GULF WAR ILLNESS

No Updates this Week for Gulf War Illness or Chronic Multisymptom Illness.

CHRONIC FATIGUE SYNDROME

Myalgic encephalomyelitis or chronic fatigue syndrome: how could the illness develop?

Morris G[1], Maes M[1,2], Berk M[1,3,4,5], Puri BK[6] .

Metab Brain Dis. **2019 Feb 13**. doi: 10.1007/s11011-019-0388-6. PMID: 30758706. [Epub ahead of print]

A model of the development and progression of chronic fatigue syndrome (myalgic encephalomyelitis), the aetiology of which is currently unknown, is put forward, starting with a consideration of the post-infection role of damage-associated molecular patterns and the development of chronic inflammatory, oxidative and nitrosative stress in genetically predisposed individuals. The consequences are detailed, including the role of increased intestinal permeability and the translocation of commensal antigens into the circulation, and the development of dysautonomia, neuroinflammation, and neurocognitive and neuroimaging abnormalities. Increasing levels of such stress and the switch to immune and metabolic downregulation are detailed next in relation to the advent of hypernitrosylation, impaired mitochondrial performance, immune suppression, cellular hibernation, endotoxin tolerance and sirtuin 1 activation. The role of chronic stress and the development of endotoxin tolerance via indoleamine 2,3-dioxygenase upregulation and the characteristics of neutrophils, monocytes, macrophages and T cells, including regulatory T cells, in endotoxin tolerance are detailed next. Finally, it is shown how the immune and metabolic abnormalities of chronic fatigue syndrome can be explained by endotoxin tolerance, thus completing the model.

HEADACHE and MIGRAINE

Burden of migraine in Finland: health care resource use, sick-leaves and comorbidities in occupational health care.

Korolainen MA[1], Kurki S[2], Lassenius MI[3], Toppila I[3], Costa-Scharplatz M[4], Purmonen T[1], Nissilä M[5].

J Headache Pain. **2019 Feb 12**;20(1):13. doi: 10.1186/s10194-019-0964-5. PMID: 30755160.

BACKGROUND: The highest prevalence of migraine is detected among people who are of working age. The aim of this study was to assess the burden of migraine in an occupational health care setting using real world data collected as a part of routine clinical practice.

METHODS: This retrospective register study included migraineurs using occupational health care at the private health care provider Terveystalo. An age and gender matched control population was established for comparison. Electronic medical records were assessed for overall and migraine related health care visits, sick-leaves and comorbidities. Stratification to acute and prophylactic treatment groups along with prophylactic treatment lines was based on prescriptions.

RESULTS: Among the 369,383 individuals in the study cohort, 7.4% women and 2.1% men were identified having a diagnosis of migraine. Prophylactic medication was prescribed to 13% of migraine patients and exclusively acute medication to 37%. Although migraine related visits and sick-leave days were significantly lower than overall visits or sick-leave days, both increased by prophylactic treatment line. The number of visits rose from 13.8 to 26.2 and sick-leave days from 16.8 to 30.4 per patient-year, in those without prophylaxis vs. ≥3 prophylactic treatments. Moreover, migraine patients had 1.7-fold increase in visits and 1.8-fold increase in sick leave days on average per patient-year, when compared to the control population. Depression and anxiety were 1.8-fold more common among patients with migraine, and the frequency also increase by treatment line.

CONCLUSIONS: Migraine burden increased by each failed treatment line and was associated with increased comorbidity. In addition, migraine patients had significantly higher extent of visits and sick-leave days as well as extent of comorbidities when compared to their age- and gender-matched counterparts.

HEADACHE and MIGRAINE (Continued)

Migraine and increased risk of developing open angle glaucoma: a population-based cohort study.

Huang JY[1,2], Su CC[3,4,5], Wang TH[1,2], Tsai IJ[6].

BMC Ophthalmol. **2019 Feb 13**;19(1):50. doi: 10.1186/s12886-019-1062-9. PMID: 30760249.

