Methods S1. Description of the scales/ questionnaires.

All the participants, cases and controls, were assessed following a systematic clinical interview that included age, height, weight, demographic data, family history of FM and years since diagnosis of FM.

The participants were administered the following scales/questionnaires:

- Visual Analogue Scales (VAS) created *ad-hoc* to assess Pain, Health State, Morning Stiffness, Fatigue, Mood, Headache, and Sleep Quality. Each scale consisted of a 10-cm line from "no problem" (score 0) to "extreme problem" (score 10), where the participants had to mark the interference of each symptom or their state in the last month.
- The Fibromyalgia Survey Questionnaire (FSQ; Wolfe *et al., 2011) is based on Wolfe et al. (2010) proposed criteria for FM. It provides two indices the Symptom Severity Scale (SSS: fatigue, cognitive troubles and non-restorative sleep, among others) and the Widespread Pain Index (WPI or number of areas with pain). We used the Spanish-validated version (Carrillo-de-la-Peña et al., 2014).*
- The Fibromyalgia Impact Questionnaire (FIQ) (52) is a specific questionnaire to assess quality of life in FM patients. The FIQ is a validated tool that reflects the overall effect of fibromyalgia on different functional areas such as the realization of daily activities or the accomplishment of job or housework (28). It also assesses the severity of symptoms- namely, pain, fatigue, stiffness, quality of sleep, anxiety and depression- in the last week. The FIQ total score ranges from 0-100 and a higher value indicates greater impact of FM. We used the Spanish FIQ (S-FIQ), adapted and validated with the same properties of the original version (Monterde *et al*., 2004)
- The Pittsburgh Sleep Quality Index (PSQI) (53, 54). It is s a self-rated questionnaire for the assessment of sleep quality and dysfunction over a 1-month time interval. It is composed of 7 subscales that explore different aspects of sleep disturbance and that are rated from 0 (no difficulty) to 3 (maximum difficulty). Global PSQI score has a range of 0-21 and higher punctuations indicate worse sleep quality. We used the Spanish version by Macías & Royuela (1996).
- The Beck Depression Inventory (BDI) (Beck *et al*., 1988) is a 21-item self-report scale that assesses the degree of severity of depression symptoms. BDI total score ranges to 0-63 and higher total scores indicate more severe depressive mood. We used the Spanish-validated version (56).

Methods S2. Description of the DNA extraction and the genotyping assays procedure.

DNA extraction

Blood was well mixed and centrifuged at 2800 rpm for 10 min, 4ºC. The white cell phase was collected and mixed with Cell Lysis Buffer; after 10 minutes at room temperature the samples were centrifuged twice at 1800 rpm for 10 min, 4ºC. Distilled water was mixed to the obtained leukocytes' pellet and centrifuged at 1800 rpm for 10 min, 4ºC. Saline solution (0.9%) was finally added to the leukocytes' pellet. Blood samples were thawed at room temperature in a biosafety cabinet and immediately subjected to the DNA purification protocol from leukocytes the QIAamp DNA Blood Midi/Maxi Kit (Spin Protocol, QIAGEN). After DNA extraction, all the samples have been quantified with NanoDrop 2000c Spectrophotometer (Thermo Scientific).

Genotyping

Genotyping assays were designed using the Agena Bioscience MassARRAY Assay Designer 4.0 software. 40 SNPs were genotyped in 2 assays, PCR reactions were set up in a 5 μl volume and contained 20 ng of template DNA, 1× PCR buffer, 2 mM $MgCl_2$, 500 μM dNTPs and 1 U/ reaction of PCR enzyme. A pool of PCR primers was made at a final concentration of each primer of 100 nM. The thermal cycling conditions for the reaction consisted of an initial denaturation step at 94°C for 2 minutes, followed by 45 cycles of 94°C for 30 seconds, 56°C for 30 seconds and 72°C for 1 minute, followed by a final extension step of 72°C for 1 minute. PCR products were treated with 0.5 U shrimp alkaline phosphatase by incubation at 37°C for 40 min, followed by enzyme inactivation by heating at 85°C for 5 min to neutralize unincorporated dNTPs.

