	4	5	6	7

Risponda alle seguenti domande apponendo un segno sulla riga sottostante

(estrema sinistra = nessun problema estrema destra = massima difficoltà)

14) SUL POSTO DI LAVORO O A CASA DURANTE I LAVORI DOMESTICI, QUANTA DIFFICOLTA' HA AVVERTITO A CAUSA DEL DOLORE O DEGLI ALTRI SINTOMI DELLA FIBROMIALGIA?

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15) QUANTO E' STATO FORTE IL SUO DOLORE?

---

16) QUANTO SI E' SENTITA STANCA?

---

17) COME SI E' SENTITA AL RISVEGLIO?

---

18) QUANTO SI E' SENTITA RIGIDA?

---

19) QUANTO SI E' SENTITA ANSIOSA O NERVOSA?

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20) QUANTO SI E' SENTITA DEPRESSA O TRISTE?

STRUMENTO PER LA VALUTAZIONE DELLO STATO DI SALUTE
SF-12

Versione italiana a cura dell'Istituto Superiore di Sanità – Roma

La preghiamo di rispondere alle seguenti domande relative al suo stato di salute. Le informazioni che ci darà rimarranno strettamente confidenziali e non saranno comunicate a nessuno senza il suo permesso. Ci serviranno per capire meglio come si sente e fino a che punto è in grado di svolgere le sue normali attività.

1. **Come giudica nel suo complesso la sua salute?**

5 - eccellente
4 - molto buona
3 – buona
2 – passabile
1 – cattiva

Le seguenti domande riguardano le attività che ptrebbe fare in un giorno qualsiasi. In che misura le sue condizioni di salute le rendono difficile, la limitano nel fare le seguenti attività:

2. **attività che richiedono discreti sforzi fisici (come spostare un tavolo, manovrare un'aspirapolvere, fare un giro in bicicletta…)**

1 – mi limitano molto
2 – mi limitano un po'
3 – non mi limtano per niente

3. **salire alcune rampe di scale**

1 – mi limitano molto
2 – mi limitano un po'
3 – non mi limtano per niente

Nelle ultime 4 settimane, a causa di malattie fisiche, ha avuto i seguenti problemi al lavoro, o nelle altre attività di tutti i giorni?

4. **ha reso meno o fatto meno bene di quello che avrebbe voluto?** SI NO

5. **ha dovuto rinunciare a fare alcune cose sul lavoro o nelle altre attività?** SI NO

Nelle ultime 4 settimane, a causa di problemi psicologici, ad esempio perché si sentiva depresso o ansioso, o perché gli altri non le credevano o volevano fargli del male:

6. **ha reso meno di quello che avrebbe voluto?** NO SI

7. **Non ha fatto le cose con la stessa cura e attenzione che avrebbe voluto?** SI NO

8. nelle ultime 4 settimane, il dolore fisico le ha reso difficile il lavoro o le altre attività, in casa e fuori?

5 – per niente
4 – un po'
3 – abbastanza
2 – molto
1 – moltissimo

Le seguenti domande riguardano il suo stato d'animo nelle ultime 4 settimane. Per quanto tempo nelle ultime 4 settimane si è sentito:

9. calmo e sereno?

6 – sempre
5- la maggior parte del tempo
4 – più o meno metà del tempo
3 – qualche volta
2 – raramente
1 – mai

10. pieno di energia?

6 – sempre
5- la maggior parte del tempo
4 – più o meno metà del tempo
3 – qualche volta
2 – raramente
1 – mai

11. scoraggiato e triste?

1 – sempre
2 - la maggior parte del tempo
3 – più o meno metà del tempo
4 – qualche volta
5 – raramente
6 – mai

12. Nelle ultime 4 settimane, per qunto tempo la sua salute fisica o le sue condizioni psicologiche le hanno causato problemi nella vita sociale (ad esempio nei suoi rapporti con parenti e amici?

1 – sempre
2 – la maggior parte del tempo
3 – qualche volta
4 – raramente
5 - mai

TAS-20

Toronto Alexithymia Scale

Taylor G.J., Bagby R.M., Parker J.D.A.,1992

Seguendo le istruzioni sotto elencate indichi quanto è d'accordo o no con ciascuna delle seguenti affermazioni segnando una X sopra il numero corrispondente.
Segnare una sola risposta per ciascuna frase.

