

GULF WAR ILLNESS

[Chronic Neurological Morbidities and Elevated Hippocampal Calcium Levels in a DFP-Based Rat Model of Gulf War Illness.](#)

[Phillips KF](#)¹, [Deshpande LS](#)^{1,2}.

Mil Med. **2018 Mar 1**;183(suppl_1):552-555. doi: 10.1093/milmed/usx148. PMID: 29635560.

Over 20 yr have elapsed since the end of the First Gulf War, yet approximately one-third of the veterans exhibit Gulf War Illness (GWI) symptoms, particularly depression and memory impairments. Exposure to organophosphate (OP) compounds is implicated for GWI development. The role of calcium (Ca²⁺) signaling in learning, memory, and mood is well established and disruptions in Ca²⁺ homeostasis are observed in many neurological disorders. However, the status of Ca²⁺ homeostasis in the development of GWI behavioral impairments is not known. Male Sprague-Dawley rats were exposed to OP agent diisopropyl fluorophosphate (DFP; 0.5 mg/kg, s.c. 5 days), and at 6 mo post-DFP exposure, rats were subjected to behavioral assays for the determination of GWI neurological morbidities. Fura-2AM loaded acutely isolated hippocampal neurons were used for [Ca²⁺]_i estimations. We observed chronic depressive symptoms and cognitive deficits in rats exposed to repeated low-dose DFP. The GWI rats also manifested elevations in hippocampal [Ca²⁺]_i along with a significant increase in the number of neurons displaying these elevations. As Ca²⁺ is a major second-messenger molecule, such sustained increases in its levels could activate multiple signaling cascades and alter gene expression of proteins involved in synaptic plasticity and possibly underlie the neuronal injury and chronic morbidities in GWI.

CHRONIC FATIGUE SYNDROME

[Lower regulatory frequency for postural control in patients with fibromyalgia and chronic fatigue syndrome.](#)

[Rasouli O](#)^{1,2}, [Vasseljen O](#)², [Fors EA](#)², [Lorås HW](#)¹, [Stensdotter AK](#)¹.

PLoS One. **2018 Apr 4**;13(4):e0195111. doi: 10.1371/journal.pone.0195111. PMID: 29617424. eCollection 2018.

As many similar symptoms are reported in fibromyalgia (FM) and chronic fatigue syndrome (CFS), underlying deficits may potentially also be similar. Postural disequilibrium reported in both conditions may thus be explained by similar deviations in postural control strategies. 75 females (25/group FM, CFS and control, age 19-49 years) performed 60 s of quiet standing on a force platform in each of three conditions: 1) firm surface with vision, 2) firm surface without vision and, 3) compliant surface with vision. Migration of center of pressure was decomposed into a slow and a fast component denoting postural sway and lateral forces controlling postural sway, analyzed in the time and frequency domains. Main effects of group for the antero-posterior (AP) and medio-lateral (ML) directions showed that patients displayed larger amplitudes (AP, $p = 0.002$; ML, $p = 0.021$) and lower frequencies (AP, $p < 0.001$; ML, $p < 0.001$) for the slow component, as well as for the fast component (amplitudes: AP, $p = 0.010$; ML, $p = 0.001$ and frequencies: AP, $p = 0.001$; ML, $p = 0.029$) compared to controls. Post hoc analyses showed no significant differences between patient groups. In conclusion, both the CFS- and the FM-group differed from the control group. Larger postural sway and insufficient control was found in patients compared to controls, with no significant differences between the two patient groups.

CHRONIC FATIGUE SYNDROME (Continued)

[Fatigue Is Associated With Altered Monitoring and Preparation of Physical Effort in Patients With Chronic Fatigue Syndrome.](#)

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Biol Psychiatry Cogn Neurosci Neuroimaging. 2018 Apr;3(4):392-404. doi: 10.1016/j.bpsc.2018.01.015. PMID: 29628071. Epub 2018 Feb 12.

