Theory of Mind and Emotional Functioning in Fibromyalgia Syndrome: An Investigation of the Relationship between Social Cognition and Executive Function

Marialaura Di Tella[1], Lorys Castelli[1]*, Fabrizio Colonna[2], Enrico Fusaro[3], Riccardo Torta[2], Rita B. Ardito[1], Mauro Adenzato[1,4]

1 Center for Cognitive Science, Department of Psychology, University of Turin, Turin, Italy, **2** Clinical Psychology and Psycho-Oncology Unit, Department of Neuroscience, University of Turin, Turin, Italy, **3** Rheumatology Unit, "Città della Salute e della Scienza" University Hospital of Turin, Turin, Italy, **4** Neuroscience Institute of Turin, Turin, Italy

* lorys.castelli@unito.it

Abstract

Background

Fibromyalgia (FM) is a syndrome primarily characterised by chronic, widespread musculo-skeletal pain. In the aetiology of this syndrome a crucial role is played by complex interactions among biological, genetic, psychological, and socio-cultural factors. Recently, researchers have started to explore emotional functioning in FM, with their attention focused on alexithymia, a personality construct that affects the regulation of a person's own emotions. On the other hand, the detection and experience of emotional signals from other people have only been sparsely investigated in FM syndrome and no studies have investigated the ability to represent other people's mental states (i.e. Theory of Mind, ToM) in these patients. Here we present the first study investigating a large set of social-cognitive abilities, and the possible relationships between these abilities and the performance on executive-function tasks, in a homogenous sample of patients with FM.

Methodology

Forty women with FM and forty-one healthy women matched for education and age were involved in the study. Social cognition was assessed with a set of validated experimental tasks. Measures of executive function were used to test the correlations between this dimension and the social-cognitive profile of patients with FM. Relationships between social-cognitive abilities and demographic, clinical and psychological variables were also investigated.

Principal Findings

Patients with FM have impairments both in the regulation of their own affect and in the recognition of other's emotions, as well as in representing other people's mental states. No

significant correlations were found between social cognition tasks and the subcomponents of the executive function that were analysed.

Conclusions

The results show the presence of several impairments in social cognition skills in patients with FM, which are largely independent of both executive function deficits and symptoms of psychological distress. The impairments reported highlight the importance of adequately assessing ToM and emotional functioning in clinical practice.

Introduction

Fibromyalgia (FM) is a syndrome primarily characterised by chronic, widespread musculoskeletal pain [1–2]. Its prevalence is estimated to be 3–6% of the world population [3], and it occurs predominantly in women, with a female to male ratio of 10:1 [4–6]. FM symptoms are not restricted to pain, but often include a heterogeneous group of other conditions, such as hyperalgesia and/or allodynia, physical and mental fatigue, disrupted or non-restorative sleep, headache, irritable bowel, psychiatric disorders, cognitive impairment, and other functional complaints [1, 7].

The aetiology of this syndrome is not completely understood, but a crucial role seems to be played by complex interactions among biological, genetic, psychological, and socio-cultural factors, such as medical illness, neuroendocrine disturbances, stress, and psychiatric disorders. In particular, high levels of stress and psychiatric symptoms may negatively influence the perception of disease severity, functional ability, and the threshold and tolerance for pain [8–11]. Some authors have indeed suggested that the development of FM might stem from stress-induced disruption of the hypothalamic-pituitary-adrenal (HPA) axis [12]. Exposure to prolonged stressful conditions can alter the function of the HPA axis, with a consequent increase in the production of corticotropin-releasing factor and potentially amplified pain perception. For this reason, FM is often defined as a *central sensitisation syndrome*, caused by increased sensitivity of the central nervous system to pain signals [13].

Among psychological factors, the high prevalence of depression (20–80%) and anxiety disorders (13–64%) has been widely reported [14–15]. Only recently, researchers have also started to explore emotional functioning in FM syndrome, with their attention focused on alexithymia, a multifaceted personality construct that affects the regulation of a person's own emotions [16–20]. Alexithymia is characterised by difficulty in identifying and describing subjective feelings, difficulty in distinguishing between feelings and bodily sensations of emotional arousal, restricted imagination processes, and a stimulus-bound, externally oriented cognitive style [21–22]. Most of these studies have reported high levels of alexithymia in patients with FM, suggesting the presence of a deficit in emotional self-awareness.

On the other hand, the detection and experience of emotional signals from other people have only been sparsely investigated in FM syndrome. A link between alexithymic traits and deficits in the processing of other people's emotions has been highlighted in both healthy individuals and specific clinical populations, e.g. affective disorders, eating disorders, borderline and psychopathic personality disorders, schizophrenia, somatoform disorders [22–26]. To the best of our knowledge, only one study to date has examined the ability to identify other people's emotions in FM syndrome [27]. The results of this study highlighted the fact that patients with FM had reduced performance in a face-recognition task, with a higher percentage of

misclassifications of emotional expressions compared with healthy controls. In addition, pain intensity, alexithymia, depression, and anxiety were inversely related to recognition performance, while psychiatric co-morbidity and medication had no impact on performance.

The ability to decipher information about the intentions and affective states of social partners is crucial for the implementation of appropriate behaviour during social interactions. This complex process is part of the so-called *social cognition domain*, defined as the ability to construct mental representations of the relations that exist between oneself and others and to flexibly use these representations to function effectively in one's social environment [28–29]. Examples of social cognition abilities are the capacity to represent other people's intentions and beliefs (i.e. Theory of Mind, ToM) [30–31], and the ability to share and recognise the emotions and sensations of others [32–33].

From a neurological point of view, ToM and emotional processing abilities are associated with overlapping but distinct brain networks [34–36]. Common areas of activation are the prefrontal cortex, the superior temporal sulcus, and the temporo-parietal junctions. These areas form the basis for making inferences about mental states [37–41]. However, these areas are not sufficient for the evaluation of one's own and other's emotions, and it is necessary to recruit the additional involvement of emotional networks, in particular those of the amygdala [34, 36, 42–43]. In fact, while the amygdala is not involved in ToM processes per se [44], its role is crucial in processing basic and social emotions, related both to the self and to others [36, 45–48].

The social cognition domain includes a series of different abilities, which gradually evolve throughout the lifetime. An open issue concerns the relationship between these capacities, particularly ToM processes, and the higher-level cognitive skills known as executive functions (EF). Growing numbers of studies are trying to address this relationship in patients with different psychiatric and neurological conditions [49–57].

EF refers to all of the skills that people use to control and coordinate their cognitive abilities and behavior. These are essential for independent everyday functioning in life, and for the establishment of adaptive social relations [58–59]. In the last decade, evidence for the multifaceted nature of EF has replaced the idea of a unitary function [60–63]. Among the several classifications that have been proposed to distinguish EF subcomponents, the model of Miyake et al. [63] identified three separate types of operations: Updating, Shifting, and Inhibition. *Updating* is related to working memory and requires monitoring and coding information as well as replacing old non-relevant information with new relevant information. *Shifting* implies the ability to shift attention between different sub-tasks or different elements of the same task. *Inhibition* is concerned with the individual's ability to withhold dominant, automatic or prepotent responses when they are inappropriate, and is considered to be a key component in planning abilities. Fisk and Sharp [64] later added a fourth subcomponent, and revised the model of Miyake and colleagues. The factor, called *Access*, refers to the processes involved in verbal fluency tasks, which are believed to mediate access to representations in long-term memory.

Currently, there are two opposing views about the relationship between ToM abilities and EF. Some authors believe that ToM is a circumscribed cognitive process, independent of general intellectual functioning and other cognitive domains, included EF [65]. Basing their ideas on theoretical and experimental data, others have suggested instead that lower-level perceptual abilities (e.g. detection of gaze direction and voice recognition) that are required for an appropriate implementation of ToM skills, may be related to specific and circumscribed cognitive domains, while higher-order ToM processes, involving interpreting and associating information as well as hypothesising, would be the result of a more general ability regarding metarepresentation and EF [66].

