## GULF WAR ILLNESS

### The Gut-Microbiome in Gulf War Veterans: A Preliminary Report.

Janulewicz PA[1], Seth RK[2], Carlson JM[3], Ajama J[3], Quinn E[4], Heeren T[5], Klimas N[6], Lasley SM[7], Horner RD[8], Sullivan K[3], Chatterjee S[2].

Int J Environ Res Public Health. **2019 Oct 4**;16(19). pii: E3751. doi: 10.3390/ijerph16193751. PMID: 31590322.

Gulf War Illness (GWI) is a chronic multi-symptom disorder affecting the central nervous system (CNS), immune and gastrointestinal (GI) systems of Gulf War veterans (GWV). We assessed the relationships between GWI, GI symptoms, gut microbiome and inflammatory markers in GWV from the Boston Gulf War Illness Consortium (GWIC). Three groups of GWIC veterans were recruited in this pilot study; GWV without GWI and no gastrointestinal symptoms (controls), GWV with GWI and no gastrointestinal symptoms (GWI-GI), GWV with GWI who reported gastrointestinal symptoms (GW+GI). Here we report on a subset of the first thirteen stool samples analyzed. Results showed significantly different gut microbiome patterns among the three groups and within the GWI +/-GI groups. Specifically, GW controls had a greater abundance of firmicutes and the GWI+GI group had a greater abundance of the phyla bacteroidetes, actinobacteria, euryarchaeota, and proteobacteria as well as higher abundances of the families Bacteroidaceae, Erysipelotrichaceae, and Bifidobacteriaceae. The GWI+GI group also showed greater plasma levels of the inflammatory cytokine TNF-RI and they endorsed significantly more chemical weapons exposure during the war and reported significantly greater chronic pain, fatigue and sleep difficulties than the other groups. Studies with larger samples sizes are needed to confirm these initial findings.

## CHRONIC FATIGUE SYNDROME

### Service based comparison of group cognitive behavior therapy to waiting list control for chronic fatigue syndrome with regard to symptom reduction and positive psychological dimensions.

Heald A[1], Barber L[2], Jones HL[2], Farman S[3], Walther A[4].

Medicine (Baltimore). **2019 Sep**;98(39):e16720. doi: 10.1097/MD.0000000000016720. PMID: 31574792.

BACKGROUND: Although chronic fatigue syndrome (CFS) sometimes referred to as myalgic encephalomyelitis (ME) is a very challenging condition to treat, there is evidence that individual cognitive behavioral therapy (ICBT) can be effective for treatment and management of its symptoms. Furthermore, group cognitive behavioral therapy (GCBT) is emerging as promising treatment for the condition. The aim of the present study was to explore further the effectiveness of GCBT in a routine clinical setting and to investigate associated positive psychological effects related to GCBT.

METHODS: In this pragmatic, non-randomized, controlled trial, 28 people acted as their own waiting list control by completing a range of measures 8 weeks prior to taking part in the GCBT. The intervention consisted of 8 consecutive weeks of 2.5-hour sessions.

RESULTS: Repeated measures analysis of covariance revealed significant improvements in physical fatigue ($F=28.31$, $P<.01$, effect size $d=0.52$), mental fatigue ($F=7.72$, $P<.01$, effect size $d=0.22$), and depressive symptoms (Beck depression inventory-fast screen for medical individuals [BDI-FS]: $F=11.43$, $P<.01$, effect size $d=0.30$; hospital anxiety and depression scale [HADS-D]: $F=16.72$, $P<.01$, effect size $d=0.38$) compared with the waiting list. Improvements in quality of life ($F=7.56$, $P<.01$, effect size $d=0.23$), hope ($F=15.15$, $P<.01$, effect size $d=0.36$), and optimism ($F=8.17$, $P<.01$, effect size $d=0.23$) were also identified, but no change was reported for anxiety levels. Global outcome measures revealed that the majority of the individuals found the treatment beneficial and were satisfied with the results.