BACKGROUND: Chronic fatigue syndrome (CFS) is characterized by disabling fatigue, which is suggested to be maintained by dysfunctional beliefs. Fatigue and its maintenance are recently conceptualized as arising from abnormally precise expectations about bodily inputs and from beliefs of diminished control over bodily states, respectively. This study used functional neuroimaging to identify the neural correlates of fatigue and its maintenance by beliefs during a physical effort task.

METHODS: We isolated behavioral adjustments and cerebral activity during feedback processing and motor preparation, in the context of a task in which patients with CFS (n = 85) and healthy control subjects (n = 29) produced 30%, 50%, and 70% of their right-hand maximal voluntary contraction, and received directional feedback on performance (e.g., too little force).

RESULTS: Patients with CSF showed an effort-dependent behavioral bias toward less effort investment in response to directional feedback for the highest effort level as compared with healthy control subjects. This bias was associated with reduced feedback-related activity in the dorsolateral prefrontal cortex. These effects were proportional to state-related fatigue and prior beliefs about CFS patients' ability to perform the task. Patients with CFS also showed higher activity in the supplementary motor area, proportional to their state-related fatigue, and reduced connectivity between the supplementary motor area and sensorimotor cortex during motor preparation as compared with control subjects.

CONCLUSIONS: These findings link fatigue symptoms to alterations in behavioral choices on effort investment, prefrontal functioning, and supplementary motor area connectivity, with the dorsolateral prefrontal cortex being associated with prior beliefs about physical abilities.

[Higher Prevalence of "Low T3 Syndrome" in Patients With Chronic Fatigue Syndrome: A Case-Control Study.](#)

[Ruiz-Núñez B](#)^{1,2}, [Tarasse R](#)¹, [Vogelaar EF](#)³, [Janneke Dijck-Brouwer DA](#)¹, [Muskiet FAJ](#)¹.

Front Endocrinol (Lausanne). 2018 Mar 20;9:97. doi: 10.3389/fendo.2018.00097. PMID: 29615976. eCollection 2018.

Chronic fatigue syndrome (CFS) is a heterogeneous disease with unknown cause(s). CFS symptoms resemble a hypothyroid state, possibly secondary to chronic (low-grade) (metabolic) inflammation. We studied 98 CFS patients (21-69 years, 21 males) and 99 age- and sex-matched controls (19-65 years, 23 males). We measured parameters of thyroid function, (metabolic) inflammation, gut wall integrity and nutrients influencing thyroid function and/or inflammation. Most remarkably, CFS patients exhibited similar thyrotropin, but lower free triiodothyronine (FT3) (difference of medians 0.1%), total thyroxine (TT4) (11.9%), total triiodothyronine (TT3) (12.5%), %TT3 (4.7%), sum activity of deiodinases (14.4%), secretory capacity of the thyroid gland (14.9%), 24-h urinary iodine (27.6%), and higher % reverse T3 (rT3) (13.3%). FT3 below the reference range, consistent with the "low T3 syndrome," was found in 16/98 CFS patients vs. 7/99 controls (OR 2.56; 95% confidence interval = 1.00-6.54). Most observations persisted in two sensitivity analyses with more stringent cutoff values for body mass index, high-sensitive C-reactive protein (hsCRP), and WBC. We found possible evidence of (chronic) low-grade metabolic inflammation (ferritin and HDL-C). FT3, TT3, TT4, and rT3 correlated positively with hsCRP in CFS patients and all subjects. TT3 and TT4 were positively related to hsCRP in controls. Low circulating T3 and the apparent shift from T3 to rT3 may reflect more severely depressed tissue T3 levels. The present findings might be in line with recent metabolomic studies pointing at a hypometabolic state. They resemble a mild form of "non-thyroidal illness syndrome" and "low T3 syndrome" experienced by a subgroup of hypothyroid patients receiving T4 monotherapy. Our study needs confirmation and extension by others. If confirmed, trials with, e.g., T3 and iodide supplements might be indicated.