The present study is based on both clinical evidence, which has highlighted high levels of emotional distress (depression, anxiety, and in particular, alexithymia) in patients with FM, and neuroimaging and neuropsychological data that has reported functional and structural alterations in brain areas crucial for ToM and emotional processing abilities (i.e. the prefrontal cortex and amygdala) in these patients [67–70], as well as cognitive deficits in the EF domain [69–72]. On these bases, the present study aimed to address two main objectives. The first goal was to evaluate the social-cognitive profile of patients with FM, and analyse ToM and emotional processing abilities. In particular, four different areas of the social cognition domain were examined: (1) regulation of one's own emotions; (2) empathic capacities; (3) recognition of other's emotions; (4) representation of other people's affective mental states (i.e., affective ToM). The second goal was to explore the possible relationships between the performance on executive-function tasks and performance on social-cognition tasks in patients with FM. Furthermore, relationships between social-cognitive abilities and demographic, clinical and psychological variables were also investigated for explorative purposes.

Materials and Methods

Ethics Statement

The study was approved by the San Giovanni Battista University Hospital's ethics committee and was conducted in accordance with the Declaration of Helsinki. All the participants gave their written informed consent to participate in the study.

Participants and procedure

Forty female participants with FM (51.75 ± 7.76 years of age) were consecutively recruited from the Fibromyalgia Integrated Outpatient Unit (FIOU), a multidisciplinary unit based on the collaboration between rheumatologists, psychologists, and psychiatrists at the San Giovanni Battista University Hospital of Turin. All patients had a main diagnosis of fibromyalgia, made by rheumatologists who are experts in the field. In addition, a psychiatric interview based on DSM IV-TR axis II criteria (Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision) [75] was performed by an expert psychiatrist, in order to exclude FM patients with personality disorders. Exclusion criteria were as follows: less than 18 years old, low education level (<5 years), and the presence or history of a neurological or a severe psychiatric disorder. Forty-one healthy women (51.83 ± 7.78 years of age) were recruited to the HC group. Exclusion criteria for the HC group were the presence of rheumatic diseases or chronic pain, as well as the presence or history of a neurological or psychiatric disorder.

Pain evaluation

As an index of pain intensity, the item "Pain" of the Italian version of the Fibromyalgia Impact Questionnaire (FIQ) [76–77] was used to assess the average intensity of pain in the previous week on a scale ranging between 0 and 10.

Psychological assessment

The presence of symptoms of depression and anxiety was assessed using the Italian version of the Hospital Anxiety and Depression Scale (HADS) [78–79]. It consists of 14 items on a 0 to 3 range, and is divided into two subscales, one for depression (HADS-D) and one for anxiety (HADS-A). Each subscale score ranges from 0 to 21 and a score of 8 (cut-off) or more suggests a level of depression/anxiety symptoms that is clinically relevant [80].

Neuropsychological assessment

Neuropsychological assessment was performed, using tests for short-term memory (Digit Span-Forward—DS F) [81], learning (Rey auditory-verbal learning test—AVLT) [82], and attention (Trail-making test—TMT—A-B) [83]. For the investigation of executive functions, four different tests were used, specific for each one of the four subcomponents into which EF has been divided according to the models of Miyake et al. [63] and Fisk and Sharp [64]. Specifically, the Digit Span-Backward (DS B) [81] was employed for evaluating the Updating component, the TMT B [83] for Shifting, the Tower of London (ToL) [84–85] for Inhibition, and the verbal fluency (FAS) [82, 86] for Access.

Social cognition assessment

Twenty-Item Toronto Alexithymia Scale (TAS-20). Alexithymia was assessed using the Italian version of the Toronto Alexithymia Scale (TAS-20) [87–88]. Subjects were asked to indicate the extent to which they agreed or disagreed with each statement on a five-point Likert scale. The results provide a TAS-20 total score, and three subscale scores that measure different aspects of alexithymia: *difficulty identifying feelings* (Factor 1), which measures the inability to distinguish specific emotions and between emotions and the bodily sensations of emotional arousal; *difficulty describing feelings* (Factor 2), which assesses the inability to verbalise one's emotions to other people; and *externally-oriented thinking* (Factor 3), which evaluates the tendency of individuals to focus their attention externally and not on the inner emotional experience [88–89]. The TAS-20 cut-off scores are as follows: ≤51 no alexithymia, 52–60 borderline alexithymia, ≥61 alexithymia. This scale has shown good internal consistency and test-retest reliability, as well as convergent, discriminant and concurrent validity [22], and it is currently one of the most utilised instruments in studies of alexithymia and emotion.

Empathy Quotient (EQ). The EQ is a validated self-report questionnaire, employed to assess the capacity to empathise with another, i.e. to recognise another's affective state and to respond to this with an appropriate emotion [90–91]. The EQ comprises 60 items, broken down into two types: 40 items assessing empathy and 20 filler/control items, included to distract the participant from a relentless focus on empathy. For each empathy item, a person can score 2, 1, or 0, so the EQ has a maximum score of 80 (higher scores indicate greater empathy). The EQ is able to detect considerable individual, gender, and group differences, in both general-population and clinical samples.

Ekman 60 Faces. The Italian version of this test was used to assess the recognition of facial expressions pertaining to basic emotions [92]. The Ekman 60 Faces Test uses photographs of the faces of 10 actors (six female and four male) selected from the Ekman and Friesen [93] series. Each actor displays one of the six basic emotions investigated (happiness, sadness, disgust, fear, surprise, and anger). The subject is required to respond verbally, deciding which of the six labels for basic emotions that are placed below each photograph can best describe the facial expression shown. The maximum test score (indicating best performance) is 60 for all six emotions and 10 for each basic emotion.

Reading the Mind in the Eyes Test (RME). The RME was employed to assess the ability to represent other people's affective mental states [94]. In the test, the experimenter presents a set of 36 photographs of the eye region of various human faces. Participants are required to choose among four words that are printed on the page that the picture appears on, using the criterion of which word best describes the mental state of the person depicted in the photograph. Participants have unlimited time to decide, and a glossary is provided. Participants have to put themselves into the mind of another person and recognise his or her complex mental state. In the gender-recognition control task, participants are asked to judge the gender of the person in

each of the 36 photographs. For both the experimental (mental state attribution) and control (gender attribution) conditions, the maximum score indicating the best performance is 36.

Statistical analyses

All the statistical analyses were conducted using IBM SPSS Statistics, version 20.0. Normal distribution was assessed using indices of asymmetry and kurtosis. Non-parametric equivalent tests were performed on data that violated this assumption. For normally distributed variables, independent t-tests were used. In order to evaluate the possible relationships between variables, Spearman or Pearson correlations were computed, as appropriate.

Results

Demographic, clinical and psychological data

Data on the demographic and psychological variables are presented in Table 1. The two groups were matched for age and education.

For psychological assessment we used data from the HADS total score and the scores for subscales HADS-A and HADS-D. The results showed significantly higher scores in patients with FM both for the total score ($p < 0.001$) and for each of the two subscales evaluating anxiety ($p < 0.001$) and depression ($p < 0.001$). According to the cut-off scores of the HADS, 67.5% (27/40) of the patients with FM showed a clinically relevant level of both anxiety and depression, compared with 34% (14/41) for anxiety ($X^2(1) = 9.011$, $p < 0.001$) and 19.5% (8/41) for depression ($X^2(1) = 19.000$, $p < 0.001$) in the HC group.

