



**GUBBIO** | 23-25  
PARK HOTEL | MAGGIO  
CAPPUCCINI | 2024

# Trattamento dei sintomi concomitanti

Marina De Tommaso

# La fibromialgia è un puzzle...

**Table 3**  
Fibromyalgia criteria—2016 revision

**Criteria**

A patient satisfies modified 2016 fibromyalgia criteria if the following 3 conditions are met:

- (1) Widespread pain index (WPI)  $\geq 7$  and symptom severity scale (SSS) score  $\geq 5$  OR WPI of 4–6 and SSS score  $\geq 9$ .
- (2) Generalized pain, defined as pain in at least 4 of 5 regions, must be present. Jaw, chest, and abdominal pain are not included in generalized pain definition.
- (3) Symptoms have been generally present for at least 3 months.
- (4) A diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses.

**Ascertainment**

(1) **WPI:** note the number of areas in which the patient has had pain over the last week. In how many areas has the patient had pain? Score will be between 0 and 19

*Left upper region (Region 1)*

Jaw, left<sup>a</sup>  
Shoulder girdle, left  
Upper arm, left  
Lower arm, left

*Right upper region (Region 2)*

Jaw, right<sup>a</sup>  
Shoulder girdle, right  
Upper arm, right  
Lower arm, right

*Axial region (Region 5)*

Neck  
Upper back  
Lower back  
Chest<sup>a</sup>  
Abdomen<sup>a</sup>

*Left lower region (region 3)*

Hip (buttock, trochanter), left  
Upper leg, left  
Lower leg, left

*Right lower region (Region 4)*

Hip (buttock, trochanter), right  
Upper leg, right  
Lower leg, right

(2) **Symptom severity scale (SSS) score**

Fatigue  
Waking unrefreshed  
Cognitive symptoms

For the each of the 3 symptoms above, indicate the level of severity over the past week using the following scale:

- 0 = No problem
- 1 = Slight or mild problems, generally mild or intermittent
- 2 = Moderate, considerable problems, often present and/or at a moderate level
- 3 = Severe: pervasive, continuous, life-disturbing problems

**The symptom severity scale (SSS) score:** is the sum of the severity scores of the 3 symptoms (fatigue, waking unrefreshed, and cognitive symptoms) (0–9) plus the sum (0–3) of the number of the following symptoms the patient has been bothered by that occurred during the previous 6 months:

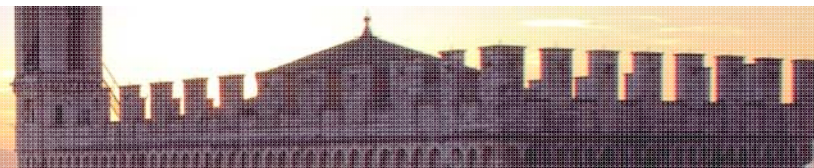
- (1) Headaches (0–1)
- (2) Pain or cramps in lower abdomen (0–1)
- (3) And depression (0–1)

The final symptom severity score is between 0 and 12

**The fibromyalgia severity (FS) scale** is the sum of the WPI and SSS

The FS scale is also known as the polysymptomatic distress (PSD) scale.

<sup>a</sup> Not included in generalized pain definition.

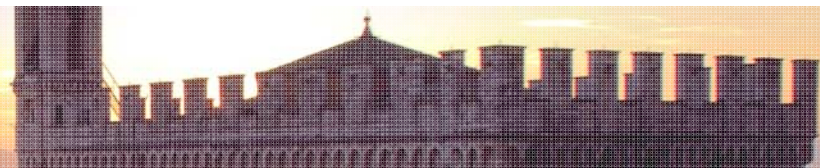
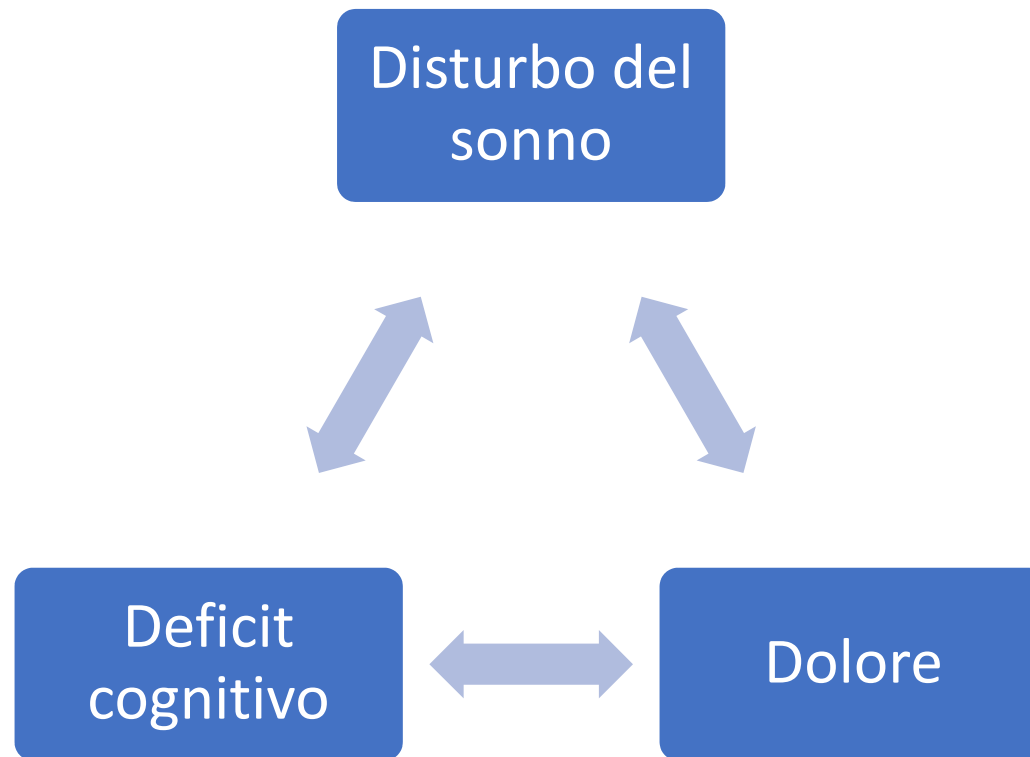


# La fibromialgia è un puzzle...trattare un tassello per trattare tutto...

- Fatica
- Disturbo del sonno
- « Nebbia cognitiva»
- Cefalea
- Depressione
- Dolore addominale



# Quanto è importante trattare il disturbo del sonno?

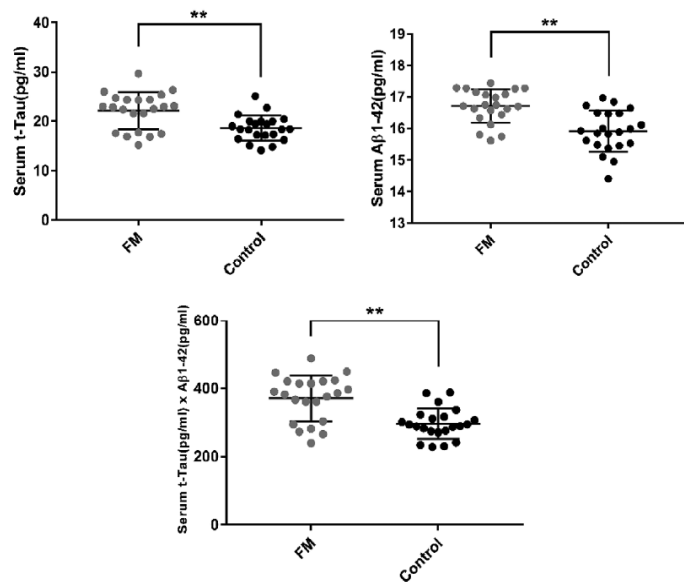


# Marcatori di neurodegenerazione e disturbo del sonno

CNS Spectrums

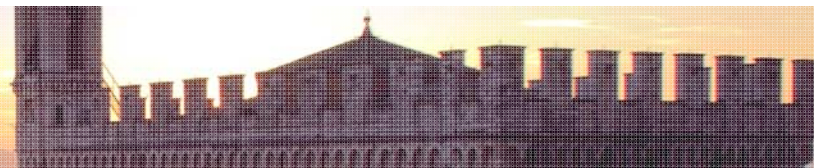
www.cambridge.org/cns

Elevated tau and  $\beta$ -amyloid in the serum of fibromyalgia patients

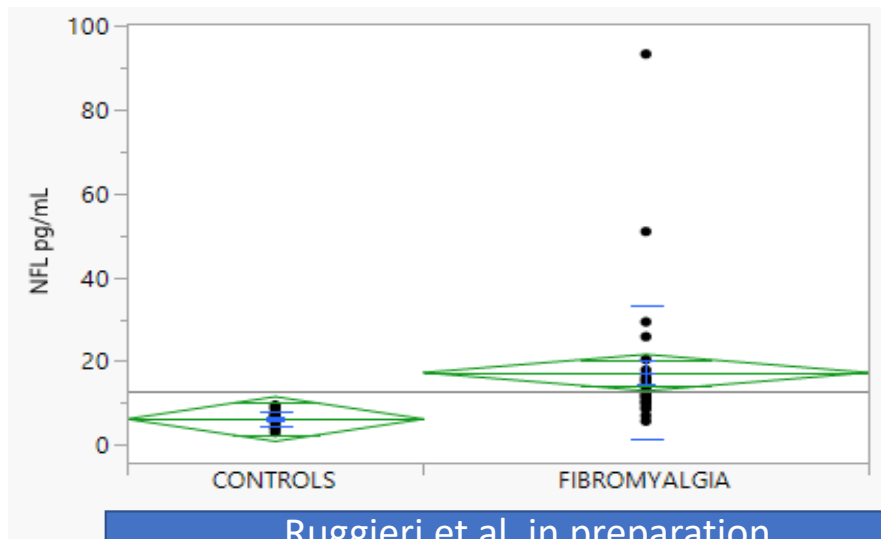


	Tau (pg/mL)	A $\beta$ -42 (pg/mL)	t-Tau $\times$ A $\beta$ 1-42 (pg/mL) <sup>2</sup>
Age			
<i>r</i>	-0.167	0.161	-0.125
<i>P</i> (2-tailed)	.458	.474	.580
PSQI			
<i>r</i>	0.476*	0.220	0.468*
<i>P</i> (2-tailed)	.025	.326	.028