CONCLUSION: GCBT is a beneficial and cost-effective treatment that individuals find amenable in routine clinical practice for CFS. Additionally we have described important effects emerged on positive psychological dimensions such as hope and optimism potentially enhancing the overall benefit.

## CHRONIC FATIGUE SYNDROME (Continued)

### Exercise therapy for chronic fatigue syndrome.

Larun L[1], Brurberg KG, Odgaard-Jensen J, Price JR.

Cochrane Database Syst Rev. **2019 Oct 2**;10:CD003200. doi: 10.1002/14651858.CD003200.pub8. PMID: 31577366.

BACKGROUND: Chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME) is a serious disorder characterised by persistent postexertional fatigue and substantial symptoms related to cognitive, immune and autonomous dysfunction. There is no specific diagnostic test, therefore diagnostic criteria are used to diagnose CFS. The prevalence of CFS varies by type of diagnostic criteria used. Existing treatment strategies primarily aim to relieve symptoms and improve function. One treatment option is exercise therapy.

OBJECTIVES: The objective of this review was to determine the effects of exercise therapy for adults with CFS compared with any other intervention or control on fatigue, adverse outcomes, pain, physical functioning, quality of life, mood disorders, sleep, self-perceived changes in overall health, health service resources use and dropout.

SEARCH METHODS: We searched the Cochrane Common Mental Disorders Group controlled trials register, CENTRAL, and SPORTDiscus up to May 2014, using a comprehensive list of free-text terms for CFS and exercise. We located unpublished and ongoing studies through the World Health Organization International Clinical Trials Registry Platform up to May 2014. We screened reference lists of retrieved articles and contacted experts in the field for additional studies.

SELECTION CRITERIA: We included randomised controlled trials (RCTs) about adults with a primary diagnosis of CFS, from all diagnostic criteria, who were able to participate in exercise therapy.

DATA COLLECTION AND ANALYSIS: Two review authors independently performed study selection, 'Risk of bias' assessments and data extraction. We combined continuous measures of outcomes using mean differences (MDs) or standardised mean differences (SMDs). To facilitate interpretation of SMDs, we re-expressed SMD estimates as MDs on more common measurement scales. We combined dichotomous outcomes using risk ratios (RRs). We assessed the certainty of evidence using GRADE.

