transporters, previously obtained in HC. Changes in modified fatigue impact scale (MFIS) score and monoaminergic-dependent RS FC were assessed.
Results: S patients showed baseline abnormalities*vs* HC in all three networks, with decreased monoamine-related RS FC in temporal, occipital, insular and cerebellar regions, and increased RS FC in frontal, parietal and subcortical areas. At W4, MFIS scores decreased in all patients' groups, with no time-by-treatment interaction. At W4, fampridine and amantadine patients showed increased dopamine- and noradrenaline-dependent RS FC in the insular cortex, as well as increased serotonin-dependent RS FC in the precuneus/posterior cingulate cortex. Amantadine patients also showed increased dopamine- and noradrenaline-dependent RS FC in the anterior cingulate cortex (ACC). Conversely, placebo patients mostly showed increased noradrenaline-dependent RS FC in the precuneus and middle cingulate cortex. In fampridine and placebo groups, there were trends towards significant correlations between RS FC modifications and MFIS improvements (r=-0.49:-0.52, p=0.07-0.08).
Conclusions: Fatigue improved in all MS groups. Concomitant monoaminergic-dependent RS FC modifications were found in insular, ACC and parietal regions for fampridine and amantadine MS patients, and in medial parietal regions for placebo patients.

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Cognitive improvements in ocrelizumab-treated patients with relapsing-remitting multiple sclerosis: 96-week CASTING study data

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Background: Cognitive impairment is highly prevalent in people with multiple sclerosis (PwMS) and is associated with reduced quality of life. The Symbol Digit Modalities Test (SDMT) measures cognitive processing speed and can be used as a screening test for cognitive impairment in PwMS.
Aims: To report changes in SDMT scores over 96 weeks in ocrelizumab (OCR)-treated patients with relapsing-remitting MS (RRMS) in the Phase IIIb CASTING trial (NCT02861014).
Methods: Patients (Expanded Disability Status Scale score ⩽4.0) with a suboptimal response to one or two prior disease-modifying therapies received intravenous OCR 600 mg every 24 weeks for 96 weeks. SDMT was measured at baseline, Week 48 and Week 96. Scores were translated to z-scores with a cut-off of −1 to define cognitive impairment; baseline z-score ⩽−1 defined the cognitively impaired subgroup and baseline z-score >−1 the minimally impaired subgroup. In both subgroups an increase of ⩾4 SDMT points was considered a clinically relevant improvement, and a decrease of ⩾4 SDMT points was considered clinically relevant worsening.
Results: Overall baseline mean z-score was −1.36. From baseline to Week 96, mean SDMT score changed from 53.8 to 55.2 (p=0.0047) in the overall population (N=680), and from 46.5 to 49.5 (p<0.001), and 65.6 to 64.1 (p=0.0073) in the impaired (N=392) and minimally impaired (N=245) subgroups, respectively. From baseline to Week 96 in the overall population, 29.0% (n/N=197/680) of patients had an improvement of ⩾4 points, 22.6% (n/N=154/680) had worsening of ⩾4 points and 32.8% (n/N=223/680) remained stable. In the impaired subgroup, 38.3% (n/N=150/392) of patients had an improvement of ⩾4 points, 18.6% (n/N=73/392) had worsening of ⩾4 points and 33.4% (n/N=131/392) remained stable. In the minimally impaired subgroup, 19.2% (n/N=47/245) of patients had an improvement of ⩾4 points, 33.1% (n/N=81/245) had worsening of ⩾4 points and 37.6% (n/N=92/245) remained stable.
Conclusions: There was a significant improvement in SDMT score over 96 weeks in patients with RRMS treated with ocrelizumab, mainly observed in the cognitively impaired subgroup. An increased proportion of patients in the cognitively impaired subgroup experienced clinically relevant improvements in SDMT score over 96 weeks, compared with the less impaired subgroup.

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A randomized, controlled trial of low-fat diet for fatigue in multiple sclerosis

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Introduction: Fatigue is a common and disabling symptom of multiple sclerosis (MS). A dietary intervention to improve fatigue is desirable given the minimal risk of adverse events.
Objectives and aims: To determine if a low-fat diet was effective at ameliorating fatigue in people with MS (PwMS), as measured by Modified Fatigue Impact Scale (MFIS) through a randomized controlled trial (RCT). Primary outcome was reduction in fatigue assessed via MFIS at 14 weeks. Secondary outcomes included evaluation of blood markers of inflammation, lipid metabolism, and clinical outcomes including cognitive function, mobility, and body composition. Additional outcomes included changes on actigraphy, gut microbiome and blood metabolomics.
Methods: This was a two-arm open-label, RCT where PwMS were assigned to a low-fat diet or wait-list control group. The diet group received 1-2 weeks of nutrition counseling followed by strict adherence to the diet for 12 weeks. The control group was offered the same nutrition counseling after 14 weeks. We measured diet adherence using monthly Food Frequency Questionnaire and 24-hr food recall. The principal statistical analysis used linear mixed models, with a random effect for subject to account for the within-subject correlation, in an intent-to-treat (ITT) framework to determine the effect of diet on the outcomes of MFIS and Fatigue Severity Scale (FSS). Sensitivity analysis was conducted by excluding potential outliers in both groups.
Results: A total of 39 participants were recruited with 20 in the diet group and 19 in the wait-list group. At baseline participants mean age was 50 years ($\pm$12 years), mean BMI was 31 kg/m^2($\pm$7 kg/m^2), and mean EDSS score was 3.8 ($\pm$1.4). Mean MFIS decreased by -4.00 (95% CI: -12.04, 4.04) and mean FSS decreased by -0.41 (95% CI: -1.18, 0.36) from baseline to the end of the RCT in diet group compared to wait-list. Sensitivity analysis strengthened the magnitude of association with a mean MFIS decrease of -13.93 (95% CI: -20.65, -7.20) and mean FSS decrease of -1.22 (95% CI: -1.94, -0.50) in diet group compared to wait-list. Percent calories from fat, assessed by 24-hr food recall, decreased by 10.56% (95% CI: -18.50%, -2.97%) in diet group compared to wait-list. Additional data analysis is under process.
Conclusions: This 12-week long low-fat dietary intervention reduced the fatigue score significantly in the PwMS compared to controls. Studies with a larger sample size and longer follow-up are needed.

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