ME/CFS Functional Imaging Task Summaries

Title	Low putamen activity associated with poor reward sensitivity in childhood chronic fatigue syndrome.
Authors	Mizuno K, Kawatani J, Tajima K, Sasaki AT, Yoneda T, Komi M, Hirai T, Tomoda A, Joudoi T, Watanabe Y.
Publication Details	Neuroimage Clin. 2016 Sep 26;12:600-606. eCollection 2016.
EntrezUID/PMID	27709065
Population; Task Domain	Pediatric population; Reward sensitivity; DV: Reaction time
Behavioral Questionnaires	All participants were right-handed according to the Edinburgh handedness inventory (Oldfield, 1971) and scored > 80 on the full-scale intelligence quotient derived from the Wechsler Intelligence Scale for Children (Wechsler, 1991). The severity of fatigue was evaluated using the Chalder Fatigue Scale (Chalder et al., 1993; Tanaka et al., 2008). The balance between effort and reward was evaluated using the effort-reward imbalance for learning model questionnaire (LERI) (Fukuda et al., 2010).
Tasks Used for fMRI	During scanning, participants performed four repeats of each of the four conditions HMR, LMR, NMR, and fixation rest (24 s per condition of 8 × 3 s trials) for a total of 6 min 24 s. In each session, the HMR and LMR conditions were ordered differently, and the order of the four sessions was counterbalanced across participants. All participants were paid a fixed amount for their participation at the end of the experiment.
Results	In this study, we demonstrated that neural activity of the putamen in CCFS patients was decreased during perception of low-value rewards, but not during perception of high-value rewards, indicating that neural processing in the putamen related to reward sensitivity is impaired in CCFS patients. In addition, putamen activity was correlated with reward from learning in CCFS patients. In conclusion, neural processing of reward sensitivity in the putamen was impaired in CCFS patients. For daily tasks with low perceived reward, low putamen activity may induce low motivation to learn. Low putamen activity may be due to dopaminergic dysfunction, and thus, dopamine agents may be an effective treatment for CCFS patients.
Task Summary	Behavioral tasks: Edinburgh Handedness Inventory, WISC 5, Chalder Fatigue Scale (Fatigue Severity), effort-reward imbalance for learning model questionnaire (LERI). Neuroimaging task experimental condition: simple gambling task-- high and low monetary reward conditions, Control condition: no-monetary-reward condition.

Title	Static and dynamic functional connectivity in patients with chronic fatigue syndrome: use of arterial spin labelling fMRI.
Authors	Boissoneault J, Letzen J, Lai S, Robinson ME, Staud R.
Publication Details	Clin Physiol Funct Imaging. 2016 Sep 28. doi: 10.1111/cpf.12393. [Epub ahead of print]
EntrezUID/PMID	27678090
Population; Task Domain	Adults; Fatigue Induction; Information Processing. PASAT task previously published.
Behavioral Questionnaires	Pennebaker Inventory of Limbic Languidness, a questionnaire designed to measure individual somatic focus (Pennebaker, 1983). Reported perceived role and physical function ranging from 'no function' to 'no impairment in function' using mechanical visual analog scales (VAS; 0–100). Immediately prior to scanning, all participants also rated their overall pain, depression, anxiety and fatigue. These VAS ranged from 'no pain/depression/anxiety/fatigue at all' to 'most intense pain/depression/anxiety/fatigue imaginable' (Price et al., 1994).
Tasks Used for fMRI	The Paced Auditory Serial Addition Test (PASAT; Gronwall, 1977) is a well-validated cognitive task of auditory information processing speed and flexibility, as well as calculation ability (Tagliazucchi & Laufs, 2015). It has good psychometric properties including high levels of internal consistency and test–retest reliability (Tombaugh, 2006). Critically, the PASAT has been successfully used as a cognitive challenge in functional neuroimaging studies of fatigue (Cook et al., 2007). To ensure standardization of presentation, auditory stimuli consisting of single- or double-digit numbers were computer-generated and presented in pseudorandom order at two different interstimulus intervals (ISIs). During the first 3 min of the PASAT, stimuli were presented with an ISI of 3 s. During the subsequent 9 min, the ISI was decreased to 2 s. Subjects added each number to the preceding one and determined whether they summed to 13 (target value). Across the duration of the PASAT, 35% of number combinations added to 13. Performance feedback (i.e. correct versus incorrect) was provided after each subject response. Subjects indicated their response (yes or no) using a keypad. They continuously rated their overall fatigue on an electronic VAS from 0 ('no fatigue') to 100 ('most intense fatigue imaginable') for the duration of the scan using a scroll wheel placed in their other hand. The scale was visible during the entire scan on a large computer screen, and subjects were instructed to adjust their ratings if fatigue changed. The PASAT and VAS were implemented and presented using PsychoPy (Peirce, 2007, 2009) running on a Dell Latitude laptop (Dell Inc., Round Rock, TX, USA).

Results	This ASL study examined dFC among brain regions associated with cognitive and emotional functioning in CFS during a fatiguing cognitive task, in addition to sFC. We also measured whether dFC was associated with fatigue ratings. Results from the present study provide the first evidence that fatigue-inducing cognitive activity, implemented with a neuropsychological task involving sustained cognitive effort (PASAT), is associated with alterations in patterns of FC between brain regions associated with aspects of CFS symptomatology. As illustrated by analyses of in-scanner fatigue ratings, this procedure was effective at increasing fatigue in both CFS and HC.
Task Summary	PILL, Bunch of VAS scales, adapted version of PASAT, not the same Cook et al. and Lange et al. used. Don't know what control task was.