MAIN RESULTS: We included eight RCTs with data from 1518 participants. Exercise therapy lasted from 12 weeks to 26 weeks. The studies measured effect at the end of the treatment and at long-term follow-up, after 50 weeks or 72 weeks. Seven studies used aerobic exercise therapies such as walking, swimming, cycling or dancing, provided at mixed levels in terms of intensity of the aerobic exercise from very low to quite rigorous, and one study used anaerobic exercise. Control groups consisted of passive control, including treatment as usual, relaxation or flexibility (eight studies); cognitive behavioural therapy (CBT) (two studies); cognitive therapy (one study); supportive listening (one study); pacing (one study); pharmacological treatment (one study) and combination treatment (one study).Most studies had a low risk of selection bias. All had a high risk of performance and detection bias. **Exercise therapy compared with 'passive' control:** Exercise therapy probably reduces fatigue at end of treatment (SMD -0.66, 95% CI -1.01 to -0.31; 7 studies, 840 participants; moderate-certainty evidence; re-expressed MD -3.4, 95% CI -5.3 to -1.6; scale 0 to 33). We are uncertain if fatigue is reduced in the long term because the certainty of the evidence is very low (SMD -0.62, 95 % CI -1.32 to 0.07; 4 studies, 670 participants; re-expressed MD -3.2, 95% CI -6.9 to 0.4; scale 0 to 33). We are uncertain about the risk of serious adverse reactions because the certainty of the evidence is very low (RR 0.99, 95% CI 0.14 to 6.97; 1 study, 319 participants). Exercise therapy may moderately improve physical functioning at end of treatment, but the long-term effect is uncertain because the certainty of the evidence is very low. Exercise therapy may also slightly improve sleep at end of treatment and at long term. The effect of exercise therapy on pain, quality of life and depression is uncertain because evidence is missing or of very low certainty. **Exercise therapy compared with CBT:** Exercise therapy may make little or no difference to fatigue at end of treatment (MD 0.20, 95% CI -1.49 to 1.89; 1 study, 298 participants; low-certainty evidence), or at long-term follow-up (SMD 0.07, 95% CI -0.13 to 0.28; 2 studies, 351 participants; moderate-certainty evidence). We are uncertain about the risk of serious adverse reactions because the certainty of the evidence is very low (RR 0.67, 95% CI 0.11 to 3.96; 1 study, 321 participants). The available evidence suggests that there may be little or no difference between exercise therapy and CBT in physical functioning or sleep (low-certainty evidence) and probably little or no difference in the effect on depression (moderate-certainty evidence). We are uncertain if exercise therapy compared to CBT improves quality of life or reduces pain because the evidence is of very low certainty. **Exercise therapy compared with adaptive pacing:** Exercise therapy may slightly reduce fatigue at end of treatment (MD -2.00, 95% CI -3.57 to -0.43; scale 0 to 33; 1 study, 305 participants; low-certainty evidence) and at long-term follow-up (MD -2.50, 95% CI -4.16 to -0.84; scale 0 to 33; 1 study, 307 participants; low-certainty evidence). We are uncertain about the risk of serious adverse reactions (RR 0.99, 95% CI 0.14 to 6.97; 1 study, 319 participants; very low-certainty evidence). The available evidence suggests that exercise therapy may slightly improve physical functioning, depression and sleep compared to adaptive pacing (low-certainty evidence). No studies reported quality of life or pain. **Exercise therapy compared with antidepressants:** We are uncertain if exercise therapy, alone or in combination with antidepressants, reduces fatigue and depression more than antidepressant alone, as the certainty of the evidence is very low. The one included study did not report on adverse reactions, pain, physical functioning, quality of life, sleep or long-term results.

AUTHORS' CONCLUSIONS: Exercise therapy probably has a positive effect on fatigue in adults with CFS compared to usual care or passive therapies. The evidence regarding adverse effects is uncertain. Due to limited evidence it is difficult to draw conclusions about the comparative effectiveness of CBT, adaptive pacing or other interventions. All studies were conducted with outpatients diagnosed with 1994 criteria of the Centers for Disease Control and Prevention or the Oxford criteria, or both. Patients diagnosed using other criteria may experience different effects.

## HEADACHE and MIGRAINE

### Coronary artery calcification score in migraine patients.

Filippopulos FM[1,2], Schoeberl F[3], Becker HC[4,5], Becker-Bense S[3,6], Eren O[3], Straube A[3], Becker A[7].

Sci Rep. **2019 Oct 1**;9(1):14069. doi: 10.1038/s41598-019-50660-9. PMID: 31575978.

Epidemiological studies have shown an increased risk of cardiovascular events in migraineurs. The pathophysiological mechanisms of this observation remain largely unknown. Recent genetic and epidemiologic studies suggest, that atherosclerosis might be the overlapping pathophysiological mechanism in migraine and coronary heart disease. The aim of the present study was to evaluate if the increased cardiovascular risk in migraineurs is attributed to an increased coronary artery calcification. For this the coronary artery calcium score was assessed by computed tomography of the heart in 1.437 patients of which 337 were migraineurs. All patients had a similar cardiovascular risk profile, so that the risk for coronary calcifications could be considered similar between migraineurs and non-migraineurs. The results showed no significant differences in the amount of coronary calcifications in patients with or without migraine. This suggests that a more pronounced coronary artery calcification, as a surrogate marker of coronary atherosclerosis, does not underlie the increased cardiovascular risk in migraineurs. A distinct common pathophysiological mechanism in migraine and coronary heart disease such as endothelial dysfunction or vasospasm should be discussed instead. However, it has to be considered, that the coronary artery calcification score does not indicate the total risk of atherosclerotic changes in the coronary arteries.

