rTMS in fibromyalgia
A randomized trial evaluating QoL and its brain metabolic substrate

ABSTRACT

Objective: This double-blind, randomized, placebo-controlled study investigated the impact of repetitive transcranial magnetic stimulation (rTMS) on quality of life (QoL) of patients with fibromyalgia, and its possible brain metabolic substrate.

Methods: Thirty-eight patients were randomly assigned to receive high-frequency rTMS (n = 19) or sham stimulation (n = 19), applied to left primary motor cortex in 14 sessions over 10 weeks. Primary clinical outcomes were QoL changes at the end of week 11, measured using the Fibromyalgia Impact Questionnaire (FIQ). Secondary clinical outcomes were mental and physical QoL component measured using the 36-Item Short Form Health Survey (SF-36), but also pain, mood, and anxiety. Resting-state [18F]-fluorodeoxyglucose-PET metabolism was assessed at baseline, week 2, and week 11. Whole-brain voxel-based analysis was performed to study between-group metabolic changes over time.

Results: At week 11, patients of the active rTMS group had greater QoL improvement in the FIQ (p = 0.032) and in the mental component of the SF-36 (p = 0.019) than the sham stimulation group. No significant impact was found for other clinical outcomes. Compared with the sham stimulation group, patients of the active rTMS group presented an increase in right medial temporal metabolism between baseline and week 11 (p < 0.001), which was correlated with FIQ and mental component SF-36 concomitant changes (r = −0.38, p = 0.043; r = 0.51, p = 0.009, respectively). QoL improvement involved mainly affective, emotional, and social dimensions.

Conclusion: Our study shows that rTMS improves QoL of patients with fibromyalgia. This improvement is associated with a concomitant increase in right limbic metabolism, arguing for a neural substrate to the impact of rTMS on emotional dimensions involved in QoL.

Classification of evidence: This study provides Class II evidence that rTMS compared with sham rTMS improves QoL in patients with fibromyalgia. Neurology® 2014;82:1–8

GLOSSARY

BDI = Beck Depression Inventory; DSM-IV-R = Diagnostic and Statistical Manual of Mental Disorders, 4th edition, revised; FDG = [18F]-fluorodeoxyglucose; FIQ = Fibromyalgia Impact Questionnaire; MCS = Mental Composite Score; PCS = Physical Composite Score; QoL = quality of life; rTMS = repetitive transcranial magnetic stimulation; SF-36 = 36-Item Short Form Health Survey.

Fibromyalgia affects quality of life (QoL) to a large extent and more than other chronic pain conditions.1,2 Of interest, neuroimaging studies of fibromyalgia have suggested global dysfunction of central pain processing.3–5 Perfusion abnormalities have been in particular described at rest (i.e., without painful stimulation) with hyperperfusions of somatosensory cortex, supporting increased nociceptive perception, and with cortico-limbic hypoperfusions, supporting altered emotional regulation.6 These hypofunctional brain regions have also been involved in mental processes related to self-awareness and awareness of others, and in a range of social cognitive abilities.7

Based on the hypothesis of central dysfunction,8 2 studies have assessed the effect of high-frequency repetitive transcranial magnetic stimulation (rTMS) on the left primary motor cortex and have reported a beneficial effect on pain and QoL.9,10 However, the mechanisms underlying the
effectiveness of rolandic rTMS remain unclear. Because high-frequency stimulation is supposed to produce enhanced cortical responses (i.e., facilitation), an activation of hypofunctional systems is expected, rather than an inhibition of the somatosensory cortex. The clinical effect should thus predominantly improve hypofunctional dimensions, affective, emotional, or social, which are involved in QoL, rather than directly affect pain nociception.

We designed a double-blind, randomized, and placebo-controlled trial to investigate the impact of high-frequency rTMS over the left primary motor cortex on QoL in patients with fibromyalgia, and its brain metabolic substrate.

**METHODS** Study site and patient eligibility. This study was conducted at La Timone University Hospital, in a specialized pain treatment center, and in the Nuclear Medicine Department (Marseille, France) from October 2008 to December 2010.