Concerning the clinical characteristics of the FM group, patients reported 6.47 ($\pm$ 5.81) years of duration of illness and a high rate of pain intensity (7 $\pm$ 2.55 to the item "Pain" of the FIQ).

Neuropsychological assessment

The comparisons between the neuropsychological scores of the two groups are shown in Table 2. Patients with FM performed worse than the HC group on all the four tasks evaluating EF (p values ranging from < 0.001–0.011). Furthermore, a poorer performance in the FM group also emerged in the DS F ($p = 0.005$), in the AVLT-Delayed recall ($p = 0.006$) and in the TMT B-A ($p = 0.004$). No statistically significant differences were found on the other neuropsychological measures.

Table 1. Demographic, clinical and psychological characteristics of the FM and HC groups.

		FM Patients (N = 40)	Healthy Controls (N = 41)	Test (df)	p
Age, years	Mean rank	41.29	40.72	Z = -0.109	0.913
Years of education	Mean (SD)	11.50 (3.33)	12.76 (3.68)	t(79) = -1.610	0.111
Duration of illness, years	Mean (SD)	6.47 (5.81)	-	-	-
FIQ-Pain	Mean (SD)	7.00 (2.55)	-	-	-
HADS Total	Mean (SD)	19.63 (6.57)	11.12 (5.76)	t(79) = 6.205	<0.001
	n% ($\geq$15)	33 (82.5%)	11 (26.8%)	X^2(1) = 25.289	<0.001
HADS D	Mean (SD)	9.58 (3.78)	5.05 (3.13)	t(79) = 5.874	<0.001
	n% ($\geq$8)	27 (67.5%)	8 (19.5%)	X^2(1) = 19.000	<0.001
HADS A	Mean (SD)	9.73 (3.78)	5.85 (3.49)	t(79) = 4.785	<0.001
	n% ($\geq$8)	27 (67.5%)	14 (34.1%)	X^2(1) = 9.011	0.003

FM = Fibromyalgia, df = Degrees of freedom, FIQ-Pain = item "Pain" of the Fibromyalgia Impact Questionnaire, HADS = Hospital Anxiety and Depression Scale, HADS-A and HADS-D = Anxiety and Depression subscales of the Hospital Anxiety and Depression Scale, SD = Standard deviation.

doi:10.1371/journal.pone.0116542.t001

Table 2. Neuropsychological tests scores. Mean (SD) or mean rank, t-test or Mann–Whitney *U* test are listed.

	FM Patients (N = 40)	Healthy Controls (N = 41)	Test (df)	*p*
DS F	4.93 (1.05)	5.61 (1.07)	t(79) = -2.911	0.005
AVLT	46.95 (9.43)	50.73 (8.72)	t(79) = -1.875	0.064
AVLT D	9.98 (2.90)	11.63 (2.39)	t(79) = -2.818	0.006
TMT A	45.41	36.70	Z = -1.669	0.095
TMT B-A	48.58	33.61	Z = -2.863	0.004
Executive functions measures				
FAS	38.45 (11.31)	45.73 (9.07)	t(79) = -3.640	< 0.001
DS B	3.59 (0.94)	4.54 (1.08)	t(78) = -4.299	< 0.001
ToL	26.10 (4.40)	28.78 (4.82)	t(79) = -2.610	0.011
TMT B	48.86	33.33	Z = -2.972	0.003

FM = Fibromyalgia, df = Degrees of freedom, DS F = Digit Span Forward, AVLT = Rey auditory-verbal learning test, AVLT D = Rey auditory-verbal learning test Delayed recall, TMT = Trail Making Test, FAS = verbal fluency, DS B = Digit Span Backward, ToL = Tower of London (total score—range 0–36—given by the sum of the time-based scores of the twelve configurations to solve; the higher the score the higher the performance), SD = Standard deviation.

doi:10.1371/journal.pone.0116542.t002

In order to bring out the individual differences that could be flattened by group analyses, the individual scores were analysed comparing for each test the number of subjects with impaired or borderline performance according to the age- and education-corrected scores (equivalent score ≤1). The results showed that a significantly higher number of patients with FM compared with HC had a deficient performance in the DS F (short-term memory) and B (working memory), and in the Delayed recall task of AVLT (episodic memory) (see Table 3).

Social cognition tasks

Data from social cognition tasks are reported in Table 4.

Regulation of own emotions. Concerning alexithymia, statistical analyses revealed the presence of significant differences between FM and HC on the TAS-20 total score ($p < 0.001$), and on the F1 ($p < 0.001$) and F2 subscales ($p = 0.011$); in all these comparisons patients with

Table 3. Number and percentage of patients with FM and healthy controls with impaired or borderline performance (E.S. = 0–1) at neuropsychological measures.

	FM Patients (N = 40)	Healthy Controls (N = 41)	Test (df)	*p*
DS F	17 (42.5%)	9 (22%)	X^2(1) = 3.923	0.048
AVLT	5 (12.5%)	1 (2.4%)	X^2(1) = 2.988	0.084
AVLT D	5 (12.5%)	0 (0%)	X^2(1) = 5.462	0.019
TMT A	0 (0%)	0 (0%)	-	-
TMT B-A	1 (2.5%)	0 (0%)	X^2(1) = 1.038	0.308
Executive functions measures				
FAS	2 (5%)	0 (0%)	X^2(1) = 2.102	0.147
DS B	18 (45%)	6 (14.6%)	X^2(1) = 8.954	0.003
ToL	2 (5%)	1 (2.4%)	X^2(1) = 0.372	0.542
TMT B	1 (2.5%)	0 (0%)	X^2(1) = 1.038	0.308

FM = Fibromyalgia, df = Degrees of freedom, DS F = Digit Span Forward, AVLT = Rey auditory-verbal learning test, AVLT D = Rey auditory-verbal learning test Delayed recall, TMT = Trail Making Test, FAS = verbal fluency, DS B = Digit Span Backward, ToL = Tower of London.

doi:10.1371/journal.pone.0116542.t003

Table 4. Theory of Mind and emotional functioning measures scores.

	FM Patients (N = 40)	Healthy Controls (N = 41)	Test (df)	p
Regulation of one's own emotions (Alexithymia)				
TAS-F1	21.78 (6.77)	14.24 (5.83)	t(79) = 5.368	**<0.001**
TAS-F2	15.30 (4.72)	12.61 (4.52)	t(79) = 2.619	**0.011**
TAS-F3	18.00 (3.44)	17.59 (4.66)	t(73.641) = 0.456	0.649
TAS-20 Total	54.75 (9.93)	44.56 (10.09)	t(79) = 4.579	**<0.001**
Empathic capacities				
EQ	45.95 (9.00)	48.44 (8.54)	t(79) = -1.277	0.205
Recognition of other's emotions				
Ekman Anger	7.98 (1.37)	8.61 (1.50)	t(79) = -2.002	**0.049**
Ekman Sadness	7.55 (1.55)	8.00 (1.20)	t(73.540) = -1.456	0.150
Ekman Fear	6.15 (2.53)	6.54 (2.64)	t(79) = -0.673	0.503
Ekman Surprise	37.43	44.49	Z = -1.502	0.133
Ekman Disgust	34.89	46.96	Z = -2.401	**0.016**
Ekman Happiness	38.96	42.99	Z = -1.111	0.266
Ekman Total	48.78 (4.80)	51.41 (4.23)	t(79) = -2.627	**0.010**
Representation of other people's affective mental states (Theory of Mind)				
RME Experimental	24.53 (3.81)	26.80 (3.55)	t(79) = -2.787	**0.007**
RME Control	43.38	38.68	Z = -0.973	0.331

FM = Fibromyalgia, df = Degrees of freedom, TAS-20 = Twenty-item Toronto Alexithymia Scale, TAS-F1 = Difficult identifying feelings factor of Toronto Alexithymia Scale, TAS-F2 = difficulty describing feelings factor of Toronto Alexithymia Scale, TAS-F3 = externally-oriented thinking factor of Toronto Alexithymia Scale, EQ = Empathy Quotient, RME = Reading the Mind in the Eyes, SD = Standard deviation.

doi:10.1371/journal.pone.0116542.t004

FM scored higher than HC. According to the TAS-20 cut-off scores, 27.5% (11/40) of the patients with FM were alexithymic and 45% (18/40) were borderline, compared with 7% (3/41) and 19.5% (8/41), respectively, in the HC group.