BACKGROUND: Migraine is linked to endothelial dysfunction and is considered to be a systemic vasculopathy. Interestingly, systemic vascular diseases also occur in glaucoma patients and are considered to be vascular risk factors. Whether migraine is simply a concomitant condition in glaucoma patients or a risk factor per se for glaucoma remains unknown. Thus, in the present study, we investigated the risk for open angle glaucoma (OAG) in migraineurs using a 10-year follow-up study that employed a nationwide population-based dataset in Taiwan.

METHODS: This retrospective matched-cohort study used data sourced from the Longitudinal Health Insurance Database 2000. We included 17,283 subjects with migraine in the study cohort and randomly selected 69,132 subjects from the database for the comparison group. Each subject in this study was individually traced for a 10-year period to identify those subjects who subsequently received a diagnosis of OAG. The age-adjusted Charlson's comorbidity index (ACCI) score was utilized to compute the burden of comorbidity in each subject. Multivariate regression analysis was used to assess risk factors for OAG in migraineurs. Cox proportional hazards regression was performed to compare the 10-year risk of OAG between the migraineurs and the comparison cohort.

RESULTS: Migraineurs had more vascular comorbidities than the comparison cohort. The overall incidence of OAG (per 1000 person-years) was 1.29 and 1.02, respectively, for migraineurs and the comparison cohort during the 10-year follow-up period. Age, hyperlipidemia, and diabetes mellitus were three significant risk factors for OAG in migraineurs. After adjusting for patients' age and vascular comorbidities, migraineurs were found to have a 1.68-fold (95% confidence interval [CI], 1.20-2.36) greater risk of developing OAG than the comparison cohort, in subjects with an ACCI score of 0. This association became statistically nonsignificant in subjects with ACCI scores of 1-2 or ≥ 3.

CONCLUSION: Migraine is associated with a higher risk of OAG for patients with no comorbidity who are aged under 50 years.

Increased risk of neurodegenerative dementia in women with migraines: A nested case-control study using a national sample cohort.

Lee SY[1], Lim JS[2], Oh DJ[3], Kong IG[4], Choi HG[4].

Medicine (Baltimore). **2019 Feb**;98(7):e14467. doi: 10.1097/MD.0000000000014467. PMID: 30762763.

The present study aimed to evaluate the association between migraines and dementia. Data were collected from 11,438 dementia participants who were 1:4 matched by age, sex, income, region of residence, hypertension, diabetes, and dyslipidemia with 45,752 controls from the Korean National Health Insurance Service-National Sample Cohort from 2002 to 2013. Dementia was diagnosed using the International Classification of Disease-10 (ICD-10) codes (G30 or F00). For the integrity of diagnoses, we included only participants ≥60 years old who had been diagnosed with an ICD-10 code twice or more during ambulatory visits for the same episode. For migraine (ICD-10 code, G43), we included participants who had visited outpatient clinics twice or more for the same episode. In both dementia and control groups, a previous history of migraine was investigated. Approximately 7.7% (881/11,438) of patients in the dementia group and 6.3% (2888/45,752) of those in the control group had a history of migraine (P < .001). The crude and adjusted odds ratios (ORs) for migraine with dementia was 1.22 (95% confidence interval [CI] = 1.13-1.32, P < .001) and 1.13 (95% CI = 1.05-1.23, P = .002), respectively. In the subgroup analyses according to age and sex, women demonstrated a significantly higher adjusted OR for migraine with dementia, whereas men did not exhibit an association between migraine and dementia. In a nested case-control study using a national sample cohort, migraine increased the risk of dementia in women.

CHRONIC PAIN

The impact of comorbid pain and depression in the United States: results from a nationally representative survey.

Dhanju S[1], Kennedy SH[2,3], Abbey S[1,3], Katz J[1,4], Weinrib A[1,4], Clarke H[1], Bhat V[2,3], Ladha K[1].