The inclusion criteria were as follows: age older than 18 years; right-handed; diagnosis of fibromyalgia according to American College of Rheumatology criteria; score of at least 4 on the average pain intensity numerical scale of the Brief Pain Inventory at screening; persistent pain for more than 6 months before enrollment; stable treatment for more than 1 month before enrollment and throughout the study; rTMS-naïve; and native French speaking. At screening, all patients underwent physical examination by the same pain specialist, followed by laboratory/imaging tests if necessary. The exclusion criteria were as follows: reduced capacity to consent; inflammatory rheumatic disease, autoimmune disease, or other painful disorders that might confound the assessment of fibromyalgia pain; current primary psychiatric condition, including major depression or major personality disorders according to DSM-IV-R criteria; or a history of substance abuse; neurologic disorders; and contraindications for rTMS and [18F]-fluorodeoxyglucose (FDG)-PET, including history of seizures, brain trauma, brain surgery, intracranial hypertension, a pacemaker or other metallic implants, and pregnancy/breastfeeding. Concomitant medication for pain and sleep disorders was allowed, provided the dose administered had been stable for at least 1 month before enrollment and remained stable throughout the study.

Standard protocol approvals, registrations, and patient consents. The patients were provided with both oral and written information regarding the study before obtaining their informed consent. The local ethics committee and the French drug and device regulation agency approved this study. The international standard randomized controlled trial number is NCT00697398.

Design. The present study was prospective, randomized, controlled, double-blind, and monocentric. Figure e-1 on the Neurology® Web site at Neurology.org displays the flowchart. Individuals were randomized by a computer-generated list, which was maintained centrally so no investigators knew the treatment allocation of any patient. The participants were randomly assigned to 1 of the 2 following groups (random assignment 1:1): patients were assigned to receive active rTMS or sham stimulation. QoL, depression, anxiety, pain, and brain PET metabolism were assessed at 3 time points: at randomization (baseline, T0), at 2 weeks (T1), and at 11 weeks (1 week after last stimulation, T2).

rTMS protocol. The stimulation protocol consisted of 14 sessions over 10 weeks: an “induction phase” of 10 sessions over 2 weeks followed by a “maintenance phase” of 4 sessions (1 session at weeks 4, 6, 8, and 10). Sham stimulation was conducted with a sham coil of identical size, color, and shape, emitting a sound similar to that emitted by the active coil. Stimulation were administered by the same technologist. Patients and clinical raters were blinded to treatment. The characteristics of the magnetic stimulation are presented in appendix e-1.

**Evaluation criteria.** Primary criterion. The primary evaluation criterion was QoL change from baseline to T2. QoL was specifically assessed using the French version of the Fibromyalgia Impact Questionnaire (FIQ). The total score of the FIQ (range 0–100) provides an estimation of the impact of fibromyalgia, with higher scores indicating lower QoL levels.

Secondary criteria. QoL was also assessed using a generic scale, the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36), to identify the 2 QoL components, namely, the Physical Composite Score (PCS) and Mental Composite Score (MCS). Scores range from 0 to 100, with higher scores indicating higher QoL levels.

Pain was measured using a self-reported average pain intensity scale over the last 24 hours (numerical scale from 0 = no pain to 10 = maximal pain imaginable), the number of tender points (of 18 points in total), and pressure pain threshold (i.e., minimum force applied that induces pain).

Depression was assessed using the self-administered Beck Depression Inventory (BDI). The BDI score range is 0 to 63, with higher scores indicating greater depression. Anxiety was assessed using the Hospital Anxiety and Depression Scale; scores range from 0 to 21, with higher scores indicating more severe anxiety symptoms.

Brain metabolism was studied with FDG-PET/CT imaging. Brain data analysis is detailed in appendix e-2. Statistical maps were thresholded at p = 0.001 and corrected for extent to 16 voxels (4 full width at half maximum of the Gaussian filter).

**Statistical analyses.** In the 2 previous trials that have assessed the impact of rTMS in fibromyalgia, differences in the FIQ score were found between active rTMS and sham stimulation groups. Guided by these results, the sample size was initially determined to obtain an 80% power to detect a 10-point difference in QoL at T2 as evaluated by the FIQ. With a significant p value of 0.05, these calculations showed that a total of 30 patients were needed; considering a potential 20% of patients being lost to follow-up, a total of 38 patients would need to be included.

Clinical analyses were performed on the intent-to-treat population. Changes in outcomes between T0 and T1/T2 were compared across the 2 groups using Mann-Whitney U tests for continuous or ordinal variables, and χ² or Fisher exact tests for frequencies. Changes in outcome were also analyzed with mixed-effect models for continuous variables or nonparametric analysis of longitudinal data for ordinal variables (number of tender points and average daily pain).