### Correlation of 5-HTR6 gene polymorphism with vestibular migraine.

Wu X[1,2,3], Qiu F[2], Wang Z[2], Liu B[4], Qi X[2].

J Clin Lab Anal. **2019 Oct 6**:e23042. doi: 10.1002/jcla.23042. PMID: 31587366. [Epub ahead of print]

OBJECTIVE: To investigate the correlation of 5-hydroxy tryptamine receptor 6 (5-HTR6) gene polymorphism with vestibular migraine (VM).

METHODS: A total of 92 VM patients were enrolled as the observation group, and 100 healthy people receiving physical examinations as the control group. Their general clinical information was collected, and the level of 5-HT in plasma and the vestibular function test indexes were detected. Moreover, the polymorphism of 5-HTR6 rs770963777 was detected with the TaqMan-MGB probe.

RESULTS: The observation group had a lower level of 5-HT than the control group ($P < .05$), and the abnormality rates of the vestibular function tests, including the caloric test, head-shaking test, and vestibular autorotation test, were obviously higher than those in the control group ($P < .01$). The comparisons showed that the distribution frequencies of the genotypes and alleles were different between the two groups ($P < .05$). According to the analysis of the genetic mode, there were differences in recessive and additive modes between the two groups ($P < .05$), but the dominant mode was not different between the two groups ($P > .05$).

CONCLUSION: The level of 5-HT and the vestibular function test indexes can serve as the effective indicators for observing VM, and the polymorphism of 5-HTR6 rs770963777 site is correlated with VM onset.

## HEADACHE and MIGRAINE (Continued)

### Percutaneous electrical nerve stimulation (PENS) therapy for refractory primary headache disorders: a pilot study.

Weatherall MW[1], Nandi D[2].

Br J Neurosurg. **2019 Oct 3**:1-5. doi: 10.1080/02688697.2019.1671951. PMID: 31578882. [Epub ahead of print]

**Purpose:** Primary headache disorders are common, but many patients are refractory to medical treatment. Percutaneous electrical nerve stimulation (PENS) therapy involves the stimulation of one or more individual nerves or dermatomes using needle probes. We assessed whether a 'single shot with single probe' strategy would benefit patients with refractory headache disorders, including chronic migraine (CM), and chronic cluster headache (CCH).

**Materials and methods:** Service evaluation of 36 patients treated with PENS therapy between September 2012 and June 2016. Follow-up data were available for 33 patients, of whom 16 had CM, nine had CCH, and six had secondary headache disorders. PENS was given using Algotec® disposable 21 gauge PENS therapy probes (8 cm) to the occipital nerve ipsilateral to the pain (or bilaterally in cases of bilateral pain). Stimulation was delivered at 2 Hz/100 Hz, at 3 cycles/s, between 1.2 and 2.5 V depending on patient tolerability, for 25-28 min.

**Results:** Six of nine patients with CCH improved significantly after the first session. In all patients with CCH, PENS therapy was well tolerated, with no significant adverse events reported. One patient with CCH reverted to episodic cluster. Only four patients with CM experienced any benefit.

**Conclusion:** PENS therapy shows potential as a relatively non-invasive, low-risk, and inexpensive component of the treatment options for refractory primary headache disorders, particularly CCH.

### The metabolic face of migraine - from pathophysiology to treatment.

Gross EC[1], Lisicki M[2], Fischer D[1], Sándor PS[3], Schoenen J[4].