Empathic capacity. No significant difference between the two groups was found in the EQ score.

Recognition of others emotions. Concerning the Ekman 60 Faces Test, independent *t*-tests revealed the presence of significant differences between the two groups on total score (*p* = 0.010), and on two of the six emotions investigated by means of the test, i.e. anger (*p* = 0.049) and disgust (*p* = 0.016). Once again, patients with FM showed significantly lower scores, indicating a reduced ability to recognise other people's emotions, especially anger and disgust.

Representation of other people's affective mental states. No significant difference between FM and HC was found in the control task for RME. In the experimental condition, patients with FM evidenced a significantly lower performance on the mental states attribution task (*p* = 0.007).

Correlations

The second aim of this study was to investigate the possible relationships between social cognition tasks and EF measures in patients with FM. Moreover, we also evaluated the correlations between social cognition tasks and demographic, clinical and psychological data. To do that, we only considered the variables that showed a significant difference in the comparison between FM and HC, i.e. TAS-20 F1, F2, and total score; Ekman anger, disgust and total score; and RME experimental task.

Correlations between social cognition measures and EF tasks are listed in Table 5. As shown, no significant correlation was found, with the only exception of a low positive

Table 5. Pearson or Spearman correlations in FM group between the four executive function measures and TAS-20, Ekman and RME.

	FAS	DS B	ToL	TMT B
TAS-F1	r = -0.206 p = 0.203	r = -0.077 p = 0.641	r = -0.200 p = 0.215	r_s = 0.244 p = 0.129
TAS-F2	r = -0.078 p = 0.631	r = 0.198 p = 0.226	r = 0.165 p = 0.309	r_s = -0.151 p = 0.351
TAS-20 Total	r = -0.183 p = 0.258	r = 0.113 p = 0.495	r = 0.061 p = 0.708	r_s = 0.019 p = 0.906
Ekman Anger	r = -0.085 p = 0.600	r = 0.000 p = 1000	r = 0.184 p = 0.257	r_s = 0.206 p = 0.203
Ekman Disgust	r_s = 0.224 p = 0.165	r_s = 0.026 p = 0.876	r_s = -0.031 p = 0.850	r_s = -0.196 p = 0.225
Ekman Total	r = 0.259 p = 0.106	r = 0.322 p = 0.046	r = -0.125 p = 0.443	r_s = -0.311 p = 0.051
RME Experimental	r = 0.299 p = 0.061	r = 0.232 p = 0.156	r = -0.112 p = 0.492	r_s = -0.121 p = 0.457

FAS = verbal fluency, DS B = Digit Span Backward, ToL = Tower of London, TMT = Trail Making Test, TAS-20 = Twenty-item Toronto Alexithymia Scale, TAS-F1 = Difficult identifying feelings factor of Toronto Alexithymia Scale, TAS-F2 = difficulty describing feelings factor of Toronto Alexithymia Scale, RME = Reading the Mind in the Eyes.

doi:10.1371/journal.pone.0116542.t005

correlation between the Ekman total score and the DS B. In addition, we verified the possible relationships between social cognition measures, EF tasks and duration of illness (DI) in FM group and no significant correlation emerged (DI and FAS: r = -0.276, p: ns; DI and DS B: r = -0.132, p: ns; DI and ToL: r = 0.196, p: ns; DI and TMT B: r_s = 0.185, p: ns; DI and TAS-20 F1: r = 0.319, p: ns; DI and TAS-20 F2: r = 0.333, p: ns; DI and TAS-20 Total: r = 0.342, p: ns; DI and Ekman Anger: r = 0.087, p: ns; DI and Ekman Disgust: r_s = -0.175, p: ns; DI and Ekman Total: r = -0.036, p: ns; DI and RME Experimental: r = -0.053, p: ns).

Regarding the relationship between social cognition measures and demographic, clinical and psychological variables, no significant correlations were detected between age, HADS-A, HADS-D, FIQ-pain, and the RME experimental or the Ekman anger, disgust and total score; a positive correlation was only found between the RME experimental and the level of education (r = 0.359, p = 0.023). However, significant correlations were detected between demographic, clinical and psychological variables and the TAS-20 scores. In particular, positive correlations were found between the TAS-20 total score and the HADS-A (r = 0.334, p = 0.035), the HADS-D (r = 0.630, p < 0.001), and the FIQ-pain (r = 0.518, p = 0.001). Likewise, positive correlations were found between the TAS-20 F1 and the HADS-A (r = 0.462, p = 0.003), the HADS-D (r = 0.476, p = 0.002) and the FIQ-pain (r = 0.442, p = 0.004). Finally, the TAS-20 F2 was positively correlated only with the HADS-D (r = 0.537, p < 0.001) and the FIQ-Pain (r = 0.344, p = 0.030).

Discussion

The present study aimed to address two main objectives. Firstly, we evaluated the social-cognitive profile of patients with FM, investigating ToM and emotional processing abilities. Secondly, we analysed the relationship between EF deficits and social cognition tasks in patients with FM. Correlations between demographic, clinical and psychological variables, and measures of social cognition were also evaluated.

The results highlighted a significant difference between patients with FM and the HC group in most of the social cognition tasks employed. In particular, the FM group showed significantly higher levels of alexithymia, especially in the subscales "Difficulty in identifying feelings" and "Difficulty describing feelings" of TAS-20, compared to the control sample. These data are in line with most of the studies that have evaluated the prevalence of alexithymia in patients with FM [16–20].

A similar significant difference was found for the experimental task of the RME, while no significant difference was observed for the control task. Patients with FM experienced specific difficulties in representing other people's affective mental states that cannot be attributed to a

basic sensory deficit. The Ekman 60 Faces Test results also showed the presence of significant differences (lower performance of patients with FM) between the two groups both for the total score and for two of the six emotions investigated by means of the test, i.e. anger and disgust; no significant differences were found for other emotions. These data are in line with the only study that has investigated the ability to recognise another's facial emotions in patients with FM [27]. As mentioned above, these authors showed that patients with FM had reduced performance in the facial affect recognition task, with a higher percentage of misclassifications of emotional expressions compared with the HC group.

The only social cognition task, in which no differences between the two groups were found, was the EQ. In this case, the FM group didn't report a lower capacity for empathy compared to the control group.

Concerning the general cognitive profile, neuropsychological assessment revealed the presence of significant differences in most of the measures. In particular, the FM group displayed significantly lower performance on the verbal fluency (FAS), the DS B and F, the AVLT-Delayed recall, and the TMT B and B-A, compared to HC. These data are consistent with previous studies that have reported cognitive deficits in attention, memory, and EF domains in patients with FM [71–74]. In particular, Park et al. [71] found that patients with FM demonstrated lower performance on measures of working memory, free recall, verbal fluency, and verbal knowledge, but showed intact speed of processing, compared with age- and education-matched controls. Significantly, patients with FM in that study performed no differently from controls who were 20 years older on most cognitive tasks, with the exception of speed of processing and vocabulary. Only self-reported pain on the Arthritis Impact Measurement Scales predicted poor cognitive performance in the FM group. Measures of depression, anxiety, and the McGill Pain Questionnaire scores were all unrelated to poor cognitive performance. Verdejo-Garcia et al. [73] observed that in the Wisconsin Card Sorting Test, women with FM showed poorer performance than healthy women on the number of categories and non-perseverative errors, but not on perseverative errors. Patients with FM also exhibited an altered learning curve in the original Iowa Gambling Task (IGT) (where reward is immediate and punishment is delayed), suggesting compromised emotion-based decision-making. This was not the case in the variant IGT (where punishment is immediate but reward is delayed), suggesting hypersensitivity to reward. Self-reported pain intensity and pain interference were significantly associated with task performance. In contrast, cognitive performance was not associated with measures of negative mood (i.e. affective distress) or duration of pharmacological treatment, and was very mildly associated with personality characteristics [73].