The models included the following: QoL scores over time as the outcome variable (FIQ, SF-36 PCS and MCS); BDI scores as covariates to isolate the effect of rTMS on QoL, independently of depression; time as a categorical variable, study group, time × study group and BDI score × study group as fixed effects; and patient as random effect. In addition to intention-to-treat analysis (sensitivity analysis), complementary per-protocol analyses were undertaken on significant clinical data.

Finally, to prevent unnecessary radiation exposure, brain imaging at T1/T2 was performed only in patients who completed the rTMS treatment. Neuroimaging analyses were based on Statistical Parametric Mapping. We then looked for associations in metabolic and clinical changes over time using Spearman correlation tests.

Statistical significance was set at p < 0.05. Statistical analyses were performed using SPSS for Windows (version 17.0; SPSS
Primary research question and classification of evidence.
We hypothesized that high-frequency rTMS would have a predominant effect on QoL rather than on pain. This study provides Class II evidence that rTMS compared with sham rTMS improves QoL in patients with fibromyalgia.

RESULTS Participants. Table 1 shows baseline data for the 38 patients randomly assigned to the active rTMS group or the sham stimulation group. The 2 groups were well balanced for pretreatment characteristics, including brain PET metabolism. All patients completed the induction phase, but 9 (23.7%) were excluded during the maintenance phase (3 in the active rTMS group and 6 in the sham rTMS group) (figure e-1). The reasons included 5 intercurrent medical conditions forcing a therapeutic shift (1 cystitis/pyelonephritis and 1 lumbago in the active rTMS group; 1 tracheitis, 1 kidney stone colic, and 1 headache in the sham rTMS group); 2 spontaneous changes in pain automedication (1 in each group); and lack of efficacy in 2 patients who decided to stop the protocol (sham rTMS group). No seizures or other side effects occurred during the follow-up study.

Effects of rTMS on FIQ and secondary clinical outcomes. At T2, the active rTMS group had a greater QoL improvement than did the control group for the primary outcome (FIQ score: \(9.6 \pm 16.7\) vs \(12.0 \pm 9.3\) points, \(p = 0.032\)) and for one secondary outcome (BDI score: \(9.1 \pm 5.9\) vs \(11.7 \pm 8.1\) points, \(p = 0.282\)).
Table 2  Changes in primary and secondary outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean change from baseline</th>
<th>p Value</th>
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<tbody>
<tr>
<td></td>
<td>Active rTMS group</td>
<td>Sham stimulation group</td>
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<tr>
<td>SF-36 score*</td>
<td></td>
<td></td>
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<tr>
<td>Physical Composite Score</td>
<td></td>
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<tr>
<td>Week 2</td>
<td>0.3 ± 18.2</td>
<td>1.3 ± 9.5</td>
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<tr>
<td>Week 11</td>
<td>−9.6 ± 16.7</td>
<td>2.0 ± 9.3</td>
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<tr>
<td>Mental Composite Score</td>
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<tr>
<td>Week 2</td>
<td>0.3 ± 8.8</td>
<td>0.9 ± 5.3</td>
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<tr>
<td>Week 11</td>
<td>1.4 ± 9.0</td>
<td>0.4 ± 4.8</td>
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<tr>
<td>BDI†</td>
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<tr>
<td>Week 2</td>
<td>−1.3 ± 2.7</td>
<td>−0.5 ± 4.0</td>
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<tr>
<td>Week 11</td>
<td>−1.9 ± 2.8</td>
<td>−0.1 ± 4.4</td>
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<tr>
<td>HADS anxiety score*</td>
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<tr>
<td>Week 2</td>
<td>0.3 ± 2.6</td>
<td>−0.8 ± 1.9</td>
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<tr>
<td>Week 11</td>
<td>0.4 ± 1.7</td>
<td>0.5 ± 2.3</td>
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<tr>
<td>Tender points, 0-18</td>
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<tr>
<td>Week 2</td>
<td>−0.2 ± 2.2</td>
<td>−1.4 ± 4.4</td>
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<tr>
<td>Week 11</td>
<td>−1.5 ± 2.7</td>
<td>−3.7 ± 6.5</td>
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<tr>
<td>Average daily pain, 0-10</td>
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<tr>
<td>Week 2</td>
<td>0.1 ± 1.8</td>
<td>−0.2 ± 2.7</td>
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<tr>
<td>Week 11</td>
<td>−0.3 ± 1.6</td>
<td>−1.5 ± 3.1</td>
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<tr>
<td>Pressure pain threshold, kPa</td>
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<tr>
<td>Right arm</td>
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<tr>
<td>Week 2</td>
<td>3.2 ± 25.0</td>
<td>4.7 ± 33.1</td>
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<tr>
<td>Week 11</td>
<td>10.5 ± 28.8</td>
<td>0.5 ± 45.4</td>
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<tr>
<td>Left arm</td>
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<tr>
<td>Week 2</td>
<td>−1.6 ± 27.1</td>
<td>−2.1 ± 37.5</td>
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<tr>
<td>Week 11</td>
<td>−1.1 ± 28.8</td>
<td>−7.9 ± 52.9</td>
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<tr>
<td>Medial temporal lobe metabolism</td>
<td></td>
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<tr>
<td>Week 2</td>
<td>6.2 ± 3.8</td>
<td>1.0 ± 3.6</td>
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<tr>
<td>Week 11</td>
<td>10.3 ± 5.9</td>
<td>−2.4 ± 5.3</td>
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</tbody>
</table>