1 = NON SONO PER NIENTE D'ACCORDO
2 = NON SONO MOLTO D'ACCORDO
3 = NON SONO NE' D'ACCORDO NE' IN DISACCORDO
4 = SONO D'ACCORDO IN PARTE
5 = SONO COMPLETAMENTE D'ACCORDO

1.	Sono spesso confuso/a circa le emozioni che provo	1	2	3	4	5
2.	Mi è difficile trovare le parole giuste per esprimere i miei sentimenti	1	2	3	4	5
3.	Provo delle sensazioni fisiche che nemmeno i medici capiscono	1	2	3	4	5
4.	Riesco facilmente a descrivere i miei sentimenti	1	2	3	4	5
5.	Preferisco approfondire i problemi piuttosto che descriverli semplicemente	1	2	3	4	5
6.	Quando sono sconvolto/a non so se sono triste, spaventato/a o arrabbiato/a	1	2	3	4	5
7.	Sono spesso disorientato dalle sensazioni che provo nel mio corpo	1	2	3	4	5
8.	Preferisco lasciare che le cose seguano il loro corso piuttosto che capire perché sono andate in quel modo	1	2	3	4	5
9.	Provo sentimenti che non riesco proprio ad identificare	1	2	3	4	5
10.	E' essenziale conoscere le proprie emozioni	1	2	3	4	5
11.	Mi è difficile descrivere ciò che provo per gli altri	1	2	3	4	5
12.	Gli altri mi chiedono di parlare di più dei miei sentimenti	1	2	3	4	5
13.	Non capisco cosa stia accadendo dentro di me	1	2	3	4	5
14.	Spesso non so perché mi arrabbio	1	2	3	4	5
15.	Con le persone preferisco parlare di cose di tutti i giorni piuttosto che delle loro emozioni	1	2	3	4	5
16.	Preferisco vedere spettacoli leggeri, piuttosto che spettacoli a sfondo psicologico	1	2	3	4	5
17.	Mi è difficile rivelare i sentimenti più profondi anche ad amici più intimi	1	2	3	4	5
18.	Riesco a sentirmi vicino ad una persona, anche se capita di stare in silenzio	1	2	3	4	5
19.	Trovo che l'esame dei miei sentimenti mi serva a risolvere i miei problemi personali	1	2	3	4	5
20.	Cercare significati nascosti in film o commedie distoglie dal piacere dello spettacolo	1	2	3	4	5

Dipartimento di Sanità Pubblica – Università degli studi di Cagliari (Italy)

Sense of Coherence – Questionario di Orientamento alla vita

Forma breve- 13 domande

Fonte: Antonovsky, Aaron Unraveling the Mystery of Health. How People Manage Stress and StayWell. San Francisco 1987.

C = comprensibilità; Ma = gestibilità; Me = significato

1. Ha la sensazione che non le importi realmente ciò che accade intorno a lei? (Me)

1	2	3	4	5	6	7
Molto raramente o mai						Molto spesso

2. Le è capitato in passato di essere sorpreso dal comportamento di persone che pensava di conoscere bene? (C)

1	2	3	4	5	6	7
Mai successo						Sempre successo

3. Le è capitato che le persone su cui contava la abbiano delusa? (Ma)

1	2	3	4	5	6	7
Mai successo						Sempre successo

4. Fino a questo momento la sua vita ha avuto: (Me)

1	2	3	4	5	6	7
Obiettivi e scopi per niente chiari						Obiettivi e scopi molto chiari

5. Ha mai la sensazione di essere trattato ingiustamente? (Ma)

1	2	3	4	5	6	7
Molto spesso						Molto raramente o mai

6. Ha mai la sensazione di trovarsi in una situazione poco familiare e non sapere cosa fare? (C)

1	2	3	4	5	6	7
Molto spesso						Molto raramente o mai

7. Fare le cose di ogni giorno è: (Me)

1	2	3	4	5	6	7
Fonte di profondo piacere e soddisfazione						Fonte di dolore e di noia

8. Ha sensazioni ed idée molto confuse? (C)

1	2	3	4	5	6	7
Molto spesso						Molto raramente o mai

9. Le capita di trovare dentro di se sensazioni che preferirebbe non provare? (C)

1	2	3	4	5	6	7
Molto spesso						Molto raramente o mai

10. Molte persone – anche quelle con un carattere forte – a volte si sentono dei perdenti in certe situazioni. Quante volte si è sentito così in passato? (Ma)

1	2	3	4	5	6	7
Mai						Molto spesso

11. Quando è capitato qualcosa, generalmente ha trovato che: (C)

1	2	3	4	5	6	7
Ne aveva sopravvalutato o sottovalutato l'importanza						Aveva visto le cose nelle giuste dimensioni