Nat Rev Neurol. **2019 Oct 4**. doi: 10.1038/s41582-019-0255-4. PMID: 31586135. [Epub ahead of print]

Migraine can be regarded as a conserved, adaptive response that occurs in genetically predisposed individuals with a mismatch between the brain's energy reserve and workload. Given the high prevalence of migraine, genotypes associated with the condition seem likely to have conferred an evolutionary advantage. Technological advances have enabled the examination of different aspects of cerebral metabolism in patients with migraine, and complementary animal research has highlighted possible metabolic mechanisms in migraine pathophysiology. An increasing amount of evidence - much of it clinical - suggests that migraine is a response to cerebral energy deficiency or oxidative stress levels that exceed antioxidant capacity and that the attack itself helps to restore brain energy homeostasis and reduces harmful oxidative stress levels. Greater understanding of metabolism in migraine offers novel therapeutic opportunities. In this Review, we describe the evidence for abnormalities in energy metabolism and mitochondrial function in migraine, with a focus on clinical data (including neuroimaging, biochemical, genetic and therapeutic studies), and consider the relationship of these abnormalities with the abnormal sensory processing and cerebral hyper-responsivity observed in migraine. We discuss experimental data to consider potential mechanisms by which metabolic abnormalities could generate attacks. Finally, we highlight potential treatments that target cerebral metabolism, such as nutraceuticals, ketone bodies and dietary interventions.

## HEADACHE and MIGRAINE (Continued)

### Delineating conditions and subtypes in chronic pain using neuroimaging.

Holmes SA[1], Upadhyay J[1], Borsook D[1].

Pain Rep. **2019 Aug 7**;4(4):e768. doi: 10.1097/PR9.0000000000000768. PMCID: PMC6727994. PMID: 31579859.

Differentiating subtypes of chronic pain still remains a challenge-both from a subjective and objective point of view. Personalized medicine is the current goal of modern medical care and is limited by the subjective nature of patient self-reporting of symptoms and behavioral evaluation. Physiology-focused techniques such as genome and epigenetic analyses inform the delineation of pain groups; however, except under rare circumstances, they have diluted effects that again, share a common reliance on behavioral evaluation. The application of structural neuroimaging towards distinguishing pain subtypes is a growing field and may inform pain-group classification through the analysis of brain regions showing hypertrophic and atrophic changes in the presence of pain. Analytical techniques such as machine-learning classifiers have the capacity to process large volumes of data and delineate diagnostically relevant information from neuroimaging analysis. The issue of defining a "brain type" is an emerging field aimed at interpreting observed brain changes and delineating their clinical identity/significance. In this review, 2 chronic pain conditions (migraine and irritable bowel syndrome) with similar clinical phenotypes are compared in terms of their structural neuroimaging findings. Independent investigations are compared with findings from application of machine-learning algorithms. Findings are discussed in terms of differentiating patient subgroups using neuroimaging data in patients with chronic pain and how they may be applied towards defining a personalized pain signature that helps segregate patient subgroups (eg, migraine with and without aura, with or without nausea; irritable bowel syndrome vs other functional gastrointestinal disorders).

## CHRONIC PAIN

### Do physical activity and body mass index modify the association between chronic musculoskeletal pain and insomnia? Longitudinal data from the HUNT study, Norway.

Skarpsno ES[1,2], Nilsen TIL[1], Sand T[3,4], Hagen K[3,4,5], Mork PJ[1].

Comment in: **Sleep hygiene, insomnia and mental health.** [J Sleep Res. 2018]

J Sleep Res. **2018 Feb**;27(1):32-39. doi: 10.1111/jsr.12580. PMID: 28744933. Epub 2017 Jul 26.

[ Note: Delayed posting in PubMed—Not previously listed in RAC Research Alerts. ]