Title	Emotional conflict processing in adolescent chronic fatigue syndrome: A pilot study using functional magnetic resonance imaging.
Authors	Wortinger LA, Endestad T, Melinder AM, Ã˜ie MG, Sulheim D, Fagermoen E, Wyller VB.
Publication Details	J Clin Exp Neuropsychol. 2017 May;39(4):355-368. doi: 10.1080/13803395.2016.1230180. Epub 2016 Sep 20.
EntrezUID/PMID	27647312
Population; Task Domain	Adolescents; emotional processing; response time slowing, decrease in accuracy. The emotional conflict task was modified from the previously described paradigm (Egner et al., 2008 Egner, T., Etkin, A., Gale, S., & Hirsch, J. (2008).
Behavioral Questionnaires	The Chalder Fatigue Questionnaire is a valid outcome measure in adult and adolescent CFS based on symptoms during the preceding month. The Mood and Feelings Questionnaire (MFQ) has been validated in children and adolescents. The state anxiety measure from the Spielberger State–Trait Anxiety Inventory.
Tasks Used for fMRI	The emotional conflict task was modified from the previously described paradigm (Egner et al., 2008 Egner, T., Etkin, A., Gale, S., & Hirsch, J. (2008). Dissociable neural systems resolve conflict from emotional versus nonemotional distracters. It consisted of 168 presentations of photographs of happy or fearful facial expressions drawn from the Karolinska database (Lundqvist & Øhman, 1998 Lundqvist, D. F., & Øhman, A. (1998). The Karolinska Directed Emotional Faces - KDEF, CD ROM. D. o. C. Neuroscience (Ed.). Solna: Psychology Department, Karolinska Institute). Faces were cropped and overlaid with the words “FRYKT” or “GLEDE” (English: fear or happy, respectively) and written in prominent red letters across the face, such that word and facial expression were either congruent or incongruent trial types (Figure 1). Stimuli were presented using E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA) and MR-compatible goggles with two LCD-displays (VisualSystems®; NordicNeuroLab, Bergen, Norway), while responses were collected using an MR-compatible response grip with two response buttons (ResponseGrip®; NordicNeuroLab, Bergen, Norway). Stimuli were presented for 1000 ms, an interstimulus interval using a fixation cross + of 3000 ms and jitter of 1250–2000 ms (mean intertrial interval, ITI = 4000) in a pseudorandom order. Trial types for expression, word, gender and response button were counterbalanced. Participants indicated facial affect with a button press response. Participants were instructed to indicate the emotional expression in the face (target), where a word was written across that was either semantically congruent or incongruent with the facial affect. Congruent conditions have semantically compatible faces and words and usually result in better performance, as there is no conflict. The congruent word thus represents a distractor that facilitates cognition. However, an incongruent word stimulus would elicit incompatible response tendencies, one of which is the overlearned prepotent response to read the word. The incongruent word represents a distractor that interferes with cognition and initiates cognitive conflict processing. Behavioral data, accuracy, and response times (excluding error trials), were analyzed in SPSS, Version 20 (SPSS, Inc., Chicago, IL).

	Interference in the response time (RT) data was calculated by subtracting the mean response times of the congruent (C) trials from the mean response times of the incongruent (I) trials. Interference in accuracy (AC) data was also calculated by subtracting mean accuracy scores on congruent trials from mean accuracy scores on incongruent trials. Emotional conflict (I – C) would be indicated on behavioral measures by producing a slowdown in I-C-RT and a reduction in I-C-AC. Behavioral effects were considered significant at a $p \leq .05$ (two-tailed) threshold.
Results	The aim of this study was to explore and link emotional conflict processing to underlying neural mechanisms in adolescent CFS. To gauge emotional conflict processing, we measured the amount of interference, response time slowing, and decrease in accuracy, observed on behavioral measures. The main findings of this study were that adolescents with CFS were less able to engage the left amygdala and left midposterior insula (mpINS) in response to conflict than the healthy comparison group. Reactivity of the amygdala was associated with accuracy interference during conflict. Conflict-related activity in the mpINS was related to response time interference. There were no associations between brain activity and depressive and anxiety symptoms. The CFS group did not produce a negative affect bias.
Task Summary	Behavioral tasks: Chalder Fatigue Questionnaire (Severity), Mood and Feelings Questionnaire, STAI. Neuroimaging tasks experimental condition: Egner et al., 2008 emotional conflict task -- Visual task

Title	Aberrant Resting-State Functional Connectivity in the Salience Network of Adolescent Chronic Fatigue Syndrome.
Authors	Wortinger LA, Endestad T, Melinder AM, Ã˜ie MG, Sevenius A, Bruun Wyller V.
Publication Details	PLoS One. 2016 Jul 14;11(7):e0159351. doi: 10.1371/journal.pone.0159351. eCollection 2016.
EntrezUID/PMID	27414048
Population; Task Domain	Adolescents; Resting state task.
Behavioral Questionnaires	All participants completed the Chalder Fatigue Questionnaire [49], Mood and Feelings Questionnaire for Depression [50], Spielberger State-Trait Anxiety Inventory [51], The Brief Pain Inventory (BPI) [52], and Wechsler Abbreviated Scale of Intelligence (WASI).
Tasks Used for fMRI	Participants were instructed to close their eyes and to rest comfortably, without moving or falling asleep, during the functional scan.
Results	Findings of insula dysfunction and its association with fatigue severity and pain intensity in adolescent CFS demonstrate an aberration of the salience network which might play a role in CFS pathophysiology.

Task Summary	Behavioral measures: Chalder, Mood and Feelings for depression, STAI, BPI, WASI II.
Title	Abnormal resting state functional connectivity in patients with chronic fatigue syndrome: an arterial spin-labeling fMRI study.
Authors	Boissoneault J, Letzen J, Lai S, O'Shea A, Craggs J, Robinson ME, Staud R.
Publication Details	Magn Reson Imaging. 2016 May;34(4):603-8. doi: 10.1016/j.mri.2015.12.008. Epub 2015 Dec 18.
EntrezUID/PMID	26708036
Population; Task Domain	Adults; Resting state task.
Behavioral Questionnaires	Prior to brain scanning, clinical fatigue, pain, depression, and anxiety were assessed using mechanical visual analog scales (VAS; [19]). Each scale was anchored on the right by “no fatigue/pain/depression/anxiety at all” and on the left by “the most intense fatigue/pain/depression/anxiety imaginable”. Perceived physical and role function were also assessed using VAS ranging from 0 (“no function”) to 100 (“no impairment in function”). VAS measures ranged from 0 to 10 and were rescaled to 0–100 by multiplying each value by 10, if necessary. Additionally, each participant completed the Pennebaker Inventory of Limbic Languidness (PILL).
Tasks Used for fMRI	Resting task, not further described.
Results	Results of our FC analyses showed abnormal connectivity patterns of ME/CFS patients for several brain regions, suggestive of functional network reorganization, including areas involved in memory (left parahippocampal gyrus), motor (bilateral pallidum), mood (ACC), and higher-order neurocognitive functions (ACC, AG, and SFG). An area of particular interest that showed altered connectivity in ME/CFS was ACC.
Task Summary	Behavioral measures: Bunch of VAS, PILL