Scand J Pain. **2019 Feb 13**. pii: /j/sjpain.ahead-of-print/sjpain-2018-0323/sjpain-2018-0323.xml. doi: 10.1515/sjpain-2018-0323. PMID: 30759071. [Epub ahead of print]

Background and Aims: The co-morbidity between pain and depression is a target of interest for treatment. However most of the published literature on the topic has used clinical cohorts as the population of interest. The goal of this study was to use a nationally representative sample to explore how health outcomes varied across pain and depression status in a cohort sampled from the general US population.

Methods: This was a cross-sectional analysis of adults ≥18 years in the 2009-2010 National Health and Nutrition Examination Survey. The cohort was stratified into: no pain/depression, pain alone, depression alone, and pain with depression. The primary outcome was self-reported general health status, and secondary outcomes were healthcare visits, overnight hospital stays and functional limitation. Survey weighted logistic regression was used to adjust for potential confounders.

Results: The cohort consisted of 4,213 individuals, of which 186 (4.4%) reported concurrent pain and depression. 597 (14.2%) and 253 (6.0%) were classified with either pain or depression alone, respectively. The majority of individuals with co-morbid pain and depression reported poor health (65.1%, p<0.001) and were significantly more likely than those with neither condition to rate their health as poor after adjustment (OR: 7.77, 95% CI: 4.24-14.26, p<0.001). Those with pain only or depression only were also more likely to rate their health as poor, albeit to a lesser extent (OR: 2.21, 95% CI: 1.21-2.34, p<0.001; OR: 3.75, 95% CI: 2.54-5.54, p<0.001, respectively). A similar pattern was noted across all secondary outcomes. Most notably, those with co-morbid pain and depression were the most likely to endorse functional limitation (OR: 13.15, 95% CI: 8.00-21.61, p<0.001). Comparatively, a similar trend was noted amongst those with pain only or depression only, though with a reduced effect size (OR: 4.23, 95% CI: 3.12-4.77, p<0.001; OR: 5.13, 95% CI: 3.38-7.82, p<0.001).

Conclusions: Co-morbid pain and depression in the general population resulted in markedly worse outcomes versus isolated pain or depression. Further, the effect appears to be synergistic. Given the substantial burdens of pain and depression, future treatments should aim to address both conditions simultaneously. Implications As a result of the co-morbidity between pain and depression, patients presenting with either condition should increase the index of suspicion among clinicians and prompt screening for the reciprocal condition. Early intervention for co-morbid pain and depression has the potential to mitigate future incidence of chronic pain and major depression.

The medial temporal lobe in nociception: a meta-analytic and functional connectivity study.

Ayoub LJ[1,2,3], Barnett A[4], Leboucher A[1], Golosky M[1], McAndrews MP[2,5], Seminowicz DA[6,7], Moayedi M[1,3,8].

Pain. **2019 Feb 8**. doi: 10.1097/j.pain.0000000000001519. PMID: 30747905. [Epub ahead of print]

Recent neuroimaging studies implicate the medial temporal lobe (MTL) in nociception and pain modulation. Here, we aim to identify which subregions of the MTL are involved in human pain and to test its connectivity in a cohort of chronic low back pain patients (CBP). We conducted two coordinate-based meta-analyses to determine which regions within the MTL showed consistent spatial patterns of functional activation (1) in response to experimental pain in healthy participants, and (2) in chronic pain compared to healthy participants. We followed PRISMA guidelines and performed activation likelihood estimate (ALE) meta-analyses. The first meta-analysis revealed consistent activation in the right anterior hippocampus (right antHC), parahippocampal gyrus and amygdala. The second meta-analysis revealed consistently less activation in patients' right antHC, compared to healthy participants. We then conducted a seed-to-voxel resting state functional connectivity of the right antHC seed with the rest of the brain in 77 CBP and 79 age-matched healthy participants. We found that CBP had significantly weaker antHC functional connectivity to the medial prefrontal cortex (mPFC) compared to healthy participants. Taken together, these data indicate that the antHC has abnormally lower activity in chronic pain, and reduced connectivity to the mPFC in CBP. Future studies should investigate the specific role of the antHC in the development and management of chronic pain.