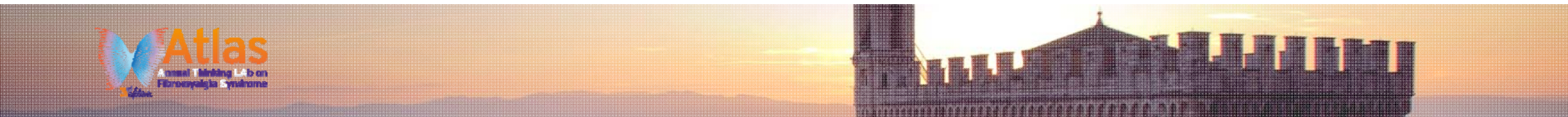
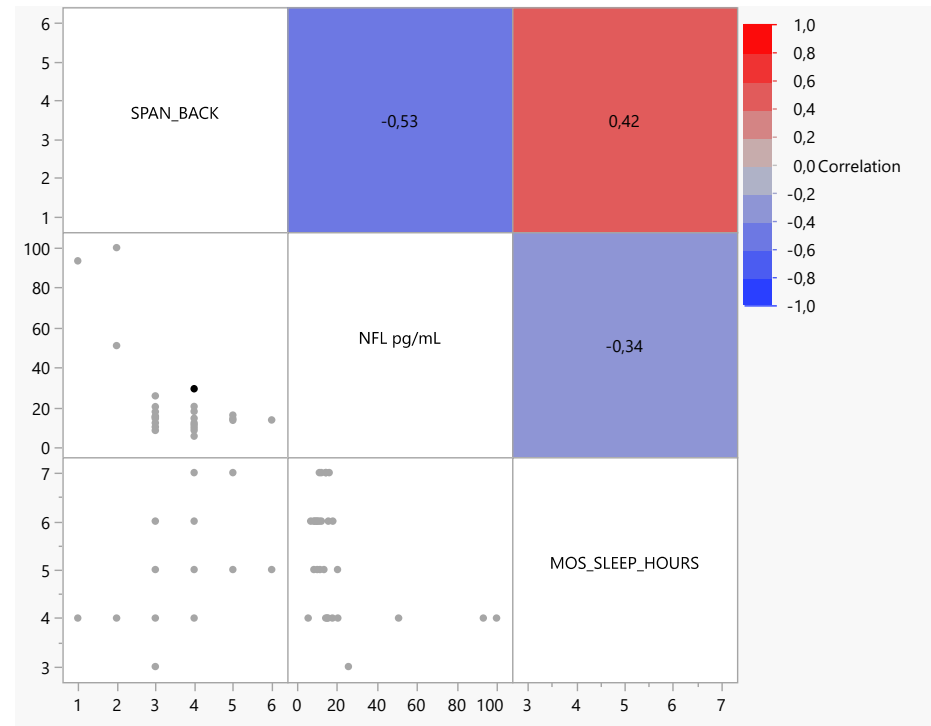
**Figure 2.** Comparisons of serum tau and A $\beta$ 1-42 protein levels between FM and control groups. (A) Serum t-tau levels in the FM group were higher than those in the control group (FM: 22.14 vs CG: 18.62 [pg/mL]). (B) Serum A $\beta$ 1-42 levels in the FM group were higher than those in the control group (FM: 16.72 vs CG: 15.92 [pg/mL]). (C) Product of tau and A $\beta$ 1-42 was also higher in the FM group than in the control group (FM: 370.99 vs CG: 296.71 [pg/mL]<sup>2</sup>). t-Tau, total tau protein; A $\beta$ 1-42, 42-amino-acid sequence of beta-amyloid protein; FM, fibromyalgia; CG, control group. \**P* < .05; \*\**P* < .01.



# Marcatori di neurodegenerazione, deficit cognitivo e disturbo del sonno



Ruggieri et al, in preparation



# Disturbo del sonno... Depressione ....



## Recommendations

**Table 1** Overview of results from selected systematic reviews of placebo-controlled pharmacological trials

Treatment (review reference)	No. of trials (no. of participants) Review quality	Dosages; durations of treatment	Overall trial quality*	Safety and comments
Amitriptyline <sup>12</sup>	10 (767) AMSTAR=6	10–50 mg/day; 8–24 weeks	Low	There was no analysis of safety but no difference in discontinuation rates compared with patients on placebo was reported.
Anticonvulsants—pregabalin <sup>24</sup>	5 (3256) AMSTAR=10	Three studies with fixed doses of 300, 450 and 600 mg/day; one with fixed doses of 150, 300 or 450 mg/day; one flexible dosing study of 300 or 450 mg/day; 8–14 weeks	High	Increased likelihood of withdrawal due to adverse events, RR 1.68, 95% CI 1.36 to 2.07; NNH 12 95% CI 9 to 17. No difference in likelihood of serious adverse events.
Cyclobenzaprine <sup>25</sup>	5 (312) AMSTAR=7	10–40 mg; 2–24 weeks	Moderate	There was no analysis of adverse outcomes in the trials reviewed although dropout across trials was large (cyclobenzaprine 29%, placebo 43%). Only two studies conducted ITT.
Growth hormone <sup>16</sup>	2 (74) AMSTAR=5	0.0125 mg/kg/day; adjusted to maintain IGF-1 level of 250 ng/mL after first month, 0.0125 mg/kg/day; 9 months to 1 year	NE	Safety concerns include sleep apnoea and carpal tunnel syndrome.
MAOIs <sup>26</sup>	3 (241) AMSTAR=9	Pirlindole 150 mg/day, moclobemide 150–300 mg/day; 4–12 weeks	Low	MAOIs are known to cause potentially fatal hypertensive crises, serotonin syndrome and psychosis when they interact with foods containing tyramine and medications (many of which are commonly used in the treatment of FM), including SSRIs, tricyclic antidepressants and tramadol. The clinical trials had restrictions on concomitant medications.
NSAIDs <sup>21</sup>	2 (242) AMSTAR=7	Ibuprofen 600 mg four times a day, tenoxicam 20 mg/day; 6–8 weeks	Low	The adverse event profile, although not considered in this review, is well established for this class of drugs.
SNRIs—duloxetine <sup>31</sup>	6 (2249) AMSTAR=10	20–120 mg/day; 12–28 weeks	Moderate	Dropout rates due to side effects across studies higher than with placebo. No difference in serious adverse events.
SNRIs—milnacipran <sup>30</sup>	5 (4118) AMSTAR=10	100 or 200 mg/day; 12–27 weeks	High	Dropout rates due to side effects across studies were double compared with placebo, but there was no difference in serious adverse events.
SSRIs <sup>36</sup>	7 (322) AMSTAR=8	20–40 mg/day citalopram, 20–80 mg/day fluoxetine, 20–60 mg/day paroxetine; 6–16 weeks	Moderate to high	Acceptability and tolerability were similar to placebo NNH 40, 95% CI 19 to 66. Although several studies excluded patients with depression/anxiety, Häuser <i>et al</i> <sup>26</sup> showed a small effect of SSRIs in improving depressed mood (SMD -0.37, 95% CI -0.66 to -0.07).
Sodium oxybate <sup>16</sup>	5 (1535) AMSTAR=5	4.5–6 g/day; 8–14 weeks	NE	There is the potential for abuse and central nervous system effects associated with abuse such as seizure, respiratory depression and decreased levels of consciousness.
Tramadol <sup>22</sup>	1 (313) AMSTAR=3	37.5 mg tramadol/325 mg paracetamol 4x/day; 3 months	High	No significant difference in discontinuation due to adverse events (RR 1.62, 95% CI 0.94 to 2.80). A high-quality review (AMSTAR score 7) identified a single study, which, among persons who tolerated and benefitted from tramadol, demonstrated a lower discontinuation rate in a double-blind phase compared with placebo (RR 0.51, 95% CI 0.21 to 1.22).