HEADACHE and MIGRAINE

[Remission of chronic headache: An 11-year follow-up study. Data from the Nord-Trøndelag Health Surveys 1995-1997 and 2006-2008.](#)

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Cephalalgia. 2018 Jan 1;333102418769940. doi: 10.1177/0333102418769940. PMID: 29629599. [Epub ahead of print]

Objectives To estimate remission rates of chronic headache and predictors of remission. **Methods** In this longitudinal population-based cohort study, we used validated headache questionnaire data from the second (1995-1997, baseline; n = 51,856 aged ≥ 20 years, response rate: 55%) and third wave (2006-2008, follow-up, response rate: 42%) of the Nord-Trøndelag Health Study. Chronic headache was defined as ≥15 headache days/month during the last year. Chronic headache remission was defined as headache less than 15 days/month at follow-up. Potential predictors of remission were evaluated using logistic regression. **Results** At baseline, 1266 (2.4%) participants reported chronic headache. Of these, 605 (48%) answered headache questions at follow-up. Remission was observed in 452 (74.7%), the proportion being almost identical in men and women (74.4% vs. 74.9, p = 0.92). In analyses adjusting for age, gender and education level, remission at follow-up was more than two times more likely among individuals without medication overuse headache (OR = 2.4, 95% CI 1.7-3.6) and without chronic musculoskeletal complaints (OR = 2.9, 95% CI 1.5-5.0) at baseline. **Conclusions** In this longitudinal population-based cohort study, three-quarters of chronic headache participants remitted from chronic headache. Remission was associated with no medication overuse headache and no chronic musculoskeletal complaints at baseline.

[A prospective real-world analysis of OnabotulinumtoxinA in chronic migraine post-NICE U.K. technology appraisal.](#)

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Eur J Neurol. 2018 Apr 4. doi: 10.1111/ene.13657. PMID: 29617060. [Epub ahead of print]

OBJECTIVES: The National Institute for Health and Care Excellence (NICE) in the United Kingdom (UK) recommend the use of OnabotulinumtoxinA (BoNTA, Botox®) in the management of chronic migraine (CM) following specific guidelines within the National Health Service (NHS). In view of the lack of data on the efficacy of this therapy following implementation of this guidelines in clinical practice and on the evaluation of guidance' compliance, we evaluate the effectiveness and safety of BoNTA in CM patients following the NICE guidelines.

METHODS: Prospective real-life audit.

RESULTS: After two treatments, 127/200 patients (63.5%) of patients obtained at least a 30% reduction in headache days. Those who continued the treatment up to three years reported a stable beneficial effect compared to baseline. Amongst responders, 68 patients (53.5%) were re-classified as episodic migraineurs. Fifty-seven of these patients (83.8%) converted to an episodic migraine pattern at six month follow-up. The majority of those whose migraine became episodic after BoNTA, extended the treatment intervals beyond three months (range: 4-8 months), before noticing any headache worsening. We observed no significant differences in the efficacy measures in patients treated with 155U compared to those treated with >155U.

CONCLUSION: When administered according to the NICE guidance BoNT-A produces a clinically meaningful effect in the long-term management of CM with and without MOH. Treatment discontinuation when CM become episodic may be useful in clinical practice to identify those who may benefit from extended treatment intervals. Our clinical experience indicates a lack of additional benefit from using the "follow-the-pain" paradigm. This article is protected by copyright. All rights reserved.

HEADACHE and MIGRAINE (Continued)

Functional neuroimaging biomarkers in migraine: diagnostic, prognostic and therapeutic implications.

[Russo A](#)¹, [Silvestro M](#)¹, [Tessitore A](#)¹, [Tedeschi G](#)¹.

Curr Med Chem. **2018 Apr 5**. doi: 10.2174/0929867325666180406115427. PMID: 29623825. [Epub ahead of print]

INTRODUCTION: In current migraine clinical practice conventional neuroimaging examinations are often sought to exclude possible causes of secondary headaches or migraine-associated disorders. Contrariwise, although advanced magnetic resonance imaging (MRI) has improved tremendously our understanding of human brain processes in migraine patients, to the state of the art they have not superseded the conventional neuroimaging techniques in the migraine clinical setting.