CHRONIC PAIN (Continued)

General practitioners and management of chronic noncancer pain: a cross-sectional survey of influences on opioid deprescribing.

White R[1,2], Hayes C[1], Boyes AW[2,3], Chiu S [3], Paul CL[2,3].

J Pain Res. **2019 Jan 22**;12:467-475. doi: 10.2147/JPR.S168785. PMCID: PMC6348964. PMID: 30774416. eCollection 2019.

Background: General practitioners' (GPs) views about deprescribing prescription opioid analgesics (POAs) may influence the care provided for patients experiencing chronic noncancer pain (CNCP). There are limited data addressing GPs' beliefs about deprescribing, including their decisions to deprescribe different types of POAs.

Aim: To determine the proportion of GPs who hold attitudes congruent with local pain stewardship, describe their deprescribing decisions, and determine whether type of POA influences deprescribing.

Design and Setting: In 2016, a cross-sectional survey of all GPs (n=1,570) in one mixed urban and regional primary health network (PHN) in Australia was undertaken.

Methods: A mailed self-report questionnaire assessed agreement with local guidelines for treating CNCP; influences on deprescribing POAs and likelihood of deprescribing in a hypothetical case involving either oral codeine or oxycodone.

Results: A response rate of 46% was achieved. Approximately half (54%) of GPs agreed POAs should be reserved for people with acute, cancer pain or palliative care and a third (32%) did not agree that a medication focus has limited benefits for peoples' long-term quality of life and function. Most (77%) GPs were less likely to deprescribe when effective alternate treatments were lacking, while various patient factors (eg, fear of weaning) were reported to decrease the likelihood of deprescribing for 25% of GPs. A significantly higher proportion of GPs reported being very likely to deprescribe codeine compared to the equivalent opioid dose of oxycodone for a hypothetical patient.

Conclusions: Many GPs in the PHN hold attitudes at odds with local guidance that opioids are a nonsuperior treatment for CNCP. Attitudinal barriers to deprescribing include: a lack of consistent approach to deprescribing opioids as a class of drugs, perceived lack of effective treatment alternatives and patient fear of deprescribing. Therefore, the next step in this target population is to appropriately train and support GPs in how to apply the evidence in practice and how to support patients appropriately.

The role of sleep quality on the relationship between posttraumatic stress symptoms and pain in women.

Aaron R[1,2], Noel M[3], Dudeney J[4], Wilson A[5], Holley A[5], Palermo T[4].

J Behav Med. **2019 Feb 14**. doi: 10.1007/s10865-019-00016-5. PMID: 30762157. [Epub ahead of print]

Pain frequently co-occurs with elevated posttraumatic stress symptoms (PTSS); women are at elevated risk for their co-occurrence. PTSS and pain are associated with poor sleep quality; yet, little research has examined how sleep impacts their co-occurrence. The current study examines the indirect role of sleep on the relationship between PTSS and pain. A community sample of 182 women completed psychometrically-sound questionnaires assessing PTSS, sleep quality, pain characteristics, depression and anxiety symptoms, and anxiety sensitivity. We examined how sleep quality impacted associations among PTSS and pain intensity and pain interference, while controlling for key psychological factors. Greater PTSS was associated with worse pain interference, and poor sleep quality had a significant indirect effect on this relationship. Sleep may represent a modifiable behavioral mechanism that contributes to the mutual maintenance of PTSS and pain in women. Future research is needed to further clarify the role of sleep quality in their co-occurrence.

CHRONIC PAIN (Continued)

Functional and neurochemical disruptions of brain hub topology in chronic pain.