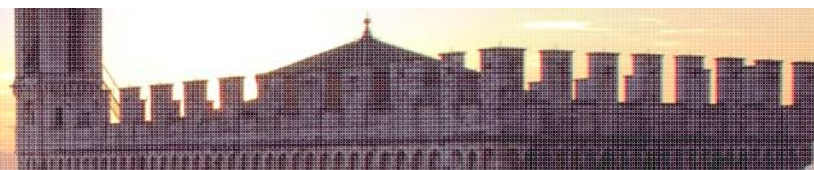
### Pharmacological management

Amitriptyline (at low dose)	Ia	A	Weak for	100
Duloxetine or milnacipran	Ia	A	Weak for	100
Tramadol	Ib	A	Weak for	100
Pregabalin	Ia	A	Weak for	94
Cyclobenzaprine	Ia	A	Weak for	75

# THERAPEUTIC APPROACH TO FIBROMYALGIA: A CONSENSUS STATEMENT ON PHARMACOLOGICAL AND NON PHARMACOLOGICAL TREATMENT FROM ITALIAN NEUROLOGICAL SOCIETY (NEUROPATHIC PAIN STUDY GROUP)

*(in preparation)-No effect of pharmacological treatments on sleep- antidepressants*

Reference	Active treatment	Comparator	Sample size	Outcome measures	Findings	Adverse events (active treatment)
<b>Antidepressants</b>						
Upadhyaya et al, 2019	Duloxetine 30/60 mg	Placebo	184 (juvenile FM)	BPI average pain severity	Negative	Nausea 25.3%, vomiting 15.4%, headache 14.3%
Bidari et al, 2019	Duloxetine 30-60 mg	Pregabalin 75-150 mg	99	WPI, BDI-2	Positive	Nausea 34.3%, constipation 31.4%, headache 22.9%, drowsiness 20%, dry mouth 17.1%, dizziness 17.1%, insomnia: 17.1%
Pickering et al, 2018	Milnacipran 100 mg	Placebo	54	Status of CPM	Negative	Gastrointestinal disorders 28.4%, nervous system symptoms 14.7%
Ahmed et al, 2016	Milnacipran 100 mg	Placebo	19	Polysomnographic measures, BPI, FIQ	Positive for pain	Nausea/vomiting 22.2%, headache 16.7%, abdominal pain 11.1%, constipation 11.1%, sinusitis 11.8%, hot flush 11.8%
Miki et al, 2016	Mirtazapine 30 mg	Placebo	422	NRS	Positive	Somnolence 32.1%, weight gain 17.7%, increased appetite 11.6%
Murakami et al, 2015	Duloxetine 60 mg	Placebo	393	BPI, average pain score	Negative	Somnolence 26.3%, nausea 21.6%, constipation 14.9%, dizziness 5.7%, liver injury in 1 patient
Staud et al, 2015	Milnacipran 100 mg	Placebo	46	VAS, mechanical and heat pain sensitivity	Negative	Gastrointestinal disorders 10.9%
Leombruni et al, 2015	Duloxetine 60 mg	acetyl L-carnitine 1500 mg	65	VAS, MADRS, HADS-D	Positive in both arms	Nausea, anxiety, insomnia, and diarrhea in 8 patients





# THERAPEUTIC APPROACH TO FIBROMYALGIA: A CONSENSUS STATEMENT ON PHARMACOLOGICAL AND NON PHARMACOLOGICAL TREATMENT FROM ITALIAN NEUROLOGICAL SOCIETY (NEUROPATHIC PAIN STUDY GROUP)

(in preparation)

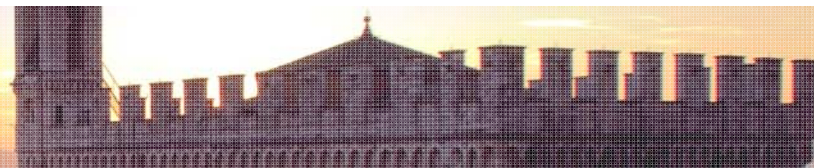
## -Weak effect of pharmacological treatments on sleep- anticonvulsants



Anticonvulsants						
Karamanlioglu et al., 2021	Pregabalin + exercise	Exercise	40	VAS, PPT, DN4, SF36	Positive	Dizziness 82.4%, somnolence 82.4%, foot edema 17.6%, weight gain 5.9%, constipation 5.9%
Arnold et al., 2019	Mirogabalin 15-30 mg	Pregabalin 300 mg Placebo	3864	ADPS; PGIC; FIQ	Negative	No unexpected adverse events
Bidari et al., 2019	Pregabalin 75-150 mg	Duloxetine 30-60 mg	99	WPI, BDI-2	Negative	Nausea 9.7%, constipation 12.9%, lightheadedness 12.9%, drowsiness 32.3%, dizziness: 32.3%
Arnold et al., 2016	Pregabalin 75-450 mg	Placebo	107	NRS (primary), PGIC, ADPS, sleep quality NRS, FIQ	Negative for primary outcome, positive for secondary outcomes	Dizziness 29.6%, nausea 22.2%, headache 18.5%, weight increase 16.7%, fatigue 14.8%
Arnold et al., 2015	Pregabalin 300- 450 mg	Placebo	197	NRS anxiety, depression, patient function, sleep	Positive	dizziness 28.2%, somnolence 19.9%, constipation 10.5%, nausea 9.4%
Combination of antidepressants + anticonvulsants						
Abdel Fattah et al., 2020	Milnacipran 100 mg + pregabalin 300 mg	Pregabalin 300 mg	58	FIQ, VAS, Leeds Sleep Evaluation Questionnaire	Negative (combination treatment not superior to pregabalin)	Disturbed sleep pattern 26.9%, dizziness and drowsiness 19.2%, gastrointestinal disorders 15.4%
Ramzy et al., 2017	Paroxetine 25 mg + pregabalin 75 mg	Pregabalin 75 mg + amitriptyline 25 mg Pregabalin 75 mg + venlafaxine 75 mg	75	SSS-8, CESDS	Positive	Dry mouth 7.7%, abnormal taste 7.7%, weight gain 11.5%
Gilron et al., 2016	Duloxetine 120 mg + pregabalin 450 mg	Placebo Pregabalin 450 mg Duloxetine 120 mg	41	NRS	Positive for active vs. placebo and pregabalin/duloxetine	Fatigue 29.4%, drowsiness 26.5%, dry mouth 23.5%, constipation 11.8%, insomnia 11.8%, headache 11.8%



La maggior parte delle terapie farmacologiche non hanno effetto/hanno effetti negativi sul sonno



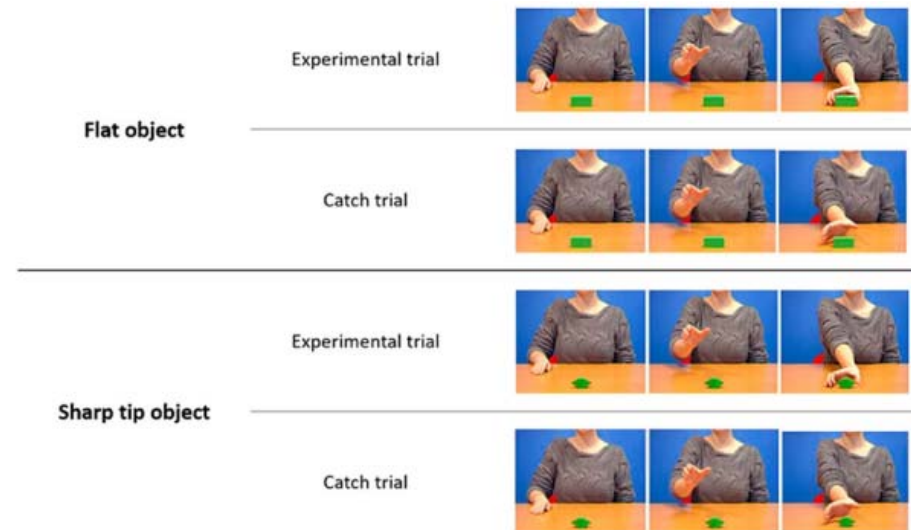
# Trattamento della fatica: fatica fisica o fatica cognitiva? Deficit corticale?

scientific reports

OPEN **Movement observation activates motor cortex in fibromyalgia patients: a fNIRS study**

Eleonora Gentile<sup>1,2</sup>, Antonio Brunetti<sup>2</sup>, Katia Ricci<sup>1</sup>, Vitoantonio Bevilacqua<sup>2</sup>, Lalla Craighero<sup>3</sup> & Marina de Tommaso<sup>1</sup>

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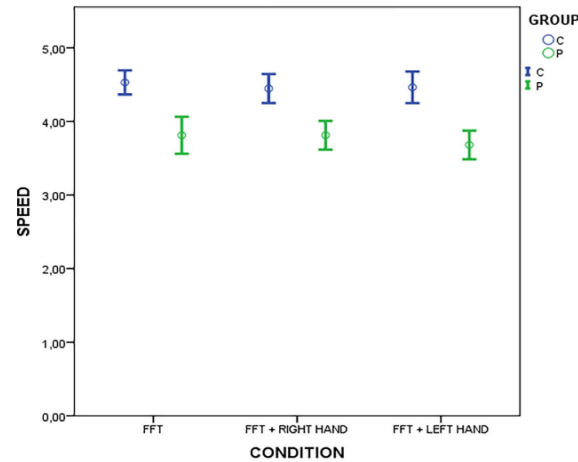
**Figure 2.** Three frames extracted from the flat object video (top) and the sharp-tip object video (bottom). Specifically, for each video, three frames extracted from the Experimental trial (Frame 1; Frame 25; Frame 66), and the Catch trial (Frame 1; Frame 25; Frame 38. Frame 38 was repeated 28 times to obtain the same duration as that of the experimental videos, 66 frames) are shown. The sharp-tip object videos were obtained by video editing the flat object videos. By means of a graphic software, the to-be-grasped parallelepiped was replaced by a polyhedron having the same size, but with sharp tips at the fingers opposition space.