Finally, from a psychological standpoint, our group of patients with FM presented with significantly higher levels of depressive and anxiety symptoms (67.5% in both cases) compared with the HC group. These results corroborate, once again, the high prevalence of psychological distress reported in previous studies of patients with FM [14–15, 19].

To the best of our knowledge, this is the first study to investigate social-cognitive abilities in a homogenous sample of patients with FM. The results show that patients with FM have impairments both in the regulation of their own affect and in the recognition of other's emotions, as well as in representing other people's affective mental states. There is evidence that appropriate behaviour in social interactions is determined by the ability to decipher information about the intentions and affective states of social partners. Thus, impairments in facial affect recognition and difficulties in accurately inferring other people's affective mental states may lead to substantial difficulties in interpersonal contacts (e.g. interaction problems with family and friends, or social isolation), which have been already reported in patients with FM [95]. Furthermore, poor psychosocial functioning and unsatisfactory relationships might contribute to the genesis and maintenance of chronic pain [96], intensifying the symptomatology in individuals with FM.

From a neurological standpoint, the brain networks relevant for pain and emotional processing partially overlap. The amygdala plays a crucial role in sharing emotional experiences and in recognising emotions in oneself and others [34, 36]. In particular, this structure is involved in the decoding of emotional expressions, and modulates the activity of the fusiform gyrus, which constitutes the most prominent face-selective area of the brain. Neuroimaging studies have indeed shown sensitivity of the amygdala to the kind and valence of facially expressed emotions [97–98]. The insular cortex may also be relevant in this context. It has been reported, for instance, that impaired disgust recognition is associated with reduced insula activity [99]. In addition to their prominent role in emotional functioning, the amygdala and the insula are integral parts of the neural network underlying pain. Specifically, both structures are involved in transmitting the affective dimension of pain perception [100] and are altered in patients with FM [69, 101]. The hyperactivity of the pain network due to central nervous system sensitisation, may lead to an increased demand on structures such as the amygdala and insula, reducing the available resources for other functions such as emotional processing.

As far as the second goal of this study is concerned, we investigated whether EF measures in the FM group were related to the different social cognition tasks that were used. In addition, we also analysed the possible relationships between demographic, clinical and psychological variables, and measures of social cognition. Concerning EF tasks, no correlations were found between social cognition tasks and each of the four subcomponents of the EF domain that were analysed. The only exception was represented by a low positive correlation between the Ekman total score and the DS B. Regarding the demographic, clinical and psychological variables, correlation analyses showed no relationship between Ekman total score, anger and disgust, RME experimental, on the one hand, and anxiety, depression and pain intensity, on the other hand. Positive correlations were only detected between the latter measures (anxiety, depression, and pain) and the total score and scores for the F1 and F2 subscales of the TAS-20. This result is consistent with previous studies that have investigated the presence of alexithymia in FM patients [18, 20, 102]. In particular, Steinweg et al. [102] found higher levels of alexithymia in FM patients compared with either general medical or rheumatoid arthritis patients. However, they also revealed that alexithymia was strongly associated with moderate-to-severe depression, but no group differences were detected when mood disturbance was controlled for.

Taken together, as far as the first aim of this study is concerned, the results show the presence of several impairments in social cognition skills in patients with FM. As for the second aim, i.e. to explore the possible relationships between the performance on executive-function tasks and the performance on social-cognition tasks in patients with FM, we found that the latter are largely independent of both EF deficits and symptoms of psychological distress. The only exception seems to be represented by alexithymia; in fact, psychological disorders, but not EF deficits, seem to play a role in explaining the high levels of alexithymia found in the FM sample. Concerning other measures of social cognition, no relationship was found with EF deficits or symptoms of psychological distress. In our sample, impairments in ToM and emotional processing ability appeared to be independent of the EF domain.

This study also has some limitations. Firstly, even though we enrolled an adequate number of patients with FM, our study is still limited by a relatively small sample size. Secondly, the self-reported measures we used might have elicited a bias towards social desirability, masking the real profile of some individuals. Thirdly, although in patients with FM there is evidence of structural and functional alterations in brain areas crucial for ToM and emotional processing abilities (i.e. the prefrontal cortex and the amygdala) [67–70], we didn't directly measure the activity in these brain structures. Future studies should include neuroimaging evaluations and use performance-based instruments for the analysis of both empathic capacity and alexithymia, in addition to traditional self-reported tests.

In spite of these limitations, the findings reported in the present study represent the first contribution towards understanding the complex social-cognitive profile of patients with FM. The impairments reported in tasks that evaluate ToM and emotional processing abilities highlight the importance of adequately assessing these abilities in clinical practice. In this way, it could be possible for clinicians to plan better pharmacological and/or psychological treatment based on each patient's needs.

Acknowledgments

The authors would like to thank Valentina Tesio, Stefania Brighenti and Francesca Monoli for their help in collecting data.

Author Contributions

Conceived and designed the experiments: MDT LC MA. Performed the experiments: MDT FC EF RT. Analyzed the data: MDT LC RBA MA. Contributed reagents/materials/analysis tools: LC RBA MA. Wrote the paper: MDT LC RBA MA.

References

1. Mease P (2005) Fibromyalgia syndrome: review of clinical presentation, pathogenesis, outcome measures, and treatment. J Rheumatol 75: 6–21.

2. Mease P, Buskila D, Sarzi-Puttini P (2009) The fibromyalgia conundrum. Clin Exp Rheumatol 27(56): S2–S4. PMID: 20074432

3. WHO (2008) World Health Organization Treatment Guideline on Non-malignant Pain in Adults. Available: http://www.who.int/en/. Accessed 14 October 2008.

4. Macfarlane GJ, Morris S, Hunt IM, Benjamin S, McBeth J, et al. (1999) Chronic widespread pain in the community: The influence of psychological symptoms and mental disorder on healthcare seeking behavior. J Rheumatol 26: 413–419. PMID: 9972978

5. Anderberg UM, Marteinsdottir I, Theorell T, von Knorring L (2000) The impact of life events in female patients with fibromyalgia and in female healthy controls. Eur Psychiatry 15: 295–301. doi: 10.1016/S0924-9338(00)00397-7 PMID: 10954873

6. Branco JC, Bannwarth B, Failde I, Abello Carbonell J, Blotman F, et al. (2010). Prevalence of fibromyalgia: a survey in five European countries. Semin Arthritis Rheum 39(6): 448–453. doi: 10.1016/j.semarthrit.2008.12.003 PMID: 19250656

7. Schmidt-Wilcke T, Clauw DJ (2011) Fibromyalgia: from pathophysiology to therapy. Nat Rev Rheumatol 7(9): 518–527. doi: 10.1038/nrrheum.2011.98 PMID: 21769128

8. Hawley DJ, Wolfe F, Cathey MA (1988) Pain, functional disability, and psychological status: a 12-month study of severity in fibromyalgia. J Rheumatol 15: 1551–1556. PMID: 3204601

9. Ledingham J, Doherty S, Doherty M (1993) Primary fibromyalgia syndrome: an outcome study. Br J Rheumatol 32: 139–142. doi: 10.1093/rheumatology/32.2.139 PMID: 8428227

10. Epstein SA, Williams DA, Osbeck L, Clauw D (1995) Effect of psychological factors on pain perception in fibromyalgia (abstract). Psychosomatics 36: 192.