Abbreviations: BDI = Beck Depression Inventory; FIQ = Fibromyalgia Impact Questionnaire; HADS = Hospital Anxiety and Depression Scale; rTMS = repetitive transcranial magnetic stimulation; SF-36 = 36-item Short Form Health Survey. Values are means ± SD.

*Scores range from 0 to 100, with higher scores indicating more severe symptoms.

†Statistically significant values.

‡Medical Outcomes Study SF-36. Scores range from 0 to 100, with higher scores indicating better health status.

§Scores range from 0 to 63, with higher scores indicating more severe symptoms.

‖Anxiety scores range from 0 to 21, with higher scores indicating more severe depressive symptoms.

¶Anxiety scores range from 0 to 21, with higher scores indicating more severe symptoms.

Per-protocol analysis: n = 16 in the active rTMS group and n = 13 in the sham stimulation group.

This randomized, double-blind, sham-controlled study showed that high-frequency rTMS over the left primary motor cortex had a delayed positive impact on patients’ QoL after 11 weeks of treatment, without effect on pain. Above all, this neuroimaging study showed that the therapeutic effect of rTMS over the left motor cortex was correlated with an increase in right medial temporal metabolism. This whole-brain voxel-based report

outcome (SF-36 MCS: +5.0 ± 6.9 vs −1.6 ± 7.6, p = 0.019) (table 2, figure 1). A difference in FIQ score and SF-36 MCS between groups from baseline to T2 was confirmed using mixed-effect models (p = 0.033 and p < 0.001, respectively) and also using per-protocol analysis (p = 0.032 and p < 0.001, respectively). The QoL was more improved in the rTMS group for all dimensions of the SF-36, but only the mental health dimension was significant (p = 0.045). The bodily pain dimension was less affected by rTMS than other dimensions involving emotional or social issues (appendix e-3). No differences for SF-36 PCS, and for other clinical outcomes (pain, mood, and anxiety), were observed over time from baseline between the 2 groups (p values >0.05). At T0, BDI scores indicated mild depression in both groups (>9 points), and at T2 the scores remained stable in the control group whereas they decreased by 2 points in the active rTMS group, indicating minimal depression. However, the difference was statistically nonsignificant (p = 0.346). In the same way, pressure pain threshold of the right arm at T2 was more increased in the rTMS group (+10.5) than in the control group (+0.5), but again this difference was not significant (p = 0.528).

Effect of rTMS on brain PET metabolism. In comparison to the sham stimulation group, the active rTMS group presented an increase in right medial temporal metabolism (hippocampus, parahippocampal and fusiform gyrus, Brodmann area 20; k = 89; t score = 3.85; p < 0.001; figure 2) between T0 and T2. It is interesting that this metabolic increase relative to baseline was already present at T1 (p = 0.002), before the improvement of QoL at T2.

We then looked for Spearman correlations between this medial temporal metabolism and QoL scores. Right medial temporal metabolism and QoL varied in the same direction between T2 and T0 (FIQ: r = −0.38, p = 0.043; SF-36 MCS: r = 0.51, p = 0.009; figure 3), especially for nonphysical dimensions, such as the feel good (r = −0.41, p = 0.031), work missed (r = −0.58, p = 0.039), depression (r = −0.37, p = 0.046), fatigue (r = −0.50, p = 0.006), rested (r = −0.40, p = 0.034), and stiffness (r = −0.45, p = 0.014) dimensions of the FIQ and the role-emotional dimension of the SF-36 (r = 0.40, p = 0.040).