Title	Less efficient and costly processes of frontal cortex in childhood chronic fatigue syndrome.
Authors	Mizuno K, Tanaka M, Tanabe HC, Joudoi T, Kawatani J, Shigihara Y, Tomoda A, Miike T, Imai-Matsumura K, Sadato N, Watanabe Y.
Publication Details	Neuroimage Clin. 2015 Sep 10;9:355-68. doi: 10.1016/j.nicl.2015.09.001. eCollection 2015.
EntrezUID/PMID	26594619
Population; Task Domain	Children and adolescents; Divided attention, multi-tasking.
Behavioral Questionnaires	The severity of fatigue was measured using the Chalder Fatigue Scale (Chalder et al., 1993); To identify the mental effort level of participants for the dual and single tasks, a visual analogue scale (VAS) for the subjective experience of motivation to each task condition was measured after the fMRI experiments (Mizuno et al., 2008). The VAS scores ranged from 0 (compete lack of motivation) to 100 (maximum motivation).
Tasks Used for fMRI	Kana Pick-out Test (KPT), which assesses participants' allocation of attentional resources to two simultaneous activities [picking out vowels (PV) and reading for story comprehension (SC). The participants performed the modified version of the KPT, which included single and dual task conditions presented on a computer screen for use with fMRI. The single task conditions were PV and SC, and the dual task required participants to perform PV and SC tasks concurrently (PV + SC). In addition, to control for the normal activation of brain areas due to visual and motor processing, the participants performed a test under control (CL) conditions. Although we used the Japanese version of the modified KPT in the present study, an English version has also been developed. In the PV condition, participants judged whether vowels included in the words were presented in the center of the screen. If the target letters were presented in the center of the screen, participants were instructed to press the right button. If the target letters did not appear in the center of the screen, participants were instructed to press the left button. In the SC condition, participants read silently each presented word as it appeared in sequence on the screen. An example sentence was “Mariko gazed at the blue sea and watched the white bird, and Takashi gazed at the blue mountain and watched the red bird.” The participants pressed the right and left buttons alternately for each word presented. In the PV + SC condition, the participants were required to simultaneously pick out vowels and understand the story. Thus, when the target letters (vowels) were presented in the center of the screen, the participants pressed the right button. If target letters did not appear in the center of the screen, the participants were instructed to press the left button. These judgments about the individual vowels and the direction of the button press were performed while reading the story for comprehension. In the CL condition, the participants were not required to perform either task and were instructed to simply press the right and left buttons alternately when presented with the word “press” on every trial.

Results	Clarifying the neural relationship between fatigue and divided attention is critical for the evaluation of cognitive development and interventional efforts in both fatigued children and adolescents and CCFS patients. Left frontal cortex of healthy students activated in verbal divided attention task
Task Summary	Behavioral measures: Chalder, VAS for subjective experience of motivation. Neuroimaging experimental task: Kana Pick out Test -- control condition was also described--visual task.

Title	Altered resting-state functional connectivity in women with chronic fatigue syndrome.
Authors	Kim BH, Namkoong K, Kim JJ, Lee S, Yoon KJ, Choi M, Jung YC.
Publication Details	Psychiatry Res. 2015 Dec 30;234(3):292-7. doi: 10.1016/j.pscychresns.2015.10.014. Epub 2015 Oct 23.
EntrezUID/PMID	26602611
Population; Task Domain	Adults; Resting state.
Behavioral Questionnaires	Chalder Fatigue Scale (Chalder et al., 1993), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and Psychological General Well-Being Index (PGWBI), to assess the subjective feelings and severity of chronic fatigue symptoms.
Tasks Used for fMRI	Resting task, not further described.
Results	It can be hypothesized that abnormal functional connectivity may result in deficits of cognition and emotion in CFS patients.
Task Summary	Behavioral measures: Chalder, BDI, BAI, PGWBI. Neuroimaging measure: resting task.

Title	Abnormal Resting-State Functional Connectivity in Patients with Chronic Fatigue Syndrome: Results of Seed and Data-Driven Analyses.
Authors	Gay CW, Robinson ME, Lai S, O'Shea A, Craggs JG, Price DD, Staud R.
Publication Details	Brain Connect. 2016 Feb;6(1):48-56. doi: 10.1089/brain.2015.0366. Epub 2015 Nov 10.
EntrezUID/PMID	26449441
Population; Task Domain	Adults; resting state.
Behavioral Questionnaires	The multidimensional fatigue inventory (MFI) is a self-reported instrument that contains 20 statements covering different aspects of fatigue (Smets et al., 1995).
Tasks Used for fMRI	Resting task, not further described.
Results	Results demonstrate that ME/CFS is associated with altered resting-state FC of several brain networks, and the degree of altered connectivity is significantly related to self-reported fatigue.
Task Summary	Behavioral measures: MFI 20 (measures presence? Of fatigue in several dimensions),

Title	Decreased basal ganglia activation in subjects with chronic fatigue syndrome: association with symptoms of fatigue.
Authors	Miller AH, Jones JF, Drake DF, Tian H, Unger ER, Pagnoni G.
Publication Details	PLoS One. 2014 May 23;9(5):e98156. doi: 10.1371/journal.pone.0098156. eCollection 2014.
EntrezUID/PMID	24858857
Population; Task Domain	Adults; Psychomotor Speed. Gambling task previously published.
Behavioral Questionnaires	Determination of reading level below grade 7 (as determined by the WRAT 3, to assure comprehension of written instructions during the gambling task). Zung Self Rating Depression Scale (Zung SDS) (indicating more than mild depressive symptoms) were also excluded [25]. Fatigue was assessed using the 20-item Multidimensional Fatigue Inventory (MFI) 20, Perceived health and function was measured by the Short Form (36) Health Survey (SF-36); Symptoms of CFS were assessed by the CFS Symptom Inventory.
Tasks Used for fMRI	A previously published gambling task, proven effective in eliciting specific activation of basal ganglia structures, was adapted for the study [19], [21]. In the task, participants had to guess which of two cards presented face-down on a screen was "red" (hearts or diamonds) by pressing one of two buttons on a MRI response box held in their right hand. Two seconds into the trial, the selected card was turned over, and, depending on its color, the participant either won (red card) or lost (black card) one dollar. Unbeknownst to the subject, the sequence of wins and losses was temporally arranged as a noisy sinusoid with a slow linear trend that favored wins over time. This procedure allowed for experimental control of the task while masking the deterministic nature of the game from the participant, thereby eliciting a realistic feeling of gambling while playing. At the beginning of the game, each participant started with a credit of $16 and ended with a total win sum of $23, which the volunteer believed was contingent on his/her specific gambling choice but was in fact fixed for all subjects.
Results	Data suggest that inflammatory stimuli including viruses, cytokines and cytokine inducers can cause fatigue through alterations in basal ganglia function. CFS subjects exhibited reduced neural activation to a reward task in caudate and globus pallidus, which in turn was correlated with symptoms of fatigue. These data suggest that basal ganglia circuits, especially those involving the globus pallidus, are associated with the expression of fatigue in CFS subjects.
Task Summary	Behavioral measures: WRAT 5, Zung, MFI 20, SF36, CFS Symptom Inventory. Neuroimaging tasks experimental condition: Capuron et al's gambling task--visual task.