Kaplan CM[1], Schrepf A[1], Vatansever D[2,3], Larkin TE[4], Mawla I[4], Ichesco E[1], Kochlefl L[1], Harte SE[1], Clauw DJ[1], Mashour GA[4,5], Harris RE[1,4].

Pain. **2019 Jan 16**. doi: 10.1097/j.pain.0000000000001480. PMID: 30763287. [Epub ahead of print]

A critical component of brain network architecture is a robust hub structure, wherein hub regions facilitate efficient information integration by occupying highly connected and functionally central roles in the network. Across a wide range of neurological disorders, hub brain regions seem to be disrupted, and the character of this disruption can yield insights into the pathophysiology of these disorders. We applied a brain network-based approach to examine hub topology in fibromyalgia, a chronic pain condition with prominent central nervous system involvement. Resting state functional magnetic resonance imaging data from 40 fibromyalgia patients and 46 healthy volunteers, and a small validation cohort of 11 fibromyalgia patients, were analyzed using graph theoretical techniques to model connections between 264 brain regions. In fibromyalgia, the anterior insulae functioned as hubs and were members of the rich club, a highly interconnected nexus of hubs. In fibromyalgia, rich-club membership varied with the intensity of clinical pain: the posterior insula, primary somatosensory, and motor cortices belonged to the rich club only in patients with the highest pain intensity. Furthermore, the eigenvector centrality (a measure of how connected a region is to other highly connected regions) of the posterior insula positively correlated with clinical pain and mediated the relationship between glutamate + glutamine (assessed by proton magnetic resonance spectroscopy) within this structure and the patient's clinical pain report. Together, these findings reveal altered hub topology in fibromyalgia and demonstrate, for the first time to our knowledge, a neurochemical basis for altered hub strength and its relationship to the perception of pain.

OTHER RESEARCH OF INTEREST

The prevalence and trend of depression among veterans in the United States.

Liu Y[1], Collins C[1], Wang K[1], Xie X[2], Bie R[3].

J Affect Disord. **2019 Feb 15**;245:724-727. doi: 10.1016/j.jad.2018.11.031. PMID: 30699861. Epub 2018 Nov 5.

BACKGROUND: Depression is a common psychiatric illness that is associated with high rates of mortality and morbidity. However, studies reporting the trends of depression among U.S. veterans are limited. Therefore, the aim of this study was to evaluate the prevalence and trend of depression among U.S. veterans and evaluate potential exploratory variables that may contribute.

METHODS: Data were from six cycles, 2005-2016, of the National Health and Nutrition Examination Survey (NHANES). Veteran status of depression was self-reported using the Patient Health Questionnaire. Rao-Scott χ^2 test measured bivariate association of depression and exploratory variables (age, gender, race/ethnicity, poverty, and education). Cochran-Armitage trend test assessed depression prevalence time-trends from 2005 to 2016.

RESULTS: Over a two-week period, 16.3% of veterans spent at least half of the days feeling tired or having little energy. Also, over 15.0% of veterans reported having trouble sleeping or sleeping too much on more than half of the days (6.5%) or nearly every day (9.1%). The overall prevalence of depression among veterans peaked in 2011-2012 at 12.3%. Among female veterans, there is a general increasing prevalence of depression, escalating from 9.0% in the 2007-2008 cycle to 14.8% in the 2015-2016 cycle. White veterans consistently had a higher prevalence of depression compared to Black and Hispanic veterans.

LIMITATIONS: NHANES data were only able to assess noninstitutionalized individuals.

CONCLUSIONS: Results indicate that disparities in prevalence of depression existed among U.S. veterans. Cost-effective strategies are needed to help prevent and treat depression among U.S. veterans.

OTHER RESEARCH OF INTEREST (Continued)

Ten-Year Prevalence of Cognitive Impairment Diagnoses and Associated Medical and Psychiatric Conditions in a National Cohort of Older Female Veterans.