DISCUSSION This randomized, double-blind, sham-controlled study showed that high-frequency rTMS over the left primary motor cortex had a delayed positive impact on patients’ QoL after 11 weeks of treatment, without effect on pain. Above all, this neuroimaging study showed that the therapeutic effect of rTMS over the left motor cortex was correlated with an increase in right medial temporal metabolism. This whole-brain voxel-based report

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corroborates the central hypothesis in fibromyalgia, while previous studies (based on region of interest) failed to demonstrate brain PET metabolism changes in these patients.

QoL was improved after rTMS maintenance on both the FIQ and mental component of the SF-36. The focus on these 2 distinct questionnaires permits a precise analytical description, with predominant QoL improvement involving affective (depression and fatigue), emotional (role-emotional), and social (work missed) dimensions. In line with this finding, the BDI scores decreased in the active rTMS group. The absence of statistical significance may be caused by a lack of sensitivity to change of this scale, as previously reported. However, the effect on QoL was not immediate; it appeared only at the end of the maintenance phase. Despite this positive outcome, there was no effect on pain. The rTMS effects may thus reflect an improvement involving the emotional dimension associated with pain, rather than a direct

Figure 1  Mean changes in quality of life and resting-state brain metabolism at 2 and 11 weeks

(A) FIQ total score (p = 0.032). (B) Total SF-36 MCS (p = 0.019). (C) Total SF-36 PCS (p = 0.874). (D) Medial temporal metabolism (p < 0.001). FIQ = Fibromyalgia Impact Questionnaire; MCS = Mental Composite Score; PCS = Physical Composite Score; rTMS = repetitive transcranial magnetic stimulation; SF-36 = 36-Item Short Form Health Survey.

Figure 2  Anatomical localization of FDG-PET findings (p < 0.001)

Increase in medial temporal metabolism (hippocampus, parahippocampal and fusiform gyrus) in the active repetitive transcranial magnetic stimulation group. FDG = [18F]-fluorodeoxyglucose.
affect on the sensory component of pain. Our findings, however, differ substantially from those of the 2 previous studies, which showed immediate effects on both QoL and pain. Considering the small sample size of these studies, one cannot exclude that the populations have different characteristics and thus different response profiles. Moreover, the stimulation protocols were not exactly the same.

Besides these methodologic considerations, the failure to detect between-group differences in pain may have several explanations. One hypothesis is that rTMS has an influence on the psychological dimensions involved in QoL, without effect on neural processing of pain. In our study, improvement of QoL would be related only to a better perception of health, but not to a pain decrease. Of interest, a recent study has suggested that 2 segregated mechanisms were involved in the neural processing of pain and of negative affect. However, we may also hypothesize that our stimulation protocol was too short to detect a global pain improvement. rTMS-induced analgesia, rather than acting directly on pain, may be mediated by the translation of changes in emotional processing associated with global pain, thus requiring a delay in action. In support of this hypothesis, a recent study suggested that catastrophizing might precede changes in pain response.

Our results are, however, not surprising from a theoretical perspective. In accordance with the metabolism increase found, high-frequency rTMS has been associated with facilitatory effects on cortical excitability. Conversely, the metabolic effects of rTMS involved contralateral interconnected brain structures, as reported in previous studies, but not the primary targeted cortical area. This absence of local effect of rTMS appears surprising, but has also been previously reported. Facilitatory effects may become weaker when the targeted cortical area is already activated, as expected for the somatosensory cortex in patients with fibromyalgia. It is interesting that the role of the limbic system, and that of the right medial temporal cortex, have been described in emotional modulation, in particular in modulation of the emotional aspects associated with pain. However, the temporal lobe has also been associated with social cognition, especially in theory of mind abilities. Similarly, a recent study reported that the superior temporal sulcus was involved in the functional substrate underlying social functioning of QoL. Moreover, neural connections have been reported between this temporal area and the limbic system. We may thus hypothesize that the effects of high-frequency rTMS over the hemisphere-dominant motor cortex mainly activate interconnected emotional and social systems, resulting in improved QoL.