METHODS: A comprehensive review was conducted of PubMed citations by entering the key word "marker" AND/OR "biomarker" combined with "migraine" AND/OR "headache." Other key words included "imaging" OR "neuroimaging", "structural" OR "functional". The only restriction was English-language publication. The abstracts of all articles meeting these criteria were reviewed, and full text was retrieved and examined for relevant references.

RESULTS: Several authors tried to identify imaging biomarkers able to identify different migraine phenotypes or, even better, to follow-up the same migraine patients during the course of the disease, to predict the evolution into more severe phenotypes and, finally, the response to specific treatment.

CONCLUSIONS: The identification of diagnostic, prognostic and therapeutic advanced neuroimaging biomarkers in the migraine clinical setting, in order to approach to patients in a more and more rational and "tailored" way, is extremely intriguing and futuristic. Unfortunately, reliable and robust neuroimaging biomarkers are still lacking for migraine, probably due to both not completely understood pathogenesis and clinical and neuroimaging heterogeneity. Although further longitudinal advanced neuroimaging studies, aimed to identify effective neuroimaging biomarkers, are needed, this review aims to collect the main and most recent works on this topic.

CHRONIC PAIN

Correlates of Use and Perceived Effectiveness of Non-pharmacologic Strategies for Chronic Pain Among Patients Prescribed Long-term Opioid Therapy.

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J Gen Intern Med. **2018 Apr 9**. doi: 10.1007/s11606-018-4325-x. PMID: 29633138. [Epub ahead of print]

OBJECTIVE: Non-pharmacologic treatments (NPTs) are recommended for chronic pain. Information is limited on patient use or perceptions of NPTs. We examined the frequency and correlates of use and self-rated helpfulness of NPTs for chronic pain among patients who are prescribed long-term opioid therapy (LTOT).

METHODS: Participants (n = 517) with musculoskeletal pain who were prescribed LTOT were recruited from two integrated health systems. They rated the frequency and utility of six clinician-directed and five self-directed NPTs for chronic pain. We categorized NPT use at four levels based on number of interventions used and frequency of use (none, low, moderate, high). Analyses examined clinical and demographic factors that differed among groups for both clinician-directed and self-directed NPTs.

RESULTS: Seventy-one percent of participants reported use of any NPT for pain within the prior 6 months. NPTs were rated as being helpful by more than 50% of users for all treatments assessed (range 51-79%). High users of clinician-directed NPTs were younger than non-users or low-frequency users and had the most depressive symptoms. In both clinician-directed and self-directed categories, high NPT users had significantly higher pain disability compared to non-NPT users. No significant group differences were detected on other demographic or clinical variables. In multivariable analyses, clinician-directed NPT use was modestly associated with younger age (OR = 0.97, 95% CI = 0.96-1.02) and higher pain disability (OR = 1.01, 95% CI = 1.00-1.02). Variables associated with greater self-directed NPT use were some college education (OR = 1.80, 95% CI = 1.13-2.84), college graduate or more (OR = 2.02, 95% CI = 1.20-3.40), and higher pain disability (OR = 1.01, 95% CI = 1.01-1.02).

CONCLUSIONS: NPT use was associated with higher pain disability and younger age for both clinician-directed and self-directed NPTs and higher education for self-directed NPTs. These strategies were rated as helpful by those that used them. These results can inform intervention implementation and be used to increase engagement in NPTs for chronic pain.