We investigated the prospective association between chronic musculoskeletal pain and risk of insomnia, and if leisure-time physical activity and body mass index modify this association. The study comprised historical data on 11 909 women and 9938 men in the Norwegian HUNT study without sleep problems at baseline in 1995-97 and followed-up for insomnia in 2006-08. Poisson regression was used to estimate adjusted risk ratios (RRs) with 95% confidence intervals (CIs). Compared to pain-free participants, any chronic pain was associated with a RR of insomnia of 2.27 (95% CI: 1.93, 2.66) in women and 1.58 (95% CI: 1.28, 1.95) in men, whereas reporting ≥5 chronic pain sites gave RRs of 3.20 (95% CI: 2.60, 3.95) and 2.40 (95% CI: 1.76, 3.27), respectively. Analysis of joint effects showed that: (i) compared to pain-free physically active people, RRs in people with ≥5 chronic pain sites were 3.77 (95% CI: 2.42-5.85) if they were inactive and 2.76 (95% CI: 2.29, 3.31) if they were active; and (ii) compared to pain-free people with normal weight, RRs in people with ≥5 chronic pain sites were 3.52 (95% CI: 2.81, 4.40) if they were obese and 2.93 (95% CI: 2.24, 3.84) if they had normal weight. In conclusion, chronic musculoskeletal pain increases the risk of insomnia, particularly among those who report several pain sites. Although there was no clear evidence of modifying effects, our results suggest that a healthy active lifestyle reduces the risk of insomnia in people with chronic musculoskeletal pain.

## IRRITABLE BOWEL SYNDROME

### Evaluation of a fluorescent immunochromatography test for fecal calprotectin.

Li R[1], Zhao X[1], Dong J[1], Zhu D[1], Wang T[1], Yang S[1], Zhao Z[1], Xiao N[1].

J Clin Lab Anal. **2019 Oct 6:**e23059. doi: 10.1002/jcla.23059. PMID: 31587371. [Epub ahead of print]

BACKGROUND: Fecal calprotectin (FC) is widely used to discriminate between patients with inflammatory diseases such as inflammatory bowel disease (IBD) and functional diseases such as irritable bowel syndrome (IBS). ELISA is a time-consuming method for the measurement of FC, whereas a fluorescent immunochromatography test can obtain results in around 30 minutes and thus enables a rapid response to clinical decision.

METHODS: Two methods, the Proglead® calprotectin (FC Proglead) and the BÜHLMANN fCAL® ELISA (FC BÜHLMANN), were used to quantitatively examine FC in 111 stool samples. The comparison and bias estimation of both assays were assessed using CLSI EP09c protocol.

RESULTS: The two methods were highly correlated (rho = .96). Deming regression was employed to calculate the regression equation, with a slope of 1.01 and an intercept of -4.98 μg/g. The estimated median bias (FC Proglead - FC BÜHLMANN) was -4.19 μg/g with the 95% limits of agreement (-55.59 to 47.21 μg/g), and the estimated median percent bias was -8.71% with the 95% limits of agreement (-50.31% to 32.90%). There was 4.50% (5/111) of values outside the 95% limits of agreement. Percent biases at the FC cutoff values of 50 and 200 μg/g between both methods evaluated by Deming regression were 8.96% and 1.49%, respectively. The biases were all less than the acceptable standard (10%). And, 99.10% of FC results were in agreement between both methods (kappa = .99, $P < .001$).

CONCLUSIONS: FC Proglead may be used as a suitable alternative to FC BÜHLMANN for the disease activity assessment for patients with IBD, considering its convenience and shorter turnaround time.

### Management of irritable bowel syndrome with diarrhea: a review of nonpharmacological and pharmacological interventions.

Cangemi DJ[1], Lacy BE[2].

Therap Adv Gastroenterol. **2019 Oct 4**;12:1756284819878950. doi: 10.1177/1756284819878950. PMCID: PMC6778998. PMID: 31632456.

Irritable bowel syndrome (IBS) is a common gastrointestinal (GI) condition involving numerous potential causative factors (e.g. alterations in gut microbiota, motility, brain-gut axis). Several interventions are available for the management of patients with IBS, but no universal management algorithm currently exists. The aim of this article is to review interventions that may be considered in the management of patients with IBS with diarrhea (IBS-D). Nonpharmacological interventions include dietary and lifestyle modification, which are generally used as first-line therapy. Probiotics have demonstrated efficacy and safety in patients with IBS, but studies are inconsistent in strains examined, dosing, and treatment duration. Psychological therapies (e.g. cognitive behavioral therapy, hypnotherapy) also may improve IBS symptoms. Pharmacological interventions for the management of IBS-D include the US Food and Drug Administration-approved agents eluxadoline, rifaximin, and alosetron, as well as loperamide, smooth muscle antispasmodics, bile acid sequestrants, and antidepressants (i.e. tricyclic antidepressants, selective serotonin reuptake inhibitors). Eluxadoline and rifaximin have been shown to improve abdominal pain and stool consistency in patients with IBS-D. In addition, data indicate that alosetron improves IBS symptoms; however, it is approved only for women with severe IBS-D. Of the three approved agents, rifaximin has the most favorable safety profile. The risk-benefit ratio is an important consideration with every medication, but is especially important in the treatment of functional GI disorders such as IBS-D. Thus, the most troublesome symptoms, quality of life, symptom intensity, and individual patient preferences should be considered when formulating a management plan for patients with IBS-D.