11. Van Houdenhove B, Luyten P (2007) Fibromyalgia and related syndromes characterised by stress intolerance and pain hypersensitivity: Do we need a new nosology? Curr Rheumatol Rev 3: 304–308. doi: 10.2174/157339707782408937

12. McBeth J, Chiu YH, Silman AJ, Ray D, Morriss R, et al. (2005) Hypothalamic-pituitary-adrenal stress axis function and the relationship with chronic widespread pain and its antecedents. Arthritis Res Ther 7: 992–1000. doi: 10.1186/ar1772

13. Ngian GS, Guymer EK, Littlejohn GO (2011) The use of opioids in fibromyalgia. Int J Rheum Dis 14: 6–11. doi: 10.1111/j.1756-185X.2010.01567.x PMID: 21303476

14. Montoya P, Sitges C, Garcia-Herrera M, Izquierdo R, Truyols M, et al. (2005) Abnormal affective modulation of somatosensory brain processing among patients with fibromyalgia. Psychosom Med 67: 957–963. doi: 10.1097/01.psy.0000188401.55394.18 PMID: 16314601

15. Fietta P, Fietta P, Manganelli P (2007) Fibromyalgia and psychiatric disorders. Acta Biomed 78: 88–95. PMID: 17933276

16. Sayar K, Gulec H, Topbas M (2004) Alexithymia and anger in patients with fibromyalgia. Clin Rheumatol 23: 441–448. doi: 10.1007/s10067-004-0918-3 PMID: 15278756

17. Pedrosa-Gil F, Weigl M, Wessels T, Irnich D, Baumüller E, et al. (2008) Parental bonding and alexithymia in adults with fibromyalgia. Psychosomatics 49: 115–122. doi: 10.1176/appi.psy.49.2.115 PMID: 18354064

18. Huber A, Suman AL, Biasi G, Carli G (2009) Alexithymia in fibromyalgia syndrome: associations with ongoing pain, experimental pain sensitivity and illness behavior. J Psychosom Res 66: 425–433. doi: 10.1016/j.jpsychores.2008.11.009 PMID: 19379959

19. Castelli L, Tesio V, Colonna F, Molinaro S, Leombruni P, et al. (2012) Alexithymia and psychological distress in fibromyalgia: prevalence and relation with quality of life. Clin Exp Rheumatol 30: 70–77. PMID: 23110722

20. Di Tella M, Castelli L (2013) Alexithymia and fibromyalgia: clinical evidence. Front Psychol 4: 909. doi: 10.3389/fpsyg.2013.00909 PMID: 24348453

21. Sifneos PE (1972) Short-term psychotherapy and emotional crisis. Cambridge: Harvard University Press.

22. Taylor GJ, Bagby RM, Parker JDA (1997) Disorders of affect regulation: Alexithymia in medical and psychiatric illness. Cambridge: Cambridge University Press.

23. Pedrosa G, Ridout N, Kessler H, Schoechlin C, Traue HC, et al. (2009). Facial emotion recognition and alexithymia in adults with somatoform disorders. Depress Anxiety 26: E26–E33. doi: 10.1002/da.20456

24. Subic-Wrana C, Beutel ME, Knebel A, Lane RD (2010) Theory of mind and emotional awareness deficits in patients with somatoform disorders. Psychosom Med 72(4): 404–411. doi: 10.1097/PSY.0b013e3181d35e83 PMID: 20223925

25. Adenzato M, Todisco P, Ardito RB (2012) Social cognition in anorexia nervosa: Evidence of preserved Theory of Mind and impaired emotional functioning. PLoS ONE 7(8): e44414. doi: 10.1371/journal.pone.0044414 PMID: 22952975

26. Cicerale A, Settanta C, D'Agata F, Caglio M, Caroppo P, et al. (2013) Neuroanatomical correlates of state of mind with respect to attachment in patients with anorexia nervosa. Clinical Neuropsychiatry 10: 217–225.

27. Weiß S, Winkelmann A, Duschek S (2013) Recognition of facially expressed emotions in patients with fibromyalgia syndrome. Behav Med 39: 146–154. doi: 10.1080/08964289.2013.818932 PMID: 24236812

28. Adolphs R (2001) The neurobiology of social cognition. Curr Opin Neurobiol 11: 231–239. doi: 10.1016/S0959-4388(00)00202-6 PMID: 11301245

29. Adolphs R (2003) Investigating the cognitive neuroscience of social behaviour. Neuropsychologia 41: 119–126. doi: 10.1016/S0028-3932(02)00142-2 PMID: 12459210

30. Premack DG, Woodruff G (1978) Does the chimpanzee have a theory of mind? Behav Brain Sci 1: 515–526. doi: 10.1017/S0140525X00076512

31. Leslie AM (1987) Pretense and representation: The origins of 'Theory of Mind'. Psychol Rev 94: 412–426. doi: 10.1037/0033-295X.94.4.412

32. Decety J, Jackson PL (2004) The functional architecture of human empathy. Behav Cogn Neurosci Rev 3: 71–100. doi: 10.1177/1534582304267187 PMID: 15537986

33. Lieberman MD (2007) Social cognitive neuroscience: A review of core processes. Annu Rev Psychol 58: 259–289. doi: 10.1146/annurev.psych.58.110405.085654 PMID: 17002553

34. Vollm BA, Taylor AN, Richardson P, Corcoran R, Stirling J, et al. (2006) Neuronal correlates of theory of mind and empathy: A functional magnetic resonance imaging study in a nonverbal task. NeuroImage 29: 90–98. doi: 10.1016/j.neuroimage.2005.07.022 PMID: 16122944

35. Decety J (2010) The neurodevelopment of empathy in human. Dev Sci 32: 257–267. doi: 10.1159/000317771

36. Lee KH, Siegle GJ (2012) Common and distinct brain networks underlying explicit emotional evaluation: A meta-analytic study. Soc Cogn Affect Neurosci 7: 521–534. doi: 10.1093/scan/nsp001 PMID: 19270039

37. Walter H, Adenzato M, Ciaramidaro A, Enrici I, Pia L, et al. (2004) Understanding intentions in social interactions: the role of the anterior parancingulate cortex. J Cogn Neurosci 16: 1854–1863. doi: 10.1162/0898929042947838 PMID: 15701234

38. Ciaramidaro A, Adenzato M, Enrici I, Erk S, Pia L, et al. (2007) The intentional network: how the brain reads varieties of intentions. Neuropsychologia 45: 3105–3113. doi: 10.1016/j.neuropsychologia.2007.05.011 PMID: 17669444

39. Enrici I, Adenzato M, Cappa S, Bara BG, Tettamanti M (2011) Intention processing in communication: a common brain network for language and gestures. J Cogn Neurosci 23: 2415–2431. doi: 10.1162/jocn.2010.21594 PMID: 20954937

40. Walter H, Ciaramidaro A, Adenzato M, Vasic N, Ardito RB, et al. (2009) Dysfunction of the social brain in schizophrenia is modulated by intention type: An fMRI study. Soc Cogn Affect Neurosci 4: 166–176. doi: 10.1093/scan/nsn047 PMID: 19287044

41. Bara BG, Ciaramidaro A, Walter H, Adenzato M (2011) Intentional minds: A philosophical analysis of intention tested through fMRI experiments involving people with schizophrenia, people with autism, and healthy individuals. Front Hum Neurosci 5: 7. doi: 10.3389/fnhum.2011.00007 PMID: 21344005