Title	Exercise challenge in Gulf War Illness reveals two subgroups with altered brain structure and function.
Authors	Rayhan RU, Stevens BW, Raksit MP, Ripple JA, Timbol CR, Adewuyi O, VanMeter JW, Baraniuk JN.
Publication Details	PLoS One. 2013 Jun 14;8(6):e63903. doi: 10.1371/journal.pone.0063903. Print 2013.
EntrezUID/PMID	23798990
Population; Task Domain	GWI; Adults; Working memory.
Behavioral Questionnaires	The Chalder Fatigue Score was used to verify presence of fatigue [20]. Quality of life (disability) was assessed by the Medical Outcomes Survey Short Form 36 (MOS-SF-36).
Tasks Used for fMRI	Provocation fMRI: pain perception in response to exercise task. Neuroimaging task: The letter variant of the 2-back task was used to gauge verbal working memory.
Results	Exercise induced two clinical Gulf War Illness subgroups. One subgroup presented with orthostatic tachycardia (n = 10). This phenotype correlated with brainstem atrophy, baseline working memory compensation in the cerebellar vermis, and subsequent loss of compensation after exercise. The other subgroup developed exercise induced hyperalgesia (n = 18) that was associated with cortical atrophy and baseline working memory compensation in the basal ganglia. Alterations in cognition, brain structure, and symptoms were absent in controls.
Task Summary	Behavioral measures: Chalder, SF-36. Neuroimaging task: 2 back working memory task.

Title	Fatigue sensation induced by the sounds associated with mental fatigue and its related neural activities: revealed by magnetoencephalography.
Authors	Ishii A, Tanaka M, Iwamae M, Kim C, Yamano E, Watanabe Y.
Publication Details	Behav Brain Funct. 2013 Jun 13;9:24. doi: 10.1186/1744-9081-9-24.
EntrezUID/PMID	23764106
Population; Task Domain	Adults; Working memory, fatigue induction, MEG study overlaid with MRI
Behavioral Questionnaires	Rating of subjective fatigue on VAS from 0 to 100.
Tasks Used for fMRI	Used two-back task trials to induce the fatigue sensation and metronome sounds as the conditioned stimuli. During the two-back task trials, one of four letters was presented on a display of a personal computer every 3s and the participants had to judge whether the letter presented on the display at the moment was the same as the one that had appeared two presentations before. If it was, they were to press the right button with their right middle finger; if it was not, they were to press the left button with their right index finger. They were instructed to perform the task trials as quickly and as correctly as possible, and had to engage in two-back task trials for 60 min.
Results	Participants underwent MEG measurement while listening to the metronome sounds for 6 min. Thereafter, fatigue-inducing mental task trials (two-back task trials), which are demanding working-memory task trials, were performed for 60 min; metronome sounds were started 30 min after the start of the task trials (conditioning session). The next day, neural activities while listening to the metronome for 6 min were measured. Levels of fatigue sensation were also assessed using a visual analogue scale. Based on our previous findings that performing two-back task trials for 30 min induces mental fatigue and mental fatigue sensation [11, 12], the metronome sounds were started 30 min after the start of the conditioning session. The level of mental fatigue sensation was increased after the two-back task trials for 60 min.
Task Summary	Neuroimaging task: visual 2-back working memory task. Fatigue conditioning with metronome sounds.

Title	Prefrontal lactate predicts exercise-induced cognitive dysfunction in Gulf War Illness.
Authors	Rayhan RU, Raksit MP, Timbol CR, Adewuyi O, Vanmeter JW, Baraniuk JN.
Publication Details	Am J Transl Res. 2013;5(2):212-23. Epub 2013 Mar 28.
EntrezUID/PMID	23573365
Population; Task Domain	GWI; Adults; Working memory. Exercise provocation study.
Behavioral Questionnaires	SF-36, Chalder, McGill Pain Scale.
Tasks Used for fMRI	We used the working memory N-back paradigm during both fMRI scans. Prior to both fMRI scans, subjects completed N-back practice sessions on a computer. Blocks of 9 randomized letters (A, B, C, D) were presented. Subjects were given instructions to respond by pressing a button for the same letter (“0-Back”) or the one seen 2 letters previously (“2-Back”). Blocks for 0-back then 2-back tasks were presented for 5 cycles. A total score of 35 letters correct were possible during the 2-back working memory cognitive paradigm.
Results	The primary observation of this study was that baseline prefrontal lactate levels predicted future exercise - induced cognitive responses in CMI subjects.
Task Summary	Behavioral: SF-36, Chalder Fatigue Scale, McGill Pain Scale. Neuroimaging -- visual letter version of 2-back.

Title	Medial orbitofrontal cortex is associated with fatigue sensation.
Authors	Tajima S, Yamamoto S, Tanaka M, Kataoka Y, Iwase M, Yoshikawa E, Okada H, Onoe H, Tsukada H, Kuratsune H, Ouchi Y, Watanabe Y.
Publication Details	Neurol Res Int. 2010;2010:671421. doi: 10.1155/2010/671421. Epub 2010 Jun 10.
EntrezUID/PMID	21188225
Population; Task Domain	Adults, fatigue induction paradigm.
Behavioral questionnaires	Handedness was assessed according to the Edinburgh handedness inventory. Rating of subjective fatigue sensation on a visual analogue scale (VAS) from 0 (no fatigue) to 100 (total exhaustion).
Tasks Used for fMRI	Subjects performed 2 types of mental tasks, which were advanced trail-making tests (ATMTs). In the ATMT, circles numbered from 11 to 35 were first randomly located on the display of a touch-panel screen. The subjects were required to touch these circles in sequence, starting with circle number 11. When they touched the first target circle, it disappeared and circle number 36 appeared in a different position on the screen. In Task 1 of ATMT, the positions of the other circles remained the same; in contrast, in Task 2, the positions of all the circles were changed. During the first session, subjects performed Task 1 of ATMT, while during the second session they performed Task 2. When they touched the circle numbered 99, the test was ended and then started again without any time intervening. They were instructed to perform these tasks as quickly and correctly as possible. The mean reaction time to touch the ATMT circles during the fatigue-inducing task trials was recorded in order to assess the task performance. Each session included 10-min fixation and 35-min fatigue-inducing task trails. The session, which included 1 fixation scan and 4 task scans, was performed with 10-min interval. During the fixation time, circles numbered from 1 to 25 were randomly located on the screen, and subjects were asked to fix their eyes on the circle number 1 placed at the center of the screen.
Results	Subjects exhibited a significant increase in subjective score of fatigue sensation, suggesting that they in fact experienced increased sensation of fatigue during the mental tasks and that the tasks used in the PET experiment were fatigue-inducing.
Task Summary	Behavioral: Edinburgh Handedness Inventory, VAS rating of subjective fatigue. Neuroimaging--visual Advanced trail making test (ATMT).