# Trattamento della fatica: fatica fisica o fatica cognitiva? Deficit corticale?

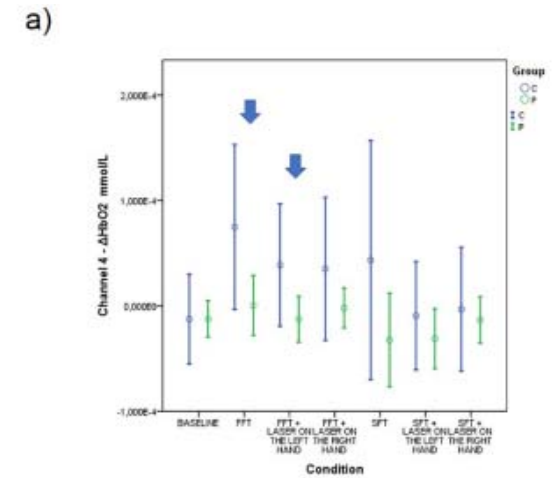
RESEARCH ARTICLE

Mutual interaction between motor cortex activation and pain in fibromyalgia: EEG-fNIRS study

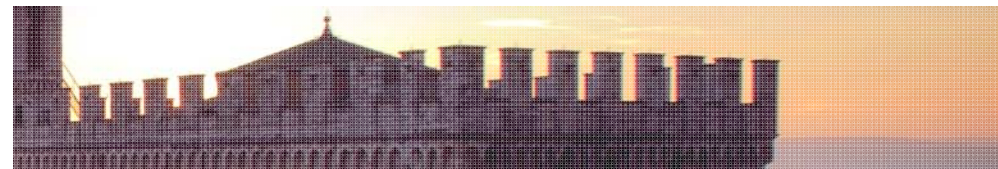
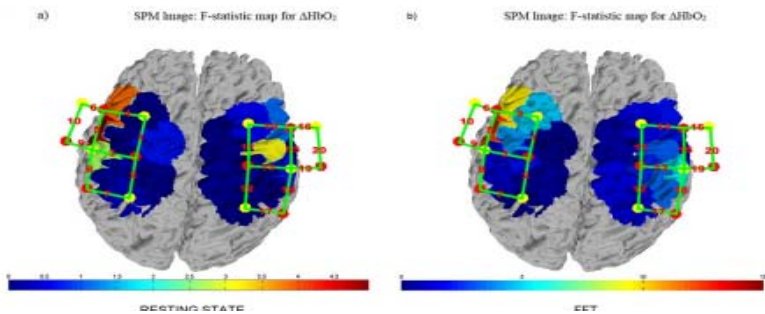
Eleonora Gentile<sup>1\*</sup>, Antonio Brunetti<sup>2</sup>, Katia Ricci<sup>1</sup>, Marianna Delussi<sup>1</sup>, Vitoantonio Bevilacqua<sup>2</sup>, Marina de Tommaso<sup>1</sup>



Lentezza ed esauribilità del movimento semplice e ripetitivo



Ridotto metabolismo della corteccia motoria

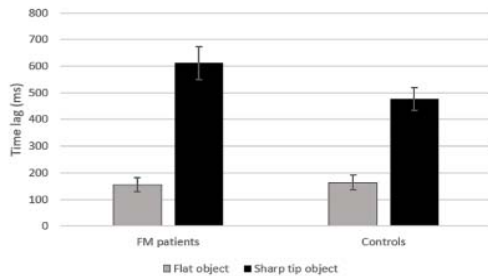


# Trattamento della fatica: fatica fisica o fatica cognitiva? Deficit corticale?

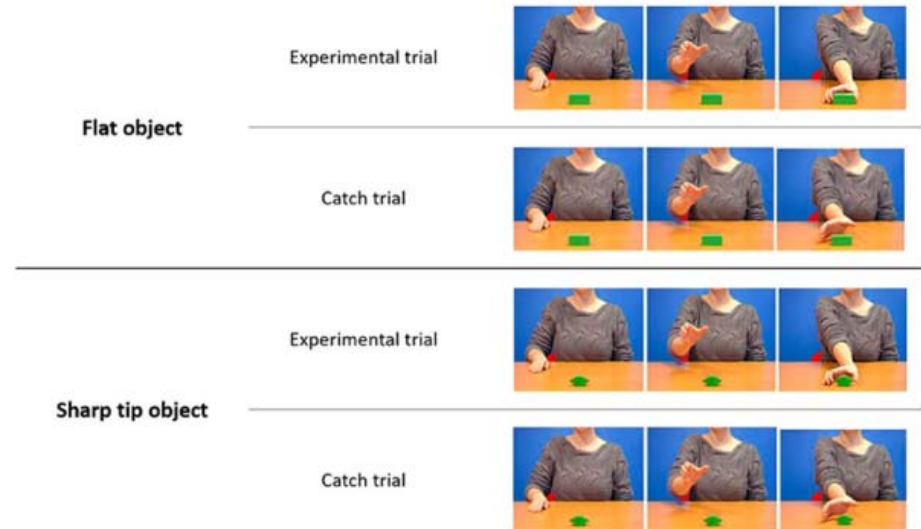
scientific reports

OPEN **Movement observation activates motor cortex in fibromyalgia patients: a fNIRS study**

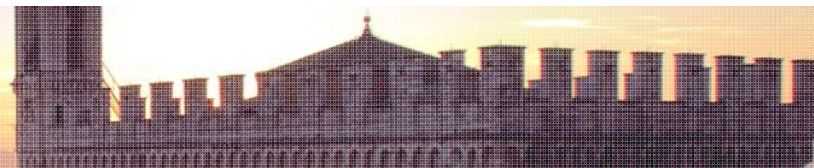
Eleonora Gentile<sup>1,2</sup>, Antonio Brunetti<sup>2</sup>, Katia Ricci<sup>1</sup>, Vitoantonio Bevilacqua<sup>2</sup>, Lalla Craighero<sup>3</sup> & Marina de Tommaso<sup>1</sup>



**Figure 3.** Detection time results. Time lag between the instant at which the agent touches the object and participant's response time. For both groups (FM patients, Controls), data for flat object trials (grey) and sharp-tip object (black) trials are shown. Thin lines above histograms indicate standard error of the mean. Ordinates are in milliseconds.



**Figure 2.** Three frames extracted from the flat object video (top) and the sharp-tip object video (bottom). Specifically, for each video, three frames extracted from the Experimental trial (Frame 1; Frame 25; Frame 66), and the Catch trial (Frame 1; Frame 25; Frame 38. Frame 38 was repeated 28 times to obtain the same duration as that of the experimental videos, 66 frames) are shown. The sharp-tip object videos were obtained by video editing the flat object videos. By means of a graphic software, the to-be-grasped parallelepiped was replaced by a polyhedron having the same size, but with sharp tips at the fingers opposition space.



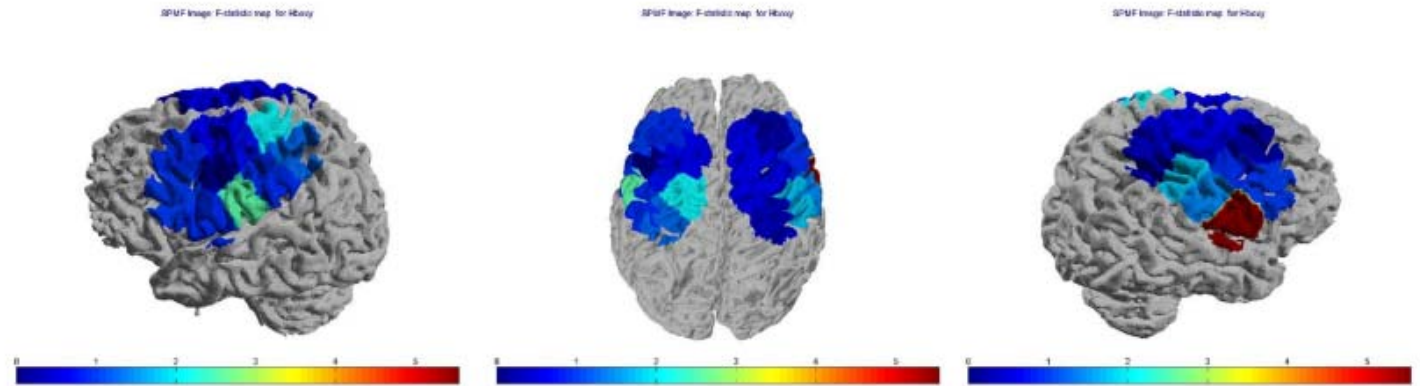
# Trattamento della fatica: fatica fisica o fatica cognitiva? Deficit corticale? L'importanza dell'azione sul programma motorio

scientific reports

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Il successo dell'approccio non farmacologico – cognitivo comportamentale- è basato verosimilmente sull'effetto positivo sui sintomi associati (depressione, fatica, sonno)  
*(NSG-in preparation)*