The increase in medial temporal lobe metabolism before the improvement of QoL could have clinical implications. Biomarkers such as neuroimaging could open interesting perspectives, to guide individual therapeutic strategy, especially to early identified responders and nonresponders to rTMS. Early detection of nonresponders to rTMS may then allow proposing more adapted treatment. Indeed, despite the safety and tolerance of rTMS found in our study, a main concern of treatment burden remains, especially in patients with chronic pain conditions.

The potential mechanism underlying high-frequency rTMS over the primary motor cortex leads us to discuss the relevance of using further rTMS protocols, in combination or alone, to optimize clinical effects. Because high-frequency stimulation has mainly produced an activation of right limbic structures, it would be preferable to directly stimulate an ipsilateral reachable cortex, highly interconnected with the deep limbic cortex, as proposed in depression for the dorsolateral prefrontal cortex and with encouraging results on affective dimensions. However, because of inhibitory effects of low-frequency stimulation on cortical excitability, low-frequency rTMS over the sensorimotor cortex should decrease nociceptive perception and then have direct analgesic effects in fibromyalgia, as reported in dystonia for the low-frequency rTMS of premotor cortex on painful muscular spasms.

Finally, rTMS remains a constraining treatment, probably not appropriate for all patients because of specific contraindications as well as the heterogeneity
of rTMS response. The absence of placebo effect can be surprising. We hypothesize that the length and the burden of our protocol exhausted the patients, which could explain the absence of placebo effect. The length of our protocol, the allocated resources in personnel and equipment, the patients’ compliance, and the absence of pain improvement should be considered in future studies to optimize the clinical practice of rTMS in patients with fibromyalgia.

This study is limited by its small sample size (n = 38), although it is close to the only other study on the efficacy of high-frequency rTMS maintenance over the motor cortex in fibromyalgia (n = 40). In addition, 9 patients did not complete the maintenance phase, reducing our sample to 29 patients. This proportion of those withdrawn (23.7%) was similar to that of the previous study (25.0%). Moderate efficacy may have been missed, especially for pain. This issue is of importance in fibromyalgia, for which treatments are known to have moderate effects. Replication with a larger sample size is needed.

Although patients were blinded to the treatment condition, the rTMS administrator who placed the active or sham stimulator in position could not be blinded to the treatment. To overcome this potential bias, she was not involved in the recruitment and evaluation of patients. A blinded rater was used for pain measures and the occurrence of adverse effects. Moreover, all patients were rTMS-naive, preventing them from recognizing the sham or active coils. Recent studies recommended that investigators test for the success of blinding, which was not done in the present trial.

Overall, our study shows that active rTMS improves QoL of patients with fibromyalgia. This improvement is associated with a concomitant increase in right limbic metabolism, arguing for a neural substrate to the impact of rTMS on the emotional dimension involved in QoL.

AUTHOR CONTRIBUTIONS
L.B.: drafting/revising the manuscript for content, including medical writing for content, analysis or interpretation of data, statistical analysis. A. Douzet: drafting/revising the manuscript for content, including medical writing for content, analysis or interpretation of data. P.R.: study concept or design, analysis or interpretation of data, acquisition of data, study supervision or coordination, obtaining funding. N.D.: study concept or design, acquisition of data. S.G.: study concept or design, acquisition of data, obtaining funding. V.P.: analysis or interpretation of data. S.K.: drafting/revising the manuscript for content, including medical writing for content, analysis or interpretation of data. O.M.: study concept or design, obtaining funding. A. Donnet: drafting/revising the manuscript for content, including medical writing for content, analysis or interpretation of data, study supervision or coordination. E.G.: drafting/revising the manuscript for content, including medical writing for content, study concept or design, analysis or interpretation of data, acquisition of data, statistical analysis, study supervision or coordination, obtaining funding.

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DISCLOSURE
The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

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REFERENCES

Complete the AAN 2014 Neurology Compensation and Productivity Survey by May 9

The AAN launched its second annual Neurology Compensation and Productivity Survey in March and needs practicing US members and their practices to contribute their data. It is critical that all US neurologists and practice managers participate in the survey to ensure the most accurate and authoritative data representing the US neurology landscape. Visit AAN.com/view/2014NeuroSurvey to review preparation documents, including an FAQ and Quick Start Guide. Complete the survey by May 9 and get free access to the online results and the Neurology Compensation and Productivity Report, available in early July 2014. The cost to access the data and report for nonparticipants is $600 for AAN members and $1200 for nonmembers.