Title	Neural correlates of "analytical-specific visual perception" and degree of task difficulty as investigated by the Mangina-Test: a functional magnetic resonance imaging (fMRI) study in young healthy adults.
Authors	Mangina CA, Beuzeron-Mangina H, Ricciardi E, Pietrini P, Chiarenza GA, Casarotto S.
Publication Details	Int J Psychophysiol. 2009 Aug;73(2):150-6. doi: 10.1016/j.ijpsycho.2009.04.009. Epub 2009 May 3.
EntrezUID/PMID	19414052
Population; Task Domain	Adults; The Mangina test to measure varying degrees of analytical-specific perceptual learning abilities and disabilities.
Behavioral Questionnaires	None
Tasks Used for fMRI	The experimental design faithfully reproduced the original psychophysical paper-and-pencil version of the Mangina-Test (Mangina, 1981; Mangina, 1994a; Mangina, 1994b; Mangina, 1994c ; Mangina, 1998). This test is composed of 44 simple and 44 complex original geometrical visual stimuli, presented with an increasing degree of difficulty (Fig. 1a). One simple and one complex stimulus are presented simultaneously. The task consists of exactly identifying and tracing completely with a fine marker the simple stimulus which is masked within a complex configuration of stimuli varying in direction, spatial orientation, size, dimension, and shape in a limited span of time. A computer-adapted version was specifically developed for the purpose of applying it during fMRI and was controlled by using Presentation® (Version 9.80, http://www.neurobs.com).
Results	A widely distributed bilateral network of brain regions, including the ventral and dorsal occipital cortex, parietal lobule, frontal and supplementary eye field, dorsolateral prefrontal cortex, and supplementary motor area, was significantly activated during test performance. In addition, increasing difficulty was associated with longer response time and significantly enhanced the neural response of ventral and dorsal occipital regions, frontal eye field, and superior parietal lobule bilaterally, and right dorsolateral prefrontal cortex. Conversely, neural activity in the left temporo-parietal junction, inferior frontal gyrus, and bilateral middle-superior temporal cortex was inversely correlated with task difficulty.
Task Summary	Neuroimaging visual task: the Mangina task

Title	The neural correlates of fatigue: an exploratory imaginal fatigue provocation study in chronic fatigue syndrome.
Authors	Caseras X, Mataix-Cols D, Rimes KA, Giampietro V, Brammer M, Zelaya F, Chalder T, Godfrey E.
Publication Details	Psychol Med. 2008 Jul;38(7):941-51. doi: 10.1017/S0033291708003450. Epub 2008 Apr 30.
EntrezUID/PMID	18447963
Population; Task Domain	Adults; fatigue induction paradigm
Behavioral Questionnaires	Chalder Fatigue Scale, SF-36, HADS, Work and social adjustment scale (WSAS). After each video, the participants were requested to produce two separate subjective ratings of fatigue (on a visual analogue scale of 0–10, where 0=no fatigue and 10=extreme fatigue) and anxiety (on a visual analogue scale of 0–10, where 0=no anxiety and 10=extreme anxiety) after imagining themselves in each situation.
Tasks Used for fMRI	Subjects were requested to imagine themselves in different situations while viewing video-clips previously selected to induce fatigue, anxiety or relaxation. To enhance the participants' experience, the video-clips were filmed from a first person's point of view and were back-projected onto a screen that could be seen through a mirror mounted on the head-coil. Before each video-clip, participants heard a pre-recorded voice file through high-fidelity pneumatic headphones telling them which situation they were required to imagine. For example, the instruction 'imagine yourself doing your shopping at the supermarket and then carrying home heavy bags' preceded a video-clip showing a person carrying heavy shopping bags. Similarly, for the anxiety-provoking videos, the instruction 'imagine yourself standing on the edge of a high cliff and looking over the edge' was followed by a video-clip showing the feet of a person on the edge of a cliff. Finally, for the relaxation videos (the control condition), the instruction 'imagine yourself sitting in a comfy armchair drinking a nice cup of tea' was followed by a clip of somebody holding a cup of tea with her feet up.
Results	The results seem to suggest that the provocation of fatigue in patients with CFS is associated with activation in brain regions implicated in emotion processing and the retrieval of emotional memories. This is consistent with the cognitive-behavioural model of CSF, which proposes that fear and avoidance are key maintaining factors for the disorder (Chalder et al. 2000). It could be argued that patients remember feeling severely fatigued in the past and that they are anxious about feeling so fatigued again. It is the fear of feeling fatigue that can lead them to avoid activity.
Task Summary	Behavioral: Chalder, SF-36, HADS, WSAS, VAS subjective fatigue. Neuroimaging: auditory fatigue and anxiety provocation task

Title	Functional neuroimaging correlates of mental fatigue induced by cognition among chronic fatigue syndrome patients and controls.
Authors	Cook DB, O'Connor PJ, Lange G, Steffener J.
Publication Details	Neuroimage. 2007 May 15;36(1):108-22. Epub 2007 Mar 3.
EntrezUID/PMID	17408973
Population; Task Domain	Adults; Perception of mental fatigue, working memory
Behavioral Questionnaires	STAI, BDI, Visual analogue scales (VAS) were used to document current ("right now, at that moment") perceived intensity of feelings of mental and physical energy and fatigue. Responses to three VAS items (same adjectives as in trait scales) were summed to provide the criterion measures for each of these mood states. The intensity of current energy and fatigue moods was scaled from 0 to 100, with zero indicating the feeling being absent and 100 indicating the strongest feeling ever experienced.
Tasks Used for fMRI	Finger tapping task: Participants were instructed to focus on a crosshair (i.e., 3″ × 3″ white + on a black background) at the center of the screen and to open and close their right hand, bringing their four fingers in contact with their thumb, at the same rate as the crosshair once it began to flash (120 min− 1). Participants were instructed not to make a fist, but instead to repeatedly bring the tips of their four fingers in contact with the tip of their thumb. Movement stopped when the crosshair stopped flashing. The task consisted of four 30-second on-periods preceded and followed by 30-second off-periods for a total of 4 min and 30 s. A second finger tapping task, identical to the first, was presented as the last task at the end of the functional imaging scanning session to determine the influence of accumulated mental fatigue on motor responses. Simple auditory monitoring task: Participants were instructed to listen to a series of numbers ranging from one to ten and to press the left mouse button when they heard the number seven. Each number was presented for 1500 ms and separated by 500 ms. The task consisted of four 30-second on-periods that were preceded and followed by 30-second off-periods for a total of 4 min and 30 s. Twenty events were presented during each 30-second on-period. Of these, seven events (35%) were correct targets (i.e., the number 7). Task performance was quantified as the percentage of correct responses and the reaction time of the correct responses. Difficult task involving attention, working memory and executive function processes: A modified version of the PASAT was used to induce feelings of mental fatigue during fMRI scanning. The PASAT requires participants to attend to and encode auditory information and retrieve it from the working memory system (Tombaugh, 2006). For the primary task, participants listened to a series of numbers ranging from one to nine. They were instructed to continually and silently add the first number to the second, the second number to the third and so on and to press the button whenever two consecutive numbers summed to the number ten. Each number was