Reference	Active treatment	Comparator	Sample size	Outcome measures	Findings	Adverse events (active treatment)
<b>Cognitive Behavioral Therapy</b>						
Luciano et al., 2014	ACT	RPT, WL	156	FIQ	Positive (compared to both control arms)	-
Simister et al., 2018	ACT + TAU	TAU	66	FIQ-R	Positive	-
Laura Andes-Rodriguez et al., 2019	MBSR + TAU	TAU	70	FIQ-R	Positive	-
Perez-Aranda et al., 2019	MBSR + TAU	FibroQoL + TAU, TAU	225	FIQ-R	Positive (compared to both control arms)	-
<b>ACT: Acceptance and Commitment Therapy; TAU: treatment as usual; MBSR: Mindfulness-Based Stress Reduction; RPT: recommended pharmacological treatment; WL: waiting list</b>						



Nessun effetto avverso su sonno , fatica e tono dell'umore

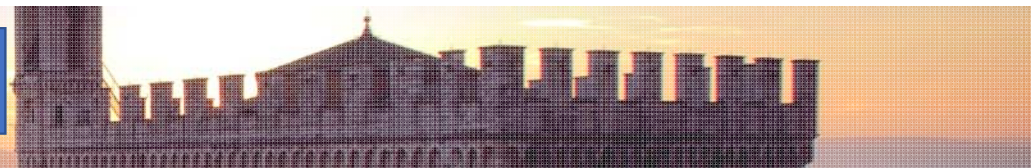


# Il successo dell'approccio non farmacologico – attività fisica-è basato verosimilmente sull'effetto positivo sui sintomi associati (depressione, fatica, sonno) (NSG-in preparation)

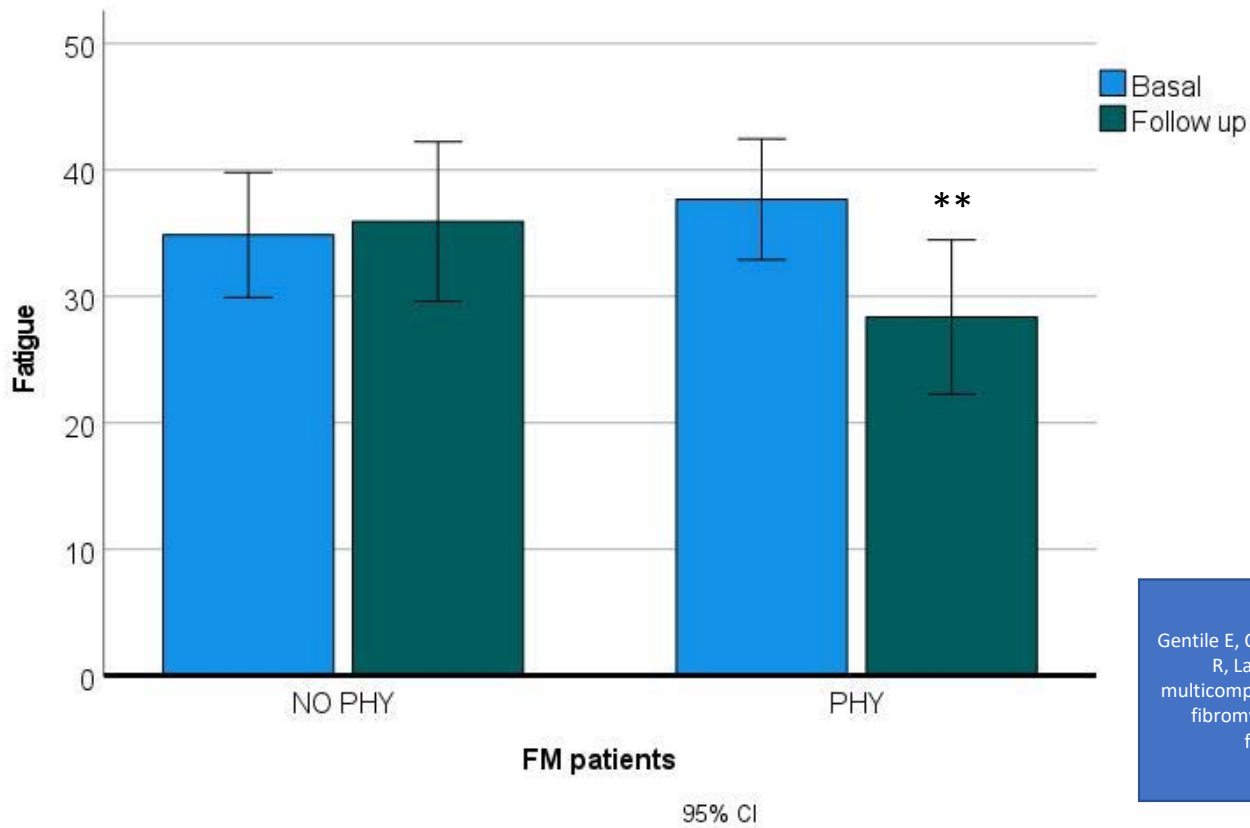
Physical activity						
Larsson et al., 2015	Resistance exercise program (60 min sessions over 15 weeks)	Active control group	130	Isometric knee-extension force	Positive	-
Collado-Mateo et al., 2017	Exergame (postural, coordination, aerobic, strength, mobility; 60 min sessions over 8 weeks)	Non-exercise group	83	FIQ	Positive	-
Wang et al., 2018	Four Tai Chi groups (60 min sessions over 12-24 weeks)	Aerobic group	226	FIQ-R	Positive (at FU)	-
Andrade et al., 2019	Aquatic physical training (60 min sessions over 16 weeks)	Non-exercise group	54	FIQ	Positive	-
Izquierdo-Alventosa et al., 2020	Low-intensity exercise (endurance training, coordination; 60 min sessions over 8 weeks)	Non-exercise group	32	PCS	Positive	-
Serrat et al., 2021	Multicomponent treatment (pain neuroscience education, therapeutic exercise, CBT, mindfulness + pharmacological trt; 60 min sessions over 12 weeks)	Pharmacological trt	272	FIQ-R	Positive	-
Gentile et al., 2023	Supervised home-based multicomponent PA intervention focused on aerobic and resistance training	Non-supervised aerobic exercise	34	Fibromyalgia-linked invalidity questionnaire Skin biopsy	Positive	-



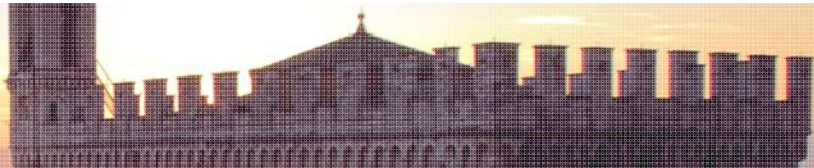
Nessun effetto avverso su sonno , fatica e tono dell'umore



# L'attività fisica adattata migliora la fatica



Gentile E, Quitadamo SG, Clemente L, Bonavolontà V, Lombardi R, Lauria G, Greco G, Fischetti F, De Tommaso M. A multicomponent physical activity home-based intervention for fibromyalgia patients: effects on clinical and skin biopsy features. Clin Exp Rheumatol. 2023 Nov 27.





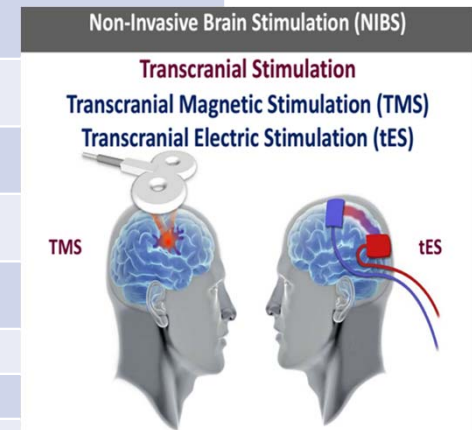
Il successo dell'approccio non farmacologico –NBS-TMS- è basato verosimilmente sull'effetto positivo sui sintomi associati (depressione, fatica, sonno)  
(NSG-in preparation)