The iPLEX GOLD reactions were set up in a final 9 μl volume and contained 0.222x iPLEX buffer Plus, 0.5x iPLEX termination mix and 0.5x iPLEX enzyme. An extension primer mix was made to give a final concentration of each primer between 0.73 μM and 1.46 μM. The thermal cycling conditions for the reaction included an initial denaturation step at 94°C for 30 seconds, followed by 40 cycles of 94°C for 5 seconds, with an internal 5 cycles loop at 52°C for 5 seconds and 80°C for 5 seconds, followed by a final extension step of 72°C for 3 minutes. The next step was to desalt the iPLEX Gold reaction products with Clean Resin following the manufacturer's protocol. The desalted products were dispensed onto a 384 Spectrochip II using an RS1000 Nanodispenser and spectra were acquired using the MA4 mass spectrometer, followed by manual inspection of spectra by trained personnel using MassARRAY Typer software, version 4.0. All assays were performed in 384-well plates, including negative controls and a trio of Coriell samples (Na10860, Na10861 and Na11984) for quality control. A 90% SNP genotyping success rate was imposed on the analysis.

Supplementary Table S1. List of the 41 candidate SNPs included in the study. SNPs: single nucleotide polymorphism; CNS: central nervous system; MAF: minor allele frequency.

n	SNP id	Consequence	Variant	Chr	Chr position start (bp)	Gene	Protein	MAF (all individuals)	PubMed ID	Association
1	rs10129666	A>G	intronic	14	78228725	NRXN3	Neurexin 3	0.365016	25387706	Electrodermal activity
2	rs10782344	G>T	intergenic	6	156457526	/	/	0.388578	24582949	Fibromyalgia
3	rs10799897	A>G,T	intronic	1	163073298	RGS4	Regulator of G protein signaling 4	0.458866	21905019 26973546	Fibromyalgia Psychiatric disorders
4	rs10821659	A>G	intronic	10	60033666	ANK3	Ankyrin 3	0.442093	23796624	Post-traumatic stress disorder
5	rs11126630	T>C	intergenic	2	77715718	/	/	0.411941	26087016	Behavioral disorders
6	rs11127292	C>T	intronic	2	2026171	MYT1L	Myelin Transcription Factor 1 Like	0.161941	24582949	Fibromyalgia & CNS
7	rs11602757	A>G	intronic	11	4032651	STIM1	Stromal interaction molecule 1	0.18151	24582949	Fibromyalgia & CNS
8	rs11923054	T>C	missense	3	167333981	ZBBX	Zinc finger B-box domain containing	0.25619	24582949	Fibromyalgia & CNS
9	rs12146962	T>A, C	intergenic	14	32911892	/	/	0.403554	19118814 22138694	Late-Onset Alzheimer Disease Ankylosing spondylitis
10	rs12556003	T>C	intronic	X	139661108	MCF2	Cell line derived transforming sequence	0.0233113	24582949	Fibromyalgia & CNS
11	rs12601358	T>A,G	intergenic	17	11190860	/	/	0.122204	27126917	Daytime resting duration
12	rs12704506	A>G	intronic	7	89991997	STEAP2-AS1	STEAP2 antisense RNA 1	0.160942	24582949	Fibromyalgia & CNS
13	rs12770855	C>T	intergenic	10	30831269	ZNF438	Zinc Finger Protein 438	0.0551118	24582949	Fibromyalgia & CNS
14	rs17512210	T>G	intronic	17	11327149	SHISA6	Shisa Family Member 6	0.214457	24582949	Fibromyalgia & CNS
15	rs1998709	C>A	intronic	10	94124817	PLCE1	phospholipase C epsilon 1	0.237819	24582949 16385451	Fibromyalgia & CNS Late-Onset Alzheimer Disease
16	rs2087017	G>A,C	downstream	3	114123166	DRD3 related	Dopamine receptor D3	0.480831	26303433	Personality traits
17	rs2194390	G>A	intronic	2	50675793	NRXN1	Neurexin 1	0.0539137	24582949	Fibromyalgia & CNS
18	rs265015	A>G	intronic	4	95439645	UNC5C	Unc-5 Netrin Receptor C	0.121605	24582949	Fibromyalgia & CNS
19	rs2701106	T>A,C	intergenic	12	114259742	TBX5 related	T-Box 5	0.359425	24582949	Fibromyalgia & CNS
20	rs2858166	A>C	5 kb_down	X	101620283	ARMCX6	Armadillo Repeat Containing X-Linked 6	0.376689	24582949	Fibromyalgia & CNS
21	rs2901761	G>A	intronic	10	94135370	PLCE1	Phospholipase C epsilon 1	0.424321	24582949	Fibromyalgia & CNS
22	rs35699176	G>A	stop gained	19	2936537	ZNF77	Zinc Finger Protein 77	0.0201677	26086970	Increase of growth hormone
23	rs4453447	G>C	intronic	15	26758325	GABRB3	Gamma-Aminobutyric Acid Type A Receptor Beta3 Subunit	0.184904	21905019	Fibromyalgia
24	rs4901530	A>G	intronic	14	54700440	SAMD4A	Sterile Alpha Motif Domain Containing 4A	0.338658	27126917	Sleep onset irregularity