CHRONIC PAIN (Continued)

[A Research Agenda for Advancing Non-pharmacological Management of Chronic Musculoskeletal Pain: Findings from a VHA State-of-the-art Conference.](#)

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J Gen Intern Med. 2018 Apr 9. doi: 10.1007/s11606-018-4345-6. PMID: 29633136. [Epub ahead of print]

Chronic pain is widely prevalent among Veterans and can have serious negative consequences for functional status and quality of life among other domains. The Veterans Health Administration (VHA) convened a state-of-the-art (SOTA) conference to develop research priorities for advancing the science and clinical practice of non-pharmacological management of chronic musculoskeletal pain. In this perspective article, we present the methods and consensus recommendations for research priorities emanating from the SOTA. In the months leading up to the SOTA, a core group of researchers defined four areas of focus: psychological/behavioral therapies; exercise/movement therapies; manual therapies; and models for delivering multi-modal pain care and divided into workgroups. Each workgroup, in their respective areas of focus, identified seminal studies capturing the state of the evidence. Herein, we present consensus recommendations ranging from efficacy to effectiveness to implementation/dissemination research depending on the state of the evidence as assessed by participants, including commentary on common elements across workgroups and future areas of innovation in study design, measurement, and outcome

[Closed-Loop Deep Brain Stimulation for Refractory Chronic Pain.](#)

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Front Comput Neurosci. 2018 Mar 26;12:18. doi: 10.3389/fncom.2018.00018. PMCID: PMC5879131. PMID: 29632482. eCollection 2018.

Pain is a subjective experience that alerts an individual to actual or potential tissue damage. Through mechanisms that are still unclear, normal physiological pain can lose its adaptive value and evolve into pathological chronic neuropathic pain. Chronic pain is a multifaceted experience that can be understood in terms of somatosensory, affective, and cognitive dimensions, each with associated symptoms and neural signals. While there have been many attempts to treat chronic pain, in this article we will argue that feedback-controlled 'closed-loop' deep brain stimulation (DBS) offers an urgent and promising route for treatment. Contemporary DBS trials for chronic pain use "open-loop" approaches in which tonic stimulation is delivered with fixed parameters to a single brain region. The impact of key variables such as the target brain region and the stimulation waveform is unclear, and long-term efficacy has mixed results. We hypothesize that chronic pain is due to abnormal synchronization between brain networks encoding the somatosensory, affective and cognitive dimensions of pain, and that multisite, closed-loop DBS provides an intuitive mechanism for disrupting that synchrony. By (1) identifying biomarkers of the subjective pain experience and (2) integrating these signals into a state-space representation of pain, we can create a predictive model of each patient's pain experience. Then, by establishing how stimulation in different brain regions influences individual neural signals, we can design real-time, closed-loop therapies tailored to each patient. While chronic pain is a complex disorder that has eluded modern therapies, rich historical data and state-of-the-art technology can now be used to develop a promising treatment.

CHRONIC PAIN (Continued)**Targeting human Mas-related G protein-coupled receptor X1 to inhibit persistent pain.**

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Proc Natl Acad Sci U S A. 2017 Mar 7;114(10):E1996-E2005. doi: 10.1073/pnas.1615255114. PMCID: PMC5347560. PMID: 28223516. Epub 2017 Feb 21.

Human Mas-related G protein-coupled receptor X1 (MRGPRX1) is a promising target for pain inhibition, mainly because of its restricted expression in nociceptors within the peripheral nervous system. However, constrained by species differences across *Mrgprs*, drug candidates that activate MRGPRX1 do not activate rodent receptors, leaving no responsive animal model to test the effect on pain in vivo. Here, we generated a transgenic mouse line in which we replaced mouse *Mrgprs* with human *MrgprX1*. This humanized mouse allowed us to characterize an agonist [bovine adrenal medulla 8-22 (BAM8-22)] and a positive allosteric modulator (PAM), ML382, of MRGPRX1. Cellular studies suggested that ML382 enhances the ability of BAM8-22 to inhibit high-voltage-activated Ca²⁺ channels and attenuate spinal nociceptive transmission. Importantly, both BAM8-22 and ML382 effectively attenuated evoked, persistent, and spontaneous pain without causing obvious side effects. Notably, ML382 by itself attenuated both evoked pain hypersensitivity and spontaneous pain in *MrgprX1* mice after nerve injury without acquiring coadministration of an exogenous agonist. Our findings suggest that humanized *MrgprX1* mice provide a promising preclinical model and that activating MRGPRX1 is an effective way to treat persistent pain.