	presented for 1500 ms and was separated by 500 ms. The task consisted of three 3-minute on-periods and four 30 s off-periods for a total of 11 min. One hundred and twenty events were presented during each three-minute on-period. Of these, forty-two (35%) were correct targets (i.e., two numbers summing ‘10’). As a secondary task, participants were instructed that, in addition to listening to the numbers presented as part of the PASAT, they were to visually focus on a set of three boxes that contained rapidly (every 500 ms) and randomly changing numbers. The rate at which the visual numbers were presented was intentionally made too rapid for any arithmetic and was purely intended to distract and interfere with the primary auditory task, thereby increasing the complexity and attentional demands of the task and inducing greater mental fatigue. Participants were instructed that no action was required on their part for the distracting numbers. Thus, the participants were instructed to listen to the numbers presented through the headphones and perform the serial addition task on these auditory numbers, while simultaneously focusing on the numbers scrolling on the screen. In order to ensure participant compliance to the task, we reiterated the task instructions prior to each 3-minute on-period and stressed the importance of keeping their eyes open. Furthermore, we instructed them that we would be able to view their performance through the projection mirror and that we would remind them to open their eyes should they accidentally close them. Ratings of mental fatigue were obtained immediately prior to and immediately following each 3-minute block of the task. Task performance was defined as the percentage of correct responses and the reaction time to the correct responses.
Results	The present investigation extends prior research by more directly examining neural systems known to be involved in cognitive operations. Brain regions that were significantly related to mental fatigue included the parietal, cingulate, inferior frontal and superior temporal cortices, cerebellum and cerebellar vermis; regions that have been demonstrated as important for several aspects of cognitive function, including those that involve the working memory network
Task Summary	Behavioral: STAI, BDI, VAS perception of intensity of feelings of mental and physical energy and fatigue. Neuroimaging: experimental tasks: auditory monitoring, mPASAT. Control task: finger tapping.

Title	Effects of elevated plasma tryptophan on brain activation associated with the Stroop task.
Authors	Morgan RM, Parry AM, Arida RM, Matthews PM, Davies B, Castell LM.
Publication Details	Psychopharmacology (Berl). 2007 Feb;190(3):383-9. Epub 2006 Dec 19.
EntrezUID/PMID	17180619
Population; Task Domain	Adults; measurement of reaction time to reflect central fatigue
Behavioral Questionnaires	None
Tasks Used for fMRI	Modified version of the counting Stroop (CS) test (Bush et al. 1998; Parry et al. 2003). A 9-min block-design with eight alternating blocks of neutral (N; 30 s) and interference (I) stimuli (30 s) was used. The paradigm started and ended with a 30-s rest period. The N stimuli consisted of animal words (e.g., cat, dog, mouse, bird), whereas the I stimuli consisted of number words (e.g., one, two, three, four). Stimuli were presented at 1.5-s intervals. Subjects were instructed to press the button corresponding to the number of words seen on the screen, to answer as quickly as possible, but not to forsake accuracy for speed.
Results	Increasing plasma Trp and consequently p[FT] and brain Trp to a concentration that should substantially increase brain 5-HT is associated with activation changes in a region of the medial parietal cortex, the activity of which is associated with arousal state and awareness. An increase was also observed in specific task-associated regions including the primary somatosensory cortex.
Task Summary	Behavioral: none. Neuroimaging--visual modified Stroop task

Title	Probing the working memory system in chronic fatigue syndrome: a functional magnetic resonance imaging study using the n-back task.
Authors	Caseras X, Mataix-Cols D, Giampietro V, Rimes KA, Brammer M, Zelaya F, Chalder T, Godfrey EL.
Publication Details	Psychosom Med. 2006 Nov-Dec;68(6):947-55. Epub 2006 Nov 1.
EntrezUID/PMID	17079703
Population; Task Domain	Adults; working memory
Behavioral Questionnaires	Physical Functioning Scale from the SF-36 (16), the Chalder Fatigue scale (17), the Work and Social Adjustment Scale (18,19), and the Hospital Anxiety and Depression Scale (20)
Tasks Used for fMRI	A verbal version of the n-back originally described by Braver et al. (13) was used. In a block design, three levels of difficulty (1-back, 2-back, and 3-back) and one control condition (0-back) were included. Participants were presented with a series of capital letters on a projection screen (which they saw through a mirror above their head) and were required to press a button whenever the letter presented was the same as that presented n trials previously (1-, 2-, or 3-back). During the control condition, participants were required to press the button whenever they saw the letter “X.” All blocks consisted of a pseudorandom sequence of 21 letters presented for 1 second each and separated by an interstimulus interval of 1 second. Three blocks of each condition were presented, totaling 12 blocks in the following order: 1-back/2-back/0-back/3-back/2-back/0-back/1-back/3-back/2-back/3-back/0-back/1-back. The task had a total duration of 9 minutes. A computer automatically recorded the participants' performance (accuracy and reaction time to target) during the task. All participants received a training session before scanning to ensure that they understood the task.
Results	This is the first fMRI study of WM in CFS using a parametric verbal WM task, which allowed us to examine the effects of load on performance and brain activation. During the low load (1-back) condition, patients with CFS showed greater activation than control subjects in medial prefrontal regions, including the anterior cingulate gyrus. However, on the high load conditions (2-back and 3-back), patients with CFS demonstrated reduced activation in working memory-related brain regions (dorsolateral prefrontal and parietal cortices) compared with healthy control subjects. Furthermore, on the 2-back and 3-back conditions, patients but not control subjects significantly activated a large cluster in the right inferior/medial temporal cortex. Finally, trend analyses of task load demonstrated statistically significant differences in brain activation between the two groups as the difficulty of the task increased. These results were uncorrelated with any demographic or clinical variables.
Task Summary	Behavioral: SF-36, Chalder Fatigue Scale, Hads, WSAS. Neuroimaging--visual parametric n-back task.