## IRRITABLE BOWEL SYNDROME (Continued)

### Use of functional magnetic resonance imaging in patients with irritable bowel syndrome and functional dyspepsia.

Skrobisz K[1], Piotrowicz G[2], Drozdowska A[3], Markiet K[3], Sabisz A[3], Naumczyk P[4], Rydzewska G[5,6], Szurowska E[3].

Prz Gastroenterol. **2019**;14(3):163-167. doi: 10.5114/pg.2019.88163. PMCID: PMC6807669. PMID: 31649785. Epub 2019 Sep 27.

Functional brain imaging (positron emission tomography - PET, functional magnetic resonance imaging - fMRI), allowing *in vivo* analysis of the brain-digestive tract interaction and the neurological mechanisms underlying visceral hypersensitivity, significantly advanced research and helped in the understanding of the interrelations in this field. Differences in this parameter can result from alterations in task-related cognitive states or from resting state processes. Nowadays, advanced imaging techniques such as fMRI are more frequently used and are acknowledged among both clinicians and radiologists in the diagnostic algorithm of digestive tract diseases. Functional dyspepsia is a condition in which neuroimaging allows for analysis of dysfunctions within the brain-gut axis (BGA) engaged in processing of visceral discomfort and pain. The results of studies in patient groups with irritable bowel syndrome prove that psychosocial factors significantly affect the mechanisms regulating visceral sensitivity within the brain. The BGA includes neuronal pathways (autonomic nervous system), neuroendocrine (hypothalamo-pituitary-adrenal axis), and neuroimmunological ones. Psychological processes affect the functioning of the digestive system and can cause dyspeptic symptoms. A patient's mental condition associated with stress can affect processes taking place in the central nervous system and trigger somatic reactions in the digestive tract through the autonomic visceral system.

## OTHER RESEARCH OF INTEREST

### SR9009 administered for one day after myocardial ischemia-reperfusion prevents heart failure in mice by targeting the cardiac inflammasome.

Reitz CJ[1], Alibhai FJ[1], Khatua TN[1], Rasouli M[1], Bridle BW[2], Burris TP[3], Martino TA[1].

Commun Biol. **2019 Oct 3**;2:353. doi: 10.1038/s42003-019-0595-z. eCollection 2019. PMCID: PMC6776554. PMID: 31602405.

Reperfusion of patients after myocardial infarction (heart attack) triggers cardiac inflammation that leads to infarct expansion and heart failure (HF). We previously showed that the circadian mechanism is a critical regulator of reperfusion injury. However, whether pharmacological targeting using circadian medicine limits reperfusion injury and protects against HF is unknown. Here, we show that short-term targeting of the circadian driver REV-ERB with SR9009 benefits long-term cardiac repair post-myocardial ischemia reperfusion in mice. Gain and loss of function studies demonstrate specificity of targeting REV-ERB in mice. Treatment for just one day abates the cardiac NLRP3 inflammasome, decreasing immunocyte recruitment, and thereby allowing the vulnerable infarct to heal. Therapy is given in vivo, after reperfusion, and promotes efficient repair. This study presents downregulation of the cardiac inflammasome in fibroblasts as a cellular target of SR9009, inviting more targeted therapeutic investigations in the future.

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