FATICA

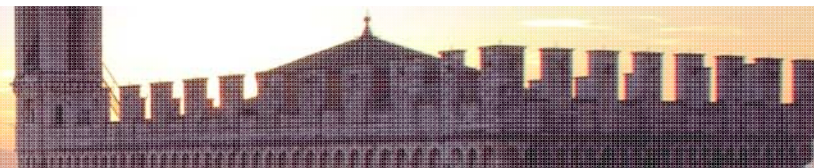
DEPRESSIONE

DEPRESSIONE


NIBS – TMS							
Boyer et al., 2014	HF rTMS (10 sessions on I-M1)	Sham	38	FIQ	Positive	None	
Fitzgibbon et al., 2018	HF rTMS (20 sessions on I-DLPFC)	Sham	26	SF-MPQ, BPI, NRS (pain), MFI-20	Positive (MFI-20)	Site discomfort (15.4%), headache (15.4%), nausea (3.8%), dizziness (3.8%), other (3.8%)	
Altas et al., 2019	HF rTMS (15 sessions on I-M1 or I-DLPFC)	Sham	30	VAS, FIQ, FSS, SF-36, BDI	Positive	NR	
Cheng et al., 2019	HF rTMS (10 sessions on I-DLPFC)	Sham	20	VAS (pain)	Positive	None	
Tanwar et al., 2020	LF rTMS (20 sessions on r-DLPFC)	Sham	90	NRS (pain)	Positive	Headache (2%)	
Bilir et al., 2021	HF rTMS (10 sessions on I-DLPFC)	Sham	20	VAS, FSS, HADS	Negative	None	
Izquierdo-Alventosa et al., 2021	HF rTMS (10 sessions on I-DLPFC)	Sham, physical exercise	49	VAS (pain)	Positive	NR	
Lacroix et al., 2021	HF rTMS (15 sessions on I-M1)	Sham	78	VAS, PGIC	Positive	None	
Argaman et al., 2022	HF rTMS (10 sessions on M1)	Sham	27	BPI, MPQ, FIQ, SF-36, STAI, BDI	Positive	NR	
Pareja et al., 2022	rTMS (8 sessions) + pharmacological trt	Pharmacological trt	560	FIQ, WPI, SSS	Positive	NR	
NIBS – combined							
Forogh et al., 2021	rTMS or tDCS (3 sessions, 20 min/session of rTMS or tDCS on DLPFC)	None	30	VAS (pain), FIQ-R, DASS-21	Positive (rTMS, VAS)	Mild, transient headache (rTMS)	



HADS: Hospital Anxiety and Depression Scale DASS-21: Depression Anxiety Stress Scale-21 MFIS: Modified Fatigue Impact Scale; BDI Beck depression Inventory

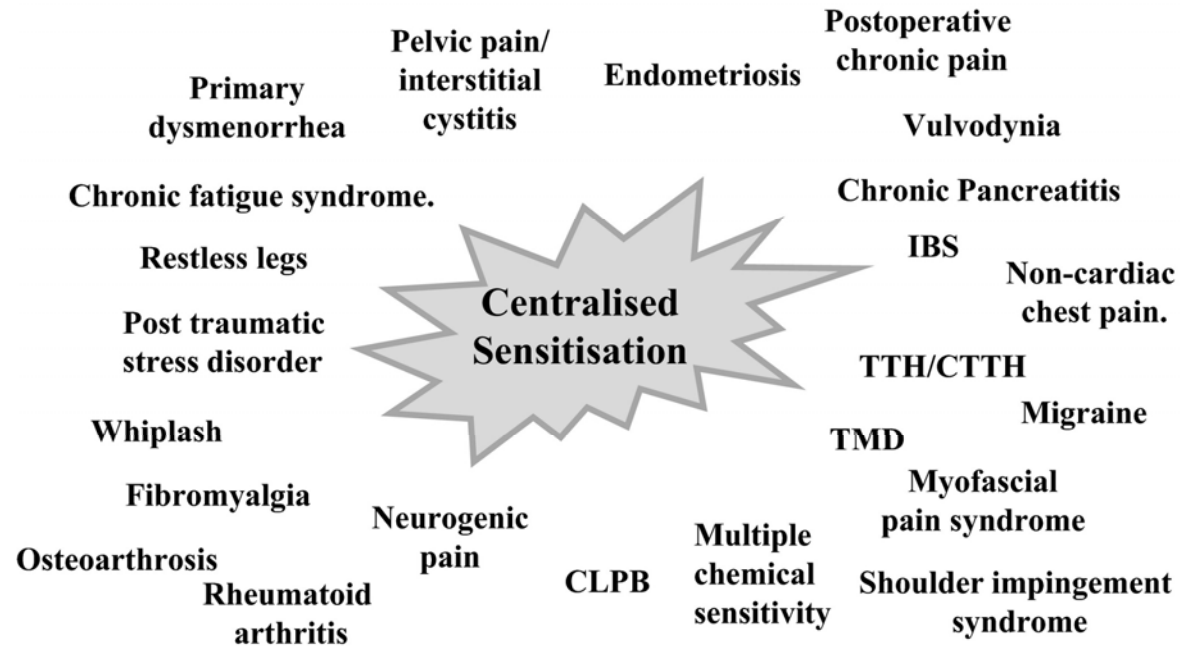


# Efficacia dell'rTMS nella depressione

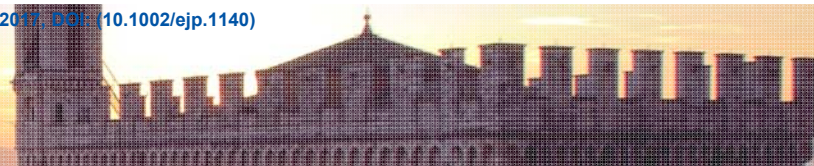
	<b>DEPARTMENT OF HEALTH &amp; HUMAN SERVICES</b>	Public Health Service
Neuronetics, Inc. % Judy P. Ways, Ph.D. Vice President Regulatory Affairs and Quality Assurance One Great Valley Parkway, Suite 2 Malvern, Pennsylvania 19355		Food and Drug Administration 9200 Corporate Boulevard Rockville MD 20850
<b>DEC 16 2008</b>		
Re: K083538 Trade/Device Name: NeuroStar TMS Therapy System Regulation Number: 21 CFR 882.5805 Regulation Name: Repetitive transcranial magnetic stimulator for treatment of major depressive disorder Regulatory Class: II Product Code: OBP Dated: November 28, 2008 Received: November 28, 2008		



Assessment and manifestation of central sensitisation across different chronic pain conditions



I SINTOMI CONCOMITANTI POSSONO CONFIGURARE SPECIFICHE PATOLOGIE: IL CASO DELLE CEFALEE PRIMARIE



# Fibromialgia: frequenza nelle cefalee primarie

**Table 2** Prevalence of fibromyalgia in patients with some types of headache

Author	N	Type of headache	Prevalence of fibromyalgia (%)	Setting	Country
Peres [48]	101	Transformed migraine	35.6	Headache clinic	Brazil
Ifergane [49]	92	Episodic migraine	17.4	Headache clinic	Israel
de Tommaso [50]	217	Primary headaches	36.4	Headache center	Italy
		Migraine	28.5		
		TTH	59.0		
de Tommaso [51]	849	Primary headaches	19.6	Pain clinic	Italy
		Migraine	17.8		
		TTH	35.1		
Tietjen [52]	1,413	Migraine	6.9	Headache clinics	USA
Tietjen [53]	223	Migraine	11.7	Headache clinic	USA
Le [54]	8,044	Migraine	1.2	Twins cohort	Denmark
		Migraine with aura	2.1		
		Migraine without aura	0.6		
Küçükşen [55]	118	Migraine	31.4	Headache clinic	Turkey

## Clinical features of headache patients with fibromyalgia comorbidity

Marina de Tommaso · Antonio Federici · Claudia Serpino · Eleonora Vecchio · Giovanni Franco · Michele Sardaro · Marianna Delussi · Paolo Livrea

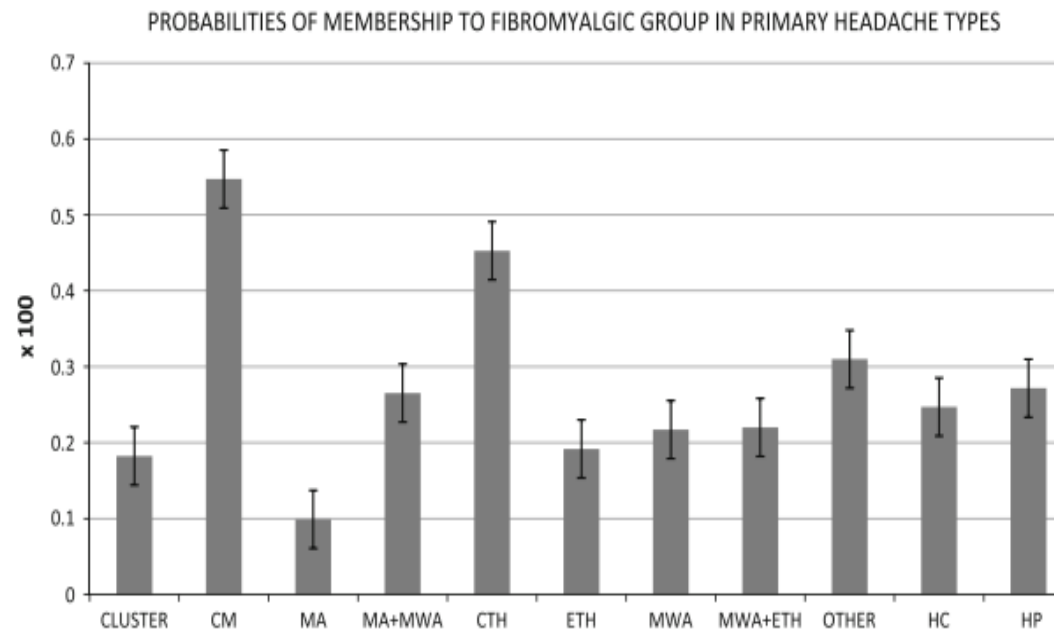
**Table 5** Classification function coefficients

	No FM	FM
Frequency	0.082	0.102
SAS	0.865	0.928
TTS	0.052	0.301
SLP9	-0.03	-0.002
PCF	0.891	0.831
Constant	-37.382	-41.132

Fisher's linear discriminant functions

Discriminating variables between fibromyalgic (FM) and not fibromyalgic patients

SAS self-rating-anxiety-scale, TTS total tenderness score, SLP9 sleep problems index, PCF physical component summary