Title	Reduced responsiveness is an essential feature of chronic fatigue syndrome: a fMRI study.
Authors	Tanaka M, Sadato N, Okada T, Mizuno K, Sasabe T, Tanabe HC, Saito DN, Onoe H, Kuratsune H, Watanabe Y.
Publication Details	BMC Neurol. 2006 Feb 22;6:9.
EntrezUID/PMID	16504053
Population; Task Domain	Adults; visual fatiguing task.
Behavioral Questionnaires	Immediately before and after the MRI experiments, subjects were asked to rate their subjective sensation of fatigue on the visual analogue scale (VAS) from 0 (no fatigue) to 10 (total exhaustion)
Tasks Used for fMRI	Subjects performed "present", "absent", or "null" trials (Figure 1), and the experiments consisted of 3 sessions: pre-fatigue, fatigue, and post-fatigue sessions (Figure 2). Each session included 2 or 3 experimental conditions: "present" and "absent" trials or "present", "absent", and "null" trials. For present and absent trials, a randomly selected digit from 20 to 99 was presented on the centre of the viewing screen for 500 ms, followed by a test sequence of digits (targets) presented for 3,500 ms. In a given trial, subjects judged whether the digit first presented was among the targets. If they thought the presented target digit matched the first digit, subjects should press the left button (present trial); if not, they should press the right button (absent trial). There was no time interval between trials. For the null trial, the word "NULL" was presented on the centre of the viewing screen for 500 ms, followed by a test sequence presented for 3,500 ms. Subjects judged whether there was a black circle among the white circles. When a black circle was presented among the white ones, subjects should press the left button; and when all of the circles were white, they should press the right button. Subjects performed pre-fatigue, fatigue, and post-fatigue sessions lying on the MRI scanner table with both ears plugged. The time interval between 2 successive sessions was approximately 1 min. We determined session time of fatigue-inducing period from the preliminary studies. For the fatigue session (fatigue-inducing period), normal subjects performed visual search trials (present or absent trials) for 1 hour. After considering the physical and mental condition of the CFS patients, we determined that 30 min was a suitable period for these patients to perform the trials. During the fatigue-inducing period, present or absent trials were given randomly and the occurrence of each trial was equal. Also during this period, only continual visual search trials were performed; null trials were not included as they might have enabled subjects to recover from fatigue to some extent. During the pre- and post-fatigue sessions, present, absent, and null trials were presented randomly, and the occurrence of each trial was equal. In the pre- or post-fatigue sessions, subjects performed trials for 6 min. During scanning, stimuli were generated by a personal computer and projected onto a semitransparent screen from a liquid crystal display projector (DLA-M200L, Victor, Yokohama, Japan). The subjects saw the stimuli through a tilted mirror attached to the

	head coil of the scanner. The visual angle of each target used as a stimulus was approximately 1°.
Results	We demonstrated that the responsiveness in the task-dependent brain regions was decreased after the fatigue-inducing continual visual search task in the normal and CFS patient groups and that the decrement of the responsiveness in those brain regions was equivalent between the 2 groups. In addition, we found that, during the fatigue-inducing period, although responsiveness in the task-independent brain regions remained constant in the normal subjects, it was attenuated in the CFS patients. Moreover, rate of attenuation in the task-independent brain regions was positively correlated with the pre-experiment subjective sensation of fatigue as measured using a fatigue VAS.
Task Summary	Behavioral: VAS subjective sensation of fatigue. Neuroimaging--visual search task.

Title	Objective evidence of cognitive complaints in Chronic Fatigue Syndrome: a BOLD fMRI study of verbal working memory.
Authors	Lange G, Steffener J, Cook DB, Bly BM, Christodoulou C, Liu WC, Deluca J, Natelson BH.
Publication Details	Neuroimage. 2005 Jun;26(2):513-24. Epub 2005 Apr 7.
EntrezUID/PMID	15907308
Population; Task Domain	Adults; information processing, working memory
Behavioral Questionnaires	WAIS III Vocabulary subtest; BDI; STAI, MFI-20.
Tasks Used for fMRI	The fMRI paradigm consisted of a set of two auditory information processing tasks. Task 1 was an auditory monitoring test measuring simple attention. Task 2 was the mPASAT, a challenging auditory verbal WM test. Both tasks were administered as two separate time-series in a fixed sequence with Task 1 always preceding Task 2. As shown in Fig. 1, each task was presented within a blocked design consisting of five blocks: a baseline period and two “ON-periods” alternating with two “OFF-periods”. The two experimental tasks were presented during “ON-periods”. In each of the tasks, numbers were presented once every 2 s for 500 ms. No task was presented during “OFF-periods” in any of the time-series and the participants were instructed to rest quietly. Task 1—auditory monitoring: a simple attention task requiring monitoring of the aurally presented numeric information. During the auditory monitoring task, study participants heard a sequence of numbers ranging from 1 to 9 presented at a rate of one number every 2 s. Whenever the number “7” was presented, participants were required to use the thumb of their right hand to press a button on a box placed at their right thigh. The response was transmitted to and recorded on a laptop computer outside the scanning chamber. Task 2—mPASAT: a modified version of the PASAT that has been used in previous studies (Christodoulou et al., 2001 ; Lange et al., 1998). This task requires encoding, maintenance, and manipulation of verbal information. During the mPASAT, study participants heard a sequence of numbers, ranging from 1 to 9 presented at the same rate as in Task 1. Study participants were instructed to add the 1st number they heard to the 2nd, the 2nd to the 3rd, and so on. Instead of answering aloud as in the standard PASAT procedure, participants were told to silently add the number dyads and to press a button with the thumb of their right hand whenever the dyad's sum equaled 10. This modification was designed to limit head movement artifacts during image acquisition. Both tasks presented to study participants were temporally and spatially balanced and differed from each other in only one dimension — task difficulty. Participants received task instructions and engaged in brief task practice

	before entering the magnet to ensure familiarity with the task protocol. The purpose of this study was to document brain activity during auditory information processing and not to image a learning effect. The audibility of both tasks (80 db) was well within the range of normal human auditory perception. It has been shown that the ambient noise level in the MR scanner does not impact on the hearing threshold of subjects. That is, subjects consistently obtained thresholds for pure tones and speech that ranged from 20 db to 30 db (Millen et al., 1995). The pitch of the auditory stimuli was randomly varied from 200 Hz to 1200 Hz to avoid adaptation. All stimuli were delivered simultaneously to both ears.
Results	The results of the present study are further evidence that symptomatology associated with a severe fatiguing illness may have an effect on brain function. Our studies do not support the notion that difficulties in cognitive function in individuals with CFS are related to poor motivation, but instead provide evidence of increased neural resource allocation when processing more complex auditory information, a task often encountered in everyday life.
Task Summary	Behavioral: wais III, Vocabulary subtest, BDI, STAI, MFI-20; Neuroimaging--auditory task: mPasat (Lange et al., 1998)