42. Van Overwalle F (2009) Social cognition and the brain: a meta-analysis. Hum Brain Mapp 30: 829–858. doi: 10.1002/hbm.20547 PMID: 18381770

43. Schnell K, Bluschke S, Konradt B, Walter H (2011) Functional relations of empathy and mentalizing: An fMRI study on the neural basis of cognitive empathy. NeuroImage 54: 1743–1754. doi: 10.1016/j.neuroimage.2010.08.024 PMID: 20728556

44. Gallagher HL, Frith CD (2003) Functional imaging of 'theory of mind'. Trends Cogn Sci 7: 77–83. doi: 10.1016/S1364-6613(02)00025-6 PMID: 12584026

45. Phan KL, Wager T, Taylor SF, Liberzon I (2002) Functional neuroanatomy of emotion: A meta-analysis of emotion activation studies in PET and fMRI. NeuroImage 16: 331–348. doi: 10.1006/nimg.2002.1087 PMID: 12030820

46. Ruby P, Decety J (2004) How would you feel versus how do you think she would feel? A neuroimaging study of perspective-taking with social emotions. J Cogn Neurosci 16: 988–999. doi: 10.1162/0898929041502661 PMID: 15298786

47. Singer T (2006) The neuronal basis and ontogeny of empathy and mind reading: Review of literature and implications for future research. Neurosci Biobehav Rev 30: 855–863. doi: 10.1016/j.neubiorev.2006.06.011 PMID: 16904182

48. Costafreda SG, Brammer MJ, David AS, Fu CH (2008) Predictors of amygdale activation during the processing of emotional stimuli: A meta-analysis of 385 PET and fMRI studies. Brain Res Rev 58: 57–70. doi: 10.1016/j.brainresrev.2007.10.012 PMID: 18076995

49. Fine C, Lumsden J, Blair RJ (2001) Dissociation between 'theory of mind' and executive functions in a patient with early left amygdala damage. Brain 124: 287–298. doi: 10.1093/brain/124.2.287 PMID: 11157556

50. Lough S, Gregory C, Hodges JR (2001) Dissociation of social cognition and executive function in frontal variant frontotemporal dementia. Neurocase 7(2): 123–130. doi: 10.1093/neucas/7.2.130 PMID: 11320160

51. Pellicano E (2007) Links between theory of mind and executive function in young children with autism: Clues to developmental primacy. Dev Psychol 43(4): 974–990. doi: 10.1037/0012-1649.43.4.974 PMID: 17605529

52. Pickup GJ (2008) Relationship between theory of mind and executive function in schizophrenia: A systematic review. Psychopathology 41: 206–213. doi: 10.1159/000125554 PMID: 18408416

53. Poletti M, Enrici I, Adenzato M (2012) Cognitive and affective Theory of Mind in neurodegenerative diseases: Neuropsychological, neuroanatomical and neurochemical levels. Neurosci Biobehav Rev 36: 2147–2164. doi: 10.1016/j.neubiorev.2012.07.004 PMID: 22819986

54. Adenzato M, Cavallo M, Enrici I (2010) Theory of Mind ability in the behavioural variant of frontotemporal dementia: An analysis of the neural, cognitive, and social levels. Neuropsychologia 48: 2–12. doi: 10.1016/j.neuropsychologia.2009.08.001 PMID: 19666039

55. Cavallo M, Adenzato M, MacPherson SE, Karwig G, Enrici I, et al. (2011) Evidence of social understanding impairment in patients with Amyotrophic Lateral Sclerosis. PLoS ONE 6(10): e25948. doi: 10.1371/journal.pone.0025948 PMID: 21998727

56. Poletti M, Enrici I, Bonuccelli U, Adenzato M (2011) Theory of Mind in Parkinson's disease. Behav Brain Res 219: 342–350. doi: 10.1016/j.bbr.2011.01.010 PMID: 21238496

57. Adenzato M, Poletti M (2013) Theory of Mind abilities in neurodegenerative diseases: An update and a call to introduce mentalizing tasks in standard neuropsychological assessments. Clinical Neuropsychiatry 10: 226–234.

58. Lezak MH, Howieson DB, Loring DW (2004) Neuropsychological assessment (4th ed.). New York: Oxford University Press.

59. Aboulafia-Brakha T, Christe B, Martory MD, Annoni JM (2011) Theory of mind tasks and executive functions: a systematic review of group studies in neurology. J Neuropsychol 5: 39–55. doi: 10.1348/174866410X533660 PMID: 21366886

60. Stuss DT, Levine B (2002) Adult clinical neuropsychology: Lessons from studies of the frontal lobes. Annu Rev Psychol 53: 401–433. doi: 10.1146/annurev.psych.53.100901.135220 PMID: 11752491

61. Collette F, Van der Linden M, Laureys S, Delfiore G, Degueldre C, et al. (2005) Exploring the unity and diversity of the neural substrates of executive functioning. Hum Brain Mapp 25(4): 409–423. doi: 10.1002/hbm.20118 PMID: 15852470

62. Jurado MB, Rosselli M (2007) The elusive nature of executive functions: A review of our current understanding. Neuropsychol Rev 17(3): 213–233. doi: 10.1007/s11065-007-9040-z PMID: 17786559

63. Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A (2000) The unity and diversity of executive functions and their contributions to complex "Frontal lobe" tasks: a latent variable analysis. Cogn Psychol 41: 49–100. doi: 10.1006/cogp.1999.0734 PMID: 10945922

64. Fisk JE, Sharp CA (2004) Age-related impairment in executive functioning: updating, inhibition, shifting and access. J Clin Exp Neuropsychol 26(7): 874–890. doi: 10.1080/13803390490510680 PMID: 15742539

65. Baron-Cohen S, Leslie AM, Frith U (1985) Does the autistic child have a "theory of mind"? Cognition 21: 37–46. doi: 10.1016/0010-0277(85)90022-8 PMID: 2934210

66. Stone VE, Gerrans P (2006) What's domain-specific about theory of mind? Soc Neurosci 1: 309–319. doi: 10.1080/17470910601029221 PMID: 18633796

67. Grant MA, Farrell MJ, Kumar R, Clauw DJ, Gracely RH (2001) fMRI evaluation of pain intensity coding in fibromyalgia patients and controls [abstract]. Arthritis Rheum 44(9): S394.

68. Burgmer M, Gaubitz M, Konrad C, Wrenger M, Hilgart S, et al. (2009) Decreased gray matter volumes in the cingulo-frontal cortex and the amygdala in patients with fibromyalgia. Psychosom Med 71(5): 566–573. doi: 10.1097/PSY.0b013e3181a32da0 PMID: 19414621

69. Gracely RH, Ambrose KR (2011) Neuroimaging of fibromyalgia. Best Pract Res Clin Rheumatol 25: 271–284. doi: 10.1016/j.berh.2011.02.003 PMID: 22094201

70. Lee SJ, Song HJ, Decety J, Seo J, Kim SH, et al. (2013) Do patients with fibromyalgia show abnormal neural responses to the observation of pain in others? Neurosci Res 75(4): 305–315. doi: 10.1016/j.neures.2013.01.013 PMID: 23419861

71. Park DC, Glass JM, Minear M, Crofford LJ (2001) Cognitive function in Fibromyalgia patients. Arthritis Rheum 44: 2125–2133. doi: 10.1002/1529-0131(200109)44:9%3C2125::AID-ART365%3E3.0.CO;2-1 PMID: 11592377

72. Glass JM (2009) Review of cognitive dysfunction in fibromyalgia: A convergence on working memory and attentional control impairments. Rheum Dis Clin North Am 35: 299–311. doi: 10.1016/j.rdc.2009.06.002 PMID: 19647144

73. Verdejo-Garcia A, Lopez-Torrecillas F, Calandre EP, Delgado-Rodriguez A, Bechara A (2009) Executive function and decision-making in women with fibromyalgia. Arch Clin Neuropsychol 24: 113–122. doi: 10.1093/arclin/acp014 PMID: 19395361

74. Miró E, Lupiáñez J, Hita E, Martínez MP, Sánchez AI, et al. (2011) Attentional deficits in fibromyalgia and its relationships with pain, emotional distress and sleep dysfunction complaints. Psychol Health 26(6): 765–780. doi: 10.1080/08870446.2010.493611 PMID: 21391131

75. American Psychiatric Association (2000) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC: American Psychiatric Publishing.