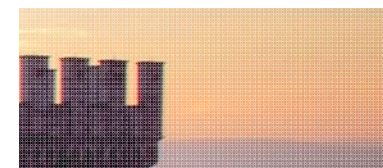
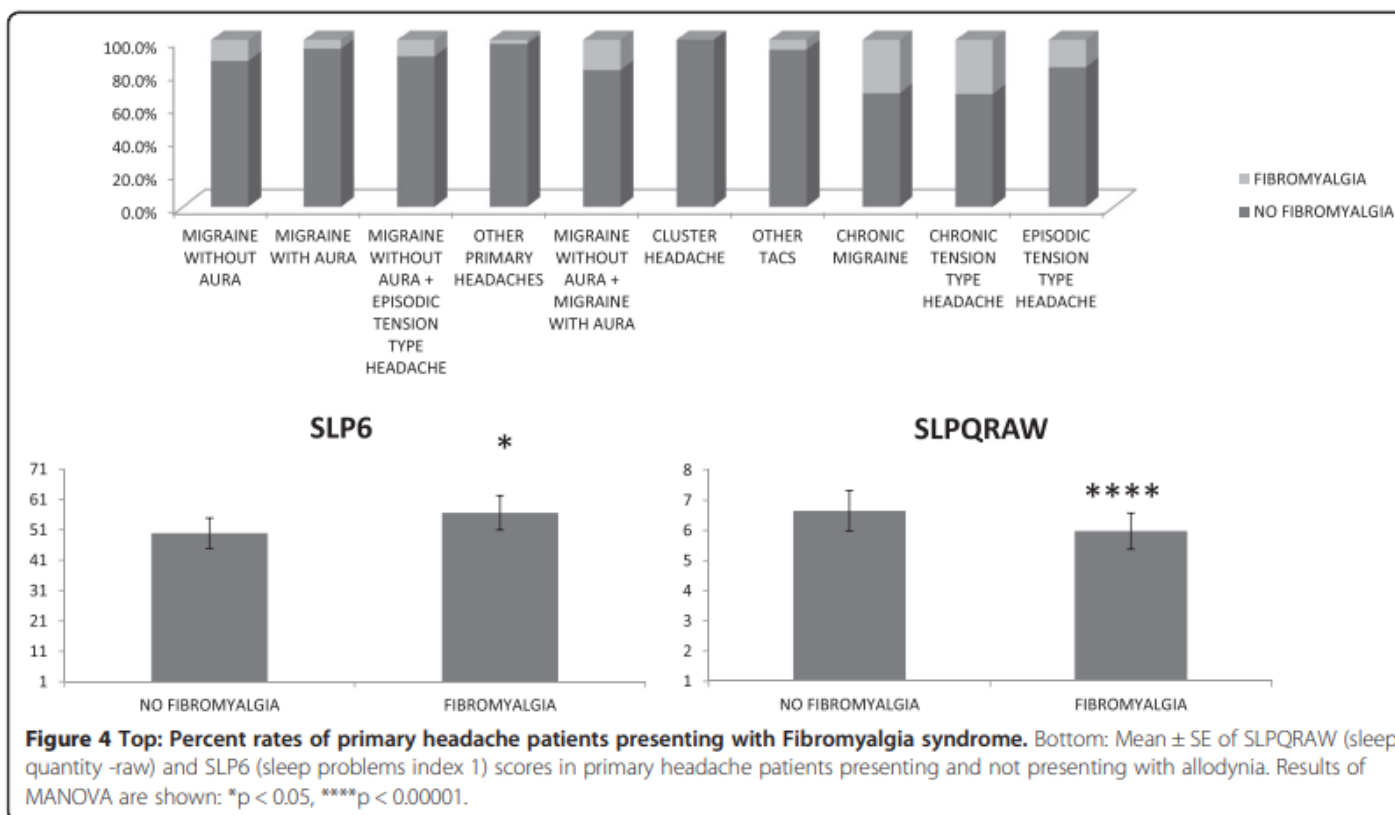


RESEARCH ARTICLE

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# Sleep features and central sensitization symptoms in primary headache patients

Marina de Tommaso<sup>1\*</sup>, Marianna Delussi<sup>1</sup>, Eleonora Vecchio<sup>1</sup>, Vittorio Scirucchio<sup>1</sup>, Sara Invitto<sup>1,2</sup> and Paolo Livrea<sup>1</sup>



RESEARCH ARTICLE

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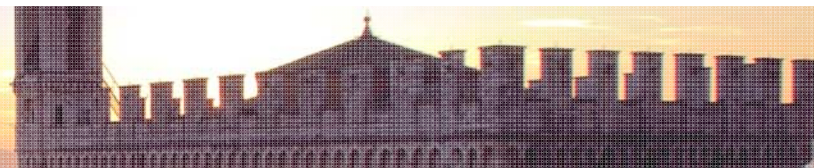
# Failure of preventive treatments in migraine: an observational retrospective study in a tertiary headache center



Marianna Delussi<sup>†</sup>, Eleonora Vecchio, Giuseppe Libro, Silvia Quitadamo and Marina de Tommaso<sup>✉</sup>

**Table 8** Effect of fibromyalgia (FM) comorbidity, gender and allodynia on the primary outcome (50% headache frequency reduction)

		Outcome		Odds ratio	95% CI	z statistic	Significance level
		< 50%	> 50%				
FM comorbidity	no	571	299	1.58	1.05 to 2.38	2.2	P = 0.02
	yes	106	35				
Gender	M	180	94	1.08	0.8 to 1.44	0.523	P = 0.6
	F	497	240				
Allodynia	No	73	67	0.5	0.35 to 0.72	3.67	P = 0.0002
	Yes	594	277				



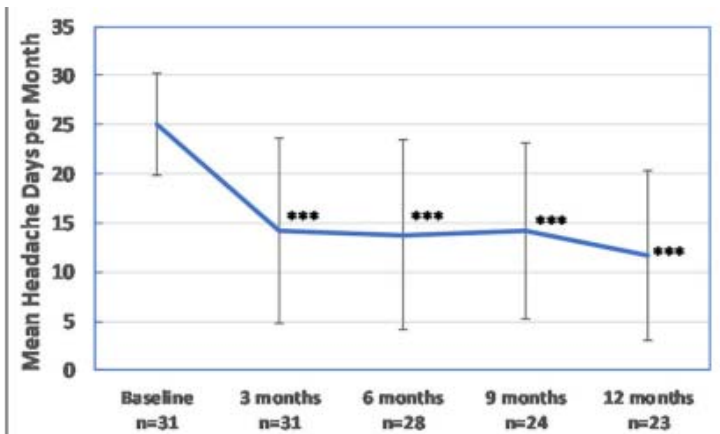


# OnabotulinumtoxinA Is an Effective Treatment for Chronic Migraine in Patients With Comorbid Fibromyalgia

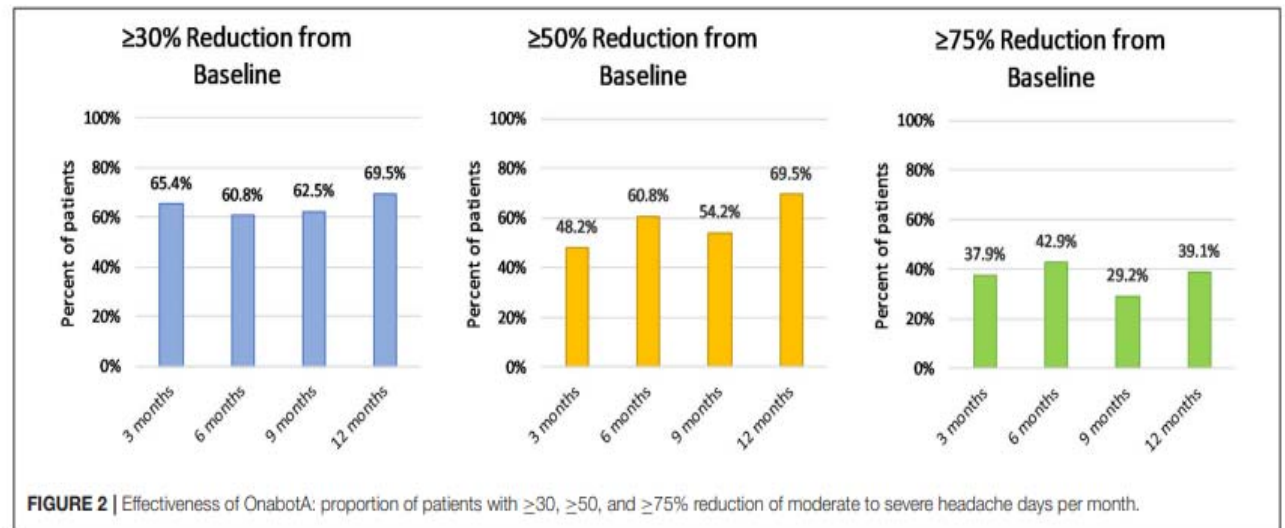
Maria Sastre Real<sup>1,2</sup> and Javier Díaz de Terán<sup>1,2\*</sup>

Sastre Real and Díaz de Terán

OnabotA Chronic Migraine Comorbid Fibromyalgia



**FIGURE 1 |** Effectiveness of OnabotA: moderate to severe headache days per month. Error bars are  $\pm 1$  standard deviation. \*\*\* $p < 0.001$  vs. baseline.