Small molecule dual-inhibitors of TRPV4 and TRPA1 for attenuation of inflammation and pain.

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Sci Rep. 2016 Jun 1;6:26894. doi: 10.1038/srep26894. PMCID: PMC4887995. PMID: 27247148.

TRPV4 ion channels represent osmo-mechano-TRP channels with pleiotropic function and wide-spread expression. One of the critical functions of TRPV4 in this spectrum is its involvement in pain and inflammation. However, few small-molecule inhibitors of TRPV4 are available. Here we developed TRPV4-inhibitory molecules based on modifications of a known TRPV4-selective tool-compound, GSK205. We not only increased TRPV4-inhibitory potency, but surprisingly also generated two compounds that potently co-inhibit TRPA1, known to function as chemical sensor of noxious and irritant signaling. We demonstrate TRPV4 inhibition by these compounds in primary cells with known TRPV4 expression - articular chondrocytes and astrocytes. Importantly, our novel compounds attenuate pain behavior in a trigeminal irritant pain model that is known to rely on TRPV4 and TRPA1. Furthermore, our novel dual-channel blocker inhibited inflammation and pain-associated behavior in a model of acute pancreatitis - known to also rely on TRPV4 and TRPA1. Our results illustrate proof of a novel concept inherent in our prototype compounds of a drug that targets two functionally-related TRP channels, and thus can be used to combat isoforms of pain and inflammation in-vivo that involve more than one TRP channel. This approach could provide a novel paradigm for treating other relevant health conditions.

CHRONIC PAIN (Continued)

[The association between severity of depression and prescription opioid misuse among chronic pain patients with and without anxiety: A cross-sectional study.](#)

[Feingold D](#)¹, [Brill S](#)², [Goor-Aryeh I](#)³, [Delayahu Y](#)⁴, [Lev-Ran S](#)⁵.

J Affect Disord. 2018 Apr 10;235:293-302. doi: 10.1016/j.jad.2018.04.058. PMID: 29660645. [Epub ahead of print]

BACKGROUND: In light of the increased rates of Prescription Opioid (PO) misuse and associated mortality in several developed countries in recent years, efforts have been made to identify populations who may be at increased risk for misuse of POs. Though the association between depression and PO misuse among pain patients is well documented, little is known regarding the effects of severity of depression on rates of misuse. In this study we explored rates of PO misuse among chronic pain patients screening positive for depression according to level of severity.

METHODS: Participants included chronic pain patients receiving POs (N = 554). All participants were screened for depression using the Patient Health Questionnaire (PHQ-9; cut-off scores of 5, 10, 15, and 20 for mild, moderate, moderate-severe and severe depression, respectively) and for opioid misuse using the Current Opioid Misuse Measure (COMM). Logistic regression analyses controlling for additional sociodemographic and clinical factors were conducted.

RESULTS: Participants who screened positive for depression were at significantly increased odds to screen positive for opioid misuse (Adjusted Odds Ratio (AOR) = 3.63; 95% Confidence Interval (CI) = 1.71-7.7) compared to those without depression. Severity of depression was significantly associated with increased odds for opioid misuse for moderate (AOR = 3.71; 95% CI = 1.01-13.76), moderate-severe (AOR = 6.28; 95% CI = 1.6-24.57) and severe (AOR = 14.66; 95% CI = 3.28-65.52) depression but not among those who screened positive for mild depression (AOR = 1.49; 95% CI = 0.39-5.68).

LIMITATIONS: Cross-sectional study.

CONCLUSIONS: Our results highlight the need to properly assess and address level of severity of co-morbid depression among chronic pain patients receiving POs.

[Effectiveness of Models Used to Deliver Multimodal Care for Chronic Musculoskeletal Pain: a Rapid Evidence Review.](#)

[Peterson K](#)¹, [Anderson J](#)², [Bourne D](#)², [Mackey K](#)², [Helfand M](#)².