n	SNP id	Consequence	Variant	Chr	Chr position start (bp)	Gene	Protein	MAF (all individuals)	PubMed ID	Association
25	rs4906902	A>G	intronic	15	26774621	GABRB3	Gamma-Aminobutyric Acid Type A Receptor Beta3 Subunit	0.199681	21905019	Fibromyalgia
									24999380	Autism spectrum disorders
									25025424	Heroin dependence
									22082659	Epilepsy
26	rs6043433	G>A	intronic	20	15678841	MACROD2	MACRO Domain Containing 2	0.163339	24582949	Fibromyalgia & CNS
27	rs6131711	C>A	intronic	20	15795773	MACROD2	MACRO Domain Containing 2	0.428914	24582949	Fibromyalgia & CNS
28	rs642544	T>G	intronic	11	105866294	GRIA4	Glutamate Ionotropic Receptor AMPA Type Subunit 4	0.33107	21905019	Fibromyalgia
29	rs6454674	T>G	intronic	6	88163211	CNR1	Cannabinoid Receptor 1	0.314097	21905019	Fibromyalgia
									20549395	PTSD
									21790903	cocaine addiction
									19052543	cocaine dependence
									25136364	Polycystic ovary syndrome
									17509535	Drug and alcohol dependence
									22085192	Alcohol dependence
									18375449	Risk for obesity
30	rs6971	A>G	missense	22	43162920	TSPO	Translocator protein	0.171725	27448744	Fibromyalgia
									23942012	Bipolar Disorder
31	rs7147705	T>C	intronic	14	79535753	NRXN3	Neurexin 3	0.49381	22959728	Amyotrophic Lateral Sclerosis
32	rs7911	A>G	intronic	1	89052437	GBP1	Guanylate Binding Protein 1	0.38099	21905019	Fibromyalgia
33	rs793108	C>T	intronic	10	31126177	ZNF438/LOC105376481	Zinc Finger Protein 438	0.341254	24390342	Rheumatoid arthritis
34	rs79448530	C>T	missense	11	4577726	C11orf40	Chromosome 11 Open Reading Frame 40	0.0189696	23762283	Fibromyalgia & Inflammatory Cytokine
35	rs7963168	T>A,C	intergenic	12	114273261	TBX5	T-Box 5	0.278754	24582949	Fibromyalgia & CNS
36	rs809	C>T	intronic	14	78090121	NRXN3	Neurexin 3	0.485024	26503763	Bipolar disorder
37	rs8192619	G>A	synonymous	6	132645209	TAAR1	Trace Amine Associated Receptor 1	0.0792732	21905019	Fibromyalgia
38	rs9381682	G>A	intergenic	6	48652502	/		0.142372	24582949	Fibromyalgia & CNS
39	rs9565180	C>T	intronic	13	75657334	LMO7	LIM Domain 7	0.298323	24582949	Fibromyalgia & CNS
40	rs981524	C>T	intronic	14	32717051	AKAP6	A-Kinase Anchoring Protein 6	0.305911	24582949	Fibromyalgia & CNS
41	rs4680	G>A	missense	22	19963748	COMT	Catechol-O-methyltransferase	0.369209	30886988	Fibromyalgia and pain sensitivity
									22528689	