76. Sarzi-Puttini P, Atzeni F, Fiorini T, Panni B, Randisi G, et al. (2003) Validation of an Italian version of the Fibromyalgia Impact Questionnaire (FIQ-I). Clin Exp Rheumatol 21: 459–464. PMID: 12942697

77. Bennett R (2005) The Fibromyalgia Impact Questionnaire (FIQ): a review of its development, current version, operating characteristics and uses. Clin Exp Rheumatol 23(39): S154–S162. PMID: 16273800

78. Costantini M, Musso M, Viterbori P, Bonci F, Del Mastro L, et al. (1999). Detecting psychological distress in cancer patients: validity of the Italian version of the Hospital Anxiety and Depression Scale. Support Care Cancer 7: 121–127. doi: 10.1007/s005200050241 PMID: 10335929

79. Bjelland I, Dahl AA, Haug TT, Neckelmann D (2002) The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 52: 69–77. doi: 10.1016/S0022-3999(01)00296-3

80. Zigmond AS, Snaith RP (1983) The Hospital Anxiety and Depression Scale. Psych Scand 67: 361–370. doi: 10.1111/j.1600-0447.1983.tb09716.x

81. Orsini A, Grossi D, Capitani E, Laiacona M, Papagno C, et al. (1987) Verbal and spatial immediate memory span: Normative data from 1355 adults and 1112 children. Ital J Neurol Sci 8: 539–548. doi: 10.1007/BF02333660 PMID: 3429213

82. Carlesimo GA, Caltagirone C, Gainotti G, Nocentini U (1995). Batteria per la valutazione del deteriora-mento mentale (Parte II): standardizzazione e affidabilità diagnostica nell'identificazione dei pazienti affetti da sindrome demenziale. Arch Psicol Neurol Psichiatr 56(4): 471–488.

83. Reitan RM (1958) Validity of the Trail Making test as an indicator of organic brain damage. Percept Mot Skills 8: 271–276. doi: 10.2466/pms.1958.8.3.271

84. Shallice T (1982) Specific impairments of planning. Phil Trans R Soc Lond B 298: 199–209. doi: 10.1098/rstb.1982.0082

85. Allamanno N, Della Sala S, Laiacona M, Pasetti C, Spinnler H (1987). Problem solving ability in aging and dementia: normative data on a non-verbal test. Ital J Neurol Sci 8: 111–119. doi: 10.1007/BF02337583 PMID: 3597050

86. Carlesimo GA, Caltagirone C, Gainotti G (1996). The Mental Deterioration Battery: normative data, diagnostic reliability and qualitative analyses of cognitive impairment. Eur Neurol 36(6): 378–384. doi: 10.1159/000117297 PMID: 8954307

87. Bressi C, Taylor G, Parker J, Bressi S, Brambilla V, et al. (1996). Cross validation of the factor struc-ture of the 20-item Toronto Alexithymia Scale: an Italian multicenter study. J Psychosom Res 41: 551–559. doi: 10.1016/S0022-3999(96)00228-0 PMID: 9032718

88. Taylor GJ, Bagby RM (2004) New trends in alexithymia research. Psychother Psychosom 73: 68–77. doi: 10.1159/000075537 PMID: 14767148

89. Lumley MA, Neely LC, Burger AJ (2007) The assessment of alexithymia in medical settings: implica-tions for understanding and treating health problems. J Pers Assess 89: 230–246. doi: 10.1080/00223890701629698 PMID: 18001224

90. Baron-Cohen S, Wheelwright S (2004) The empathy quotient: An investigation of adults with Asperger syndrome or high functioning autism, and normal sex differences. J Autism Dev Disord 34: 163–175. doi: 10.1023/B:JADD.0000022607.19833.00 PMID: 15162935

91. Preti A, Vellante M, Baron-Cohen S, Zucca G, Petretto DR, et al. (2011) The Empathy Quotient: a cross-cultural comparison of the Italian version. Cogn Neuropsychiatry 16(1): 50–70. doi: 10.1080/13546801003790982 PMID: 20737328

92. Dodich A, Cerami C, Canessa N, Crespi C, Marcone A, et al. (2014) Emotion recognition from facial expressions: a normative study of the Ekman 60-Faces Test in the Italian population. Neurol Sci 35 (7): 1015–1021. doi: 10.1007/s10072-014-1631-x PMID: 24442557

93. Ekman P, Friesen W (1976) Pictures of facial affect. Palo Alto: Consulting Psychologist Press.

94. Baron-Cohen S, Wheelwright S, Hill J, Raste Y, Plumb I (2001) The "Reading the Mind in the Eyes" test revised version: A study with normal adults, and adults with Asperger syndrome or high-function-ing autism. J Child Psychol Psychiatry 42: 241–251. doi: 10.1111/1469-7610.00715 PMID: 11280420

95. Arnold LM, Crofford LJ, Mease PJ, Burgess SM, Palmer SC, et al. (2008) Patients perspectives on the impact of fibromyalgia. Patient Educ Couns 73: 114–120. doi: 10.1016/j.pec.2008.06.005 PMID: 18640807

96. Flor H, Turk DC (2006) Cognitive and learning aspects. In: McMahon SB, Koltzenburg M, editors. Textbook of Pain. Amsterdam: Elsevier. pp. 241–258.

97. Vuilleumier P, Armony JL, Driver J, Dolan RJ (2003) Distinct spatial frequency sensitivities for pro-cessing faces and emotional expressions. Nat Neurosci 6: 624–631. doi: 10.1038/nn1057 PMID: 12740580

98. Vuilleumier P, Pourtois G (2007) Distributed and interactive brain mechanisms during emotion face perception: evidence from functional neuroimaging. Neuropsychologia 45: 174–194. doi: 10.1016/j.neuropsychologia.2006.06.003 PMID: 16854439

99. Sambataro F, Dimalta S, Di Giorgio A, Taurisano P, Blasi G, et al. (2006). Preferential responses in amygdala and insula during presentation of facial contempt and disgust. Eur J Neurosci 24: 2355–2362. doi: 10.1111/j.1460-9568.2006.05120.x PMID: 17042790

100. Apkarian AV, Bushnell MC, Treede RD, Zubieta JK (2005) Human brain mechanisms of pain percep-tion and regulation in health and disease. Eur J Pain 9: 463–484. doi: 10.1016/j.ejpain.2004.11.001 PMID: 15979027

101. Burgmer M, Pogatzki-Zahn E, Gaubitz M, Stüber C, Wessoleck E, et al. (2010) Fibromyalgia unique temporal brain activation during experimental pain: a controlled fMRI Study. J Neural Transm 117: 123–131. doi: 10.1007/s00702-009-0339-1 PMID: 19937376

102. Steinweg DL, Dallas AP, Rea WS (2011) Fibromyalgia: unspeakable suffering, a prevalence study of alexithymia. Psychosomatics 52: 255–262. doi: 10.1016/j.psym.2010.12.022 PMID: 21565597