12. Quanto spesso ha la sensazione che ci sia poco senso nelle cose che fa tutti i giorni? (Me)

1	2	3	4	5	6	7
Molto spesso						Molto raramente o mai

13. Quanto spesso prova sensazioni che non è sicuro di poter tenere sotto controllo? (Ma)

1	2	3	4	5	6	7
Molto spesso						Molto raramente o mai

INTERVISTA DI VALUTAZIONE SUI RITMI BIOLOGICI IN NEUROPSICHIATRIA

BIOLOGICAL RYTHMS INTERVIEW OF ASSESSMENT IN NEUROPSYCHIATRY (BRIAN)

Tra gli aspetti riportati di seguito indichi l'opzione che descrive meglio la condotta del paziente negli ultimi 15 giorni

SONNO	**ATTIVITA'**
1. Quanto ha difficoltà ad addormentarsi alla solita ora? (1) per nulla (2) poco (3) abbastanza (4) molto	6. quanto ha difficoltà a portare a termine tutte le attività del suo lavoro? (1) per nulla (2) poco (3) abbastanza (4) molto
2. quanto ha difficoltà a svegliarsi alla solita ora? (1) per nulla (2) poco (3) abbastanza (4) molto	7. quanto ha deifficoltà a portare a termine le sue attività abituali (pulizia di casa, fare la spesa)? (1) per nulla (2) poco (3) abbastanza (4) molto
3. quanto ha difficoltà ad alzarsi dal letto dopo essersi svegliato? (1) per nulla (2) poco (3) abbastanza (4) molto	8. quanto ha difficoltà a mantenere il suo ritmo di attività fisica (es.: prendere l'autobus/metro, o praticare uno sport – se questo fa parte delle sue abitudini)? (1) per nulla (2) poco (3) abbastanza (4) molto
4. quanto ha difficoltà a sentirsi riposato con le ore di sonno che sta facendo e (questo in riferimento alla sensazione soggettiva di sentirsi riposato per lo svolgimento delle attività quotidiane come guidare, ragionare, lavorare)? (1) per nulla (2) poco (3) abbastanza (4) molto	9. quanto ha difficoltà a rispettare il programma abituale delle sue attività? (1) per nulla (2) poco (3) abbastanza (4) molto
5. quanto ha difficoltà a "staccare" nei momenti di riposo"? (1) per nulla (2) poco (3) abbastanza (4) molto	10. quanto ha difficoltà a mantenere il suo livello di desiderio/attività sessuale? (1) per nulla (2) poco (3) abbastanza (4) molto

SOCIALE	**ALIMENTAZIONE**
11. quanto ha difficoltà a relazionarsi e comunicare con le persone del suo ambiente? (1) per nulla (2) poco (3) abbastanza (4) molto	15. quanto ha difficoltà a rispettare gli orari dei pasti (colazione, pranzo, cena)? (1) per nulla (2) poco (3) abbastanza (4) molto
12. quanto ha difficoltà a non abusare dell'uso di apparecchi elettronici come TV, internet, ecc…(senza che tale uso alteri il contatto con le persone del suo ambiente o che sottragga troppo tempo ad altre attività)? (1) per nulla (2) poco (3) abbastanza (4) molto	16. quanto ha difficoltà a rispettare le sue abitudini alimentari in termini di non saltare i pasti? (1) per nulla (2) poco (3) abbastanza (4) molto
13. quanto ha difficoltà ad adattare le sue abitudini e il suo sonno a quelli delle persone con cui vive (familiari, vicini, amici)? (1) per nulla (2) poco (3) abbastanza (4) molto	17. quanto ha difficoltà a rispettare le sue abitudini alimentari in termini di quantità di cibo? (1) per nulla (2) poco (3) abbastanza (4) molto
14. quanto a difficoltà a disporre di tempo e attenzione per le persone con cui vive (familiari, vicini, amici)? (1) per nulla (2) poco (3) abbastanza (4) molto	18. quanto ha difficoltà a non consumare in eccesso sostanze stimolanti (es.: caffè, coca cola), o cioccolato/dolci? (1) per nulla (2) poco (3) abbastanza (4) molto
RITMO PREDOMINANTE (SERALE O MATTUTINO) *Questa parte della scala è opzionale e si riferisce alle sue abitudini. Consideri qui gli <u>ultimi 12 mesi</u>*	
19. ha la tendenza a essere più attivo durante la notte (lavoro, relazioni interpersonali)? (1) mai (2) raramente (3) quasi sempre (4) sempre	21. ha la sensazione di scambiare il giorno per la notte? (1) mai (2) raramente (3) quasi sempre (4) sempre
20. ha la sensazione di essere più produttivo la mattina? (1) mai (2) raramente (3) quasi sempre (4) sempre	

Grazie…

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