**FIGURE 2 |** Effectiveness of OnabotA: proportion of patients with  $\geq 30$ ,  $\geq 50$ , and  $\geq 75$ % reduction of moderate to severe headache days per month.





Nel trattamento attuale dell'emicrania è preminente il ruolo del sistema trigemino vascolare

## CGRP and the Trigeminal System in Migraine

Smriti Ivengar, PhD; Kirk W. Johnson, PhD; Michael H. Ossipov, PhD; Sheena K. Aurora, MD

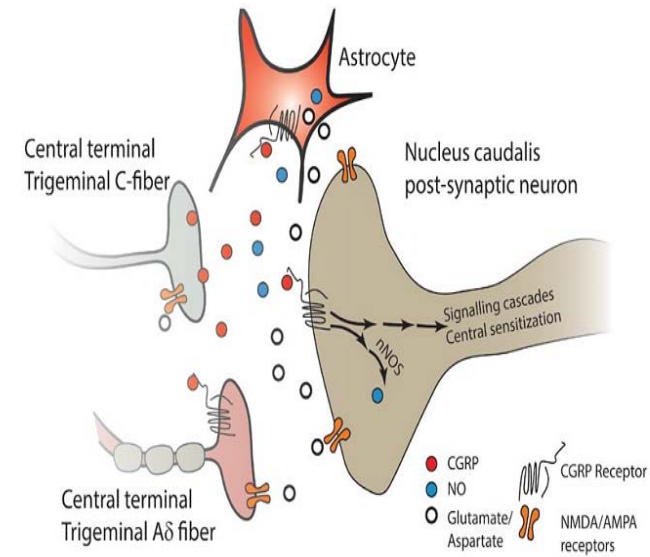
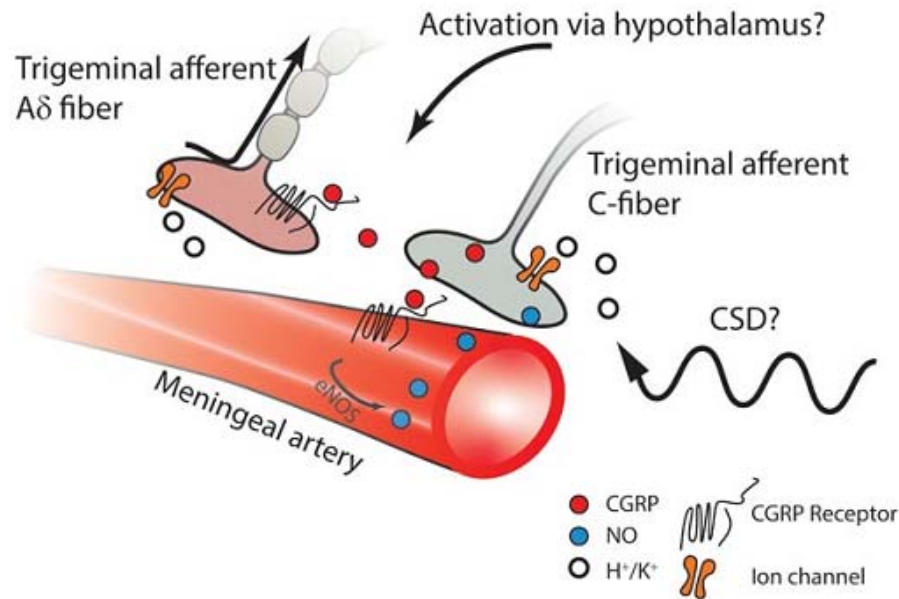
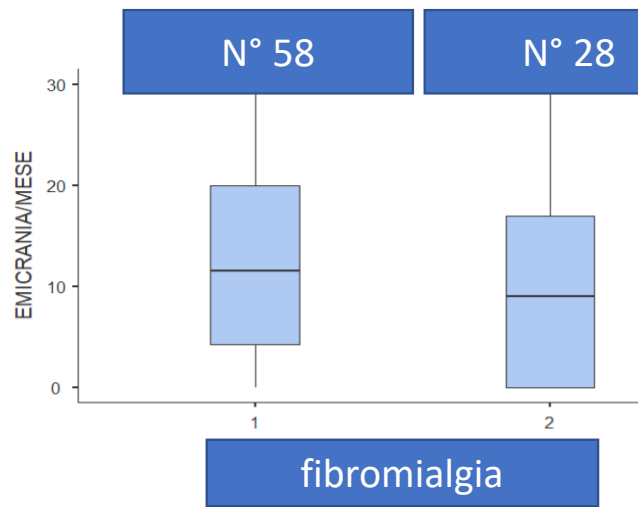
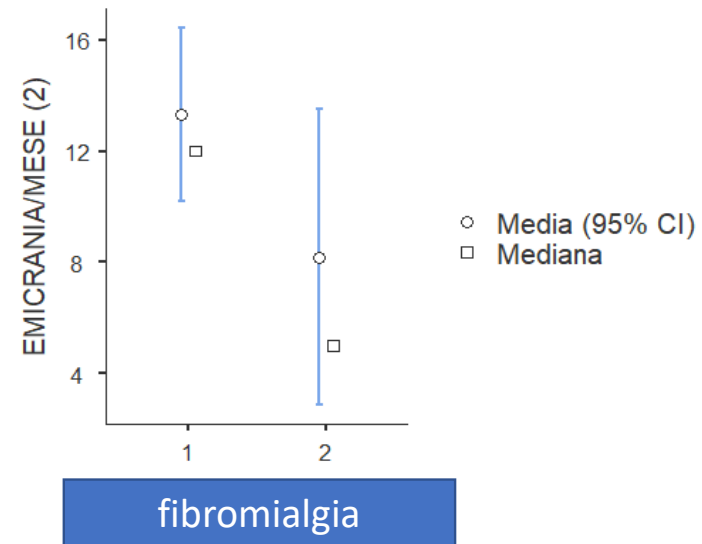
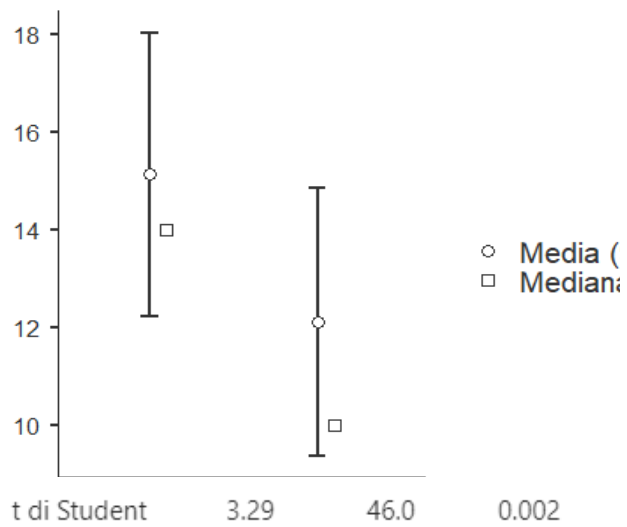


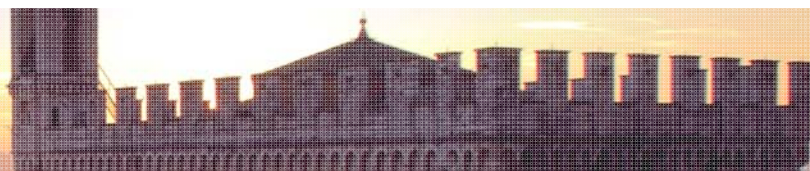
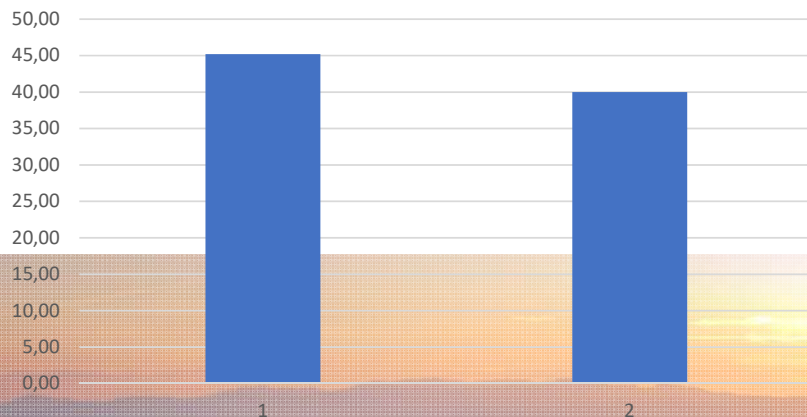
Fig. 3.—CGRP released from the central terminals of unmyelinated nociceptive C-fiber TG neurons can activate the CGRP receptors of the second-order neurons, and elicit production of NO via nNOS. NO acts as a retrograde neuromodulator and...



EMICRANIA/MESE (31) - EMICRANIA/MESE (2)



FIQ



# La fibromialgia include differenti fenotipi, cui sarà possibile attribuire sintomi associati prevalenti e peculiari approcci terapeutici

Marchi et al, 2023

## Gene-wise aggregation analysis in chronic pain reveals a mutational burden in TRPA1