J Gen Intern Med. 2018 Apr 9. doi: 10.1007/s11606-018-4328-7. PMID: 29633140. [Epub ahead of print]

BACKGROUND: Primary care providers (PCPs) face many system- and patient-level challenges in providing multimodal care for patients with complex chronic pain as recommended in some pain management guidelines. Several models have been developed to improve the delivery of multimodal chronic pain care. These models vary in their key components, and work is needed to identify which have the strongest evidence of clinically-important improvements in pain and function. Our objective was to determine which primary care-based multimodal chronic pain care models provide clinically relevant benefits, define key elements of these models, and identify patients who are most likely to benefit.

METHODS: To identify studies, we searched MEDLINE® (1996 to October 2016), CINAHL, reference lists, and numerous other sources and consulted with experts. We used predefined criteria for study selection, data abstraction, internal validity assessment, and strength of evidence grading.

RESULTS: We identified nine models, evaluated in mostly randomized controlled trials (RCTs). The RCTs included 3816 individuals primarily from the USA. The most common pain location was the back. Five models primarily coupling a decision-support component—most commonly algorithm-guided treatment and/or stepped care—with proactive ongoing treatment monitoring have the best evidence of providing clinically relevant improvement in pain intensity and pain-related function over 9 to 12 months (NNT range, 4 to 13) and variable improvement in quality of life, depression, anxiety, and sleep. The strength of the evidence was generally low, as each model was only supported by a single RCT with imprecise findings.

DISCUSSION: Multimodal chronic pain care delivery models coupling decision support with proactive treatment monitoring consistently provide clinically relevant improvement in pain and function. Wider implementation of these models should be accompanied by further evaluation of clinical and implementation effectiveness.

OTHER RESEARCH OF INTEREST

[Human Hippocampal Neurogenesis Persists throughout Aging.](#)

[Boldrini M](#)¹, [Fulmore CA](#)², [Tartt AN](#)², [Simeon LR](#)², [Pavlova I](#)³, [Poposka V](#)⁴, [Rosoklija GB](#)⁵, [Stankov A](#)⁴, [Arango V](#)⁶, [Dwork AJ](#)⁷, [Hen R](#)⁸, [Mann JJ](#)⁶.

Cell Stem Cell. **2018 Apr 5**;22(4):589-599.e5. doi: 10.1016/j.stem.2018.03.015. PMID: 29625071.

Adult hippocampal neurogenesis declines in aging rodents and primates. Aging humans are thought to exhibit waning neurogenesis and exercise-induced angiogenesis, with a resulting volumetric decrease in the neurogenic hippocampal dentate gyrus (DG) region, although concurrent changes in these parameters are not well studied. Here we assessed whole autopsy hippocampi from healthy human individuals ranging from 14 to 79 years of age. We found similar numbers of intermediate neural progenitors and thousands of immature neurons in the DG, comparable numbers of glia and mature granule neurons, and equivalent DG volume across ages. Nevertheless, older individuals have less angiogenesis and neuroplasticity and a smaller quiescent progenitor pool in anterior-mid DG, with no changes in posterior DG. Thus, healthy older subjects without cognitive impairment, neuropsychiatric disease, or treatment display preserved neurogenesis. It is possible that ongoing hippocampal neurogenesis sustains human-specific cognitive function throughout life and that declines may be linked to compromised cognitive-emotional resilience.

[Nutrigenomics and the Future of Nutrition: Proceedings of a Workshop—in Brief.](#)

Editors: National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Food and Nutrition Board; Food Forum.

Washington (DC): National Academies Press (US); **2018 March 15**. PMID: 29565524.

[The National Academies Collection: Reports funded by National Institutes of Health.](#)

[Link to Proceedings](#) full text online and download for PDF.

On December 5, 2017, the Food Forum of the National Academies of Sciences, Engineering, and Medicine hosted a public workshop in Washington, DC, to review current knowledge in the field of nutrigenomics and to explore the potential impact of personalized nutrition on health maintenance and chronic disease prevention. This publication highlights key points made by individual speakers during the workshop presentations and discussions.

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