Title	Neural correlates of the chronic fatigue syndrome--an fMRI study.
Authors	de Lange FP, Kalkman JS, Bleijenberg G, Hagoort P, van der Werf SP, van der Meer JW, Toni I.
Publication Details	Brain. 2004 Sep;127(Pt 9):1948-57. Epub 2004 Jul 7.
EntrezUID/PMID	15240435
Population; Task Domain	Adults; movement planning -- outcome measure reaction time, information processing.
Behavioral Questionnaires	CIS-R, SIP-8, SCL-90, BDI, mean actometer score
Tasks Used for fMRI	Motor imagery task and a control visual imagery task
Results	The subjects participated in alternating blocks of visual imagery (VI) and motor imagery (MI), each block consisting of eight stimuli. During VI, subjects were shown typographical characters (F, G, J and R) and their mirror images. Each stimulus could be rotated from its upright position (0°) in 30° steps until 180°, generating a set of 56 stimuli. These stimuli were serially presented to the subjects in a random order. The subjects had to report whether the displayed typographical character was a canonical letter or its mirror image, regardless of its rotation (Fig. 1, lower row). During MI, subjects were shown four different line drawings of hands (left or right hand, viewed either from the back or from the palm) or their mirror images. The same rotations and display procedures described for VI were used for MI. The subjects had to report whether the displayed hand drawing was a left or a right hand, regardless of its rotation (Fig. 1, upper row). After practising the tasks both outside and inside the scanner, subjects were scanned during task performance for ∼40 min. During scanning, subjects responded by pressing one of two buttons on a MR-compatible button box, which was positioned in their right hand. Responses were measured in the scanner for subsequent behavioural analysis. Each trial started with the presentation of a fixation cross (baseline) for a variable interval (0.75–1.25 s), followed by a visual stimulus (a typographical character or a drawing of a hand). When a response was provided, the visual stimulus was replaced by the baseline fixation cross until the presentation of the next visual stimulus. The intertrial interval (ITI) was adjusted to task performance in order to balance the time spent off-task across experimental conditions (off-task time designates the temporal intervals interposed between a behavioural response and the next stimulus presentation). We adjusted the ITI according to the formula: ITI = C + R ITI = C + R where: C = 2.0 s (VI) or 2.5 s (MI); and R is dependent on the angle of the stimulus (R = α/180 s where α is the stimulus rotation in degrees).

Task Summary	Behavioral: CIS-R, SIP-8, SCL-90, BDI, mean actometer score, Neuroimaging--motor imagery task and control visual imagery task.

Title	[Relationship between chronic fatigue and subjective symptoms of fatigue with performance status (P.S.) and subjective fatigue scale for young adults (SFS-Y)].
Authors	Kobayashi H, Demura S.
Publication Details	Nihon Koshu Eisei Zasshi. 2002 Oct;49(10):1062-9. Japanese.
EntrezUID/PMID	12462040
Population; Task Domain	Article not available in English
Behavioral Questionnaires	
Tasks Used for fMRI	
Results	
Task Summary	

Eyes closed data without an active task.

The resting-state is currently the predominant method used in neuroscience for a variety of reasons. The resting-state is an energetically costly condition and a major factor comprising ~80% of the brain's total energy budget involves spontaneous neuronal signaling processes. By contrast, the difference in signals induced by momentary environmental demands is relatively small in comparison to baseline resting activity, usually less than 5% (Raichle, 2011; Shulman, Rothman, Behar, & Hyder, 2004; Zhang & Raichle, 2010). In terms of the EEG, the electrical demands of neurons are more costly than blood oxygen and glucose, and cortical excitability is modulated by fluctuations in the delivery of glucose and adenosine triphosphate (ATP) energy to neurons (Raichle, 2011). The oscillatory processes of resting-state are indicative of the stable characteristics of intrinsic brain organization, defined as spontaneous interactions between network elements in the absence of a specific task state (Raichle, 2010). Ultimately, the resting-state represents the dynamic substrate of intrinsic oscillatory processes that are fundamental to information processing, even transcending levels of consciousness (Greicius et al., 2008). Given that intrinsic resting-state dynamics are sufficiently robust and correlate separately with task performance, it provides a highly flexible means to associate brain connectivity with scores on clinical behavioral measures or neuropsychological tests (Braun et al., 2012). When conducting a study, one measures tasks independently of the neuroimaging.

Title	Intrinsic Functional Hypoconnectivity in Core Neurocognitive Networks Suggests Central Nervous System Pathology in Patients with Myalgic Encephalomyelitis: A Pilot Study
Authors	Zinn ML, Zinn MA, Jason LA.
Publication Details	Appl Psychophysiol Biofeedback (2016) 41:283–300; DOI 10.1007/s10484-016-9331-3
EntrezUID/PMID	
Population; Task Domain	9 patients, 9 controls
Behavioral Questionnaires	None
Tasks Used	None
Results	Found widespread neural dysregulation in the DMN, the CEN and the Salience Network.
Task Summary	

Title	qEEG / LORETA in Assessment of Neurocognitive Impairment in a Patient with Chronic Fatigue Syndrome: A Case Report
Authors	Zinn ML, Zinn MA, Jason LA.
Publication Details	Zinn ML, Zinn MA, Jason LA (2016) qEEG / LORETA in Assessment of Neurocognitive Impairment in a Patient with Chronic Fatigue Syndrome: A Case Report. Clin Res 2(1): doi http://dx.doi.org/10.16966/2469-6714.110
EntrezUID/PMID	
Population; Task Domain	Single case study
Behavioral Questionnaires	
Tasks Used	
Results	
Task Summary	This case report increased our understanding of CFS from the perspective of brain functional networks by offering some possible explanations for cognitive deficits in patients with CFS. There are only a few reports of using source density analysis or qEEG connectivity analysis for cognitive deficits in CFS. While no absolute threshold exists to advise the physician as to when to conduct such analyses, the basis of his or her decision whether or not to use these tools should be a function of clinical judgment and experience. These analyses may potentially aid in clinical diagnosis, symptom management, treatment response and can alert the physician as to when intervention may be warranted.