Lwi SJ[1], Barnes DE[2], Xia F[3], Peltz C[3], Hoang T[3], Yaffe K[4].

Am J Geriatr Psychiatry. **2018 Dec 13.** pii: S1064-7481(18)30601-8. doi: 10.1016/j.jagp.2018.12.015. PMID: 30704839. [Epub ahead of print]

OBJECTIVE: Veterans are at risk for dementia because of elevated general risk factors and exposure to military risk factors; however, few studies have focused on female veterans despite their growing numbers. We sought to characterize the 10-year prevalence of cognitive impairment (i.e., mild cognitive impairment and dementia) and associated conditions in older female veterans.

METHODS: Data were extracted from Veterans Health Administration medical records of 168,111 female veterans aged 65 and older. Cognitive impairment (CI) diagnoses were defined using International Classification of Diseases, Ninth Revision (ICD-9) codes or dementia medication prescriptions. Medical comorbidities and psychiatric conditions were determined using ICD-9 codes occurring within 2 years of CI diagnosis or the last recorded medical encounter for veterans without CI.

RESULTS: Ten-year prevalence was 1.8% (3,075) for mild cognitive impairment (MCI) diagnoses and 8.1% (13,653) for dementia diagnoses. Prevalence increased with age (MCI age 65: 1.4%; age 85+: 2.7%; dementia age 65: 2.5%; age 85+: 17.7%); 37.3% had dementia subtype diagnoses, with Alzheimer's disease being the most prevalent (72.7%). 47.7% of veterans with CI had at least one medical comorbidity, whereas 22.5% had at least one psychiatric condition.

CONCLUSION: Few studies have characterized the prevalence of cognitive impairment in female veterans despite the expected increases in CI and impending demographic shifts in the military. The high prevalence of medical and psychiatric conditions in female veterans with CI highlights their healthcare burden and emphasizes the need for further investigations into the prevention, treatment, and care of cognitive impairment in this understudied population.

Pragmatic trial of brief warrior renew group therapy for military sexual trauma in VA primary care.

Katz LS[1], Sawyer WN[1].

Psychol Serv. **2019 Jan 24**. doi: 10.1037/ser0000325. PMID: 30676045. [Epub ahead of print]

This is a pragmatic trial of a brief version of Warrior Renew, an emerging evidence-based treatment for military sexual trauma (MST) delivered in a Department of Veterans Affairs women's health clinic primary care setting. The full protocol meets twice a week for 12 weeks (24 sessions); however, Brief Warrior Renew meets for 8 sessions. Brief Warrior Renew is a manualized protocol addressing coping skills for affect management (e.g., triggers and anxiety) and unique aspects of MST including anger-resentments due to injustice-betrayal, and self-blame. It also addresses interpersonal factors such as relationship patterns. In this evaluation, 39 female veterans enrolled, 38 started, and 30 completed Brief Warrior Renew treatment (21% attrition). Participant scores reflected significant decreases of anxiety, depression, posttraumatic stress disorder, and negative thinking with large to very large effect sizes. Of the sample, 73.3% had reliable clinical change in their reports of negative thinking. This brief treatment appears to be feasible and well tolerated by veterans in a primary care setting. Results suggest formal investigation of this brief protocol is warranted.

OTHER RESEARCH OF INTEREST (Continued)

Direct Electrical Stimulation of Lateral Orbitofrontal Cortex Acutely Improves Mood in Individuals with Symptoms of Depression.

Rao VR[1], Sellers KK[2], Wallace DL[2], Lee MB[2], Bijanzadeh M[2], Sani OG[3], Yang Y[3], Shanechi MM[3], Dawes HE[4], Chang EF[5].

Curr Biol. **2018 Dec 17**;28(24):3893-3902.e4. doi: 10.1016/j.cub.2018.10.026. PMID: 30503621. Epub 2018 Nov 29.

Mood disorders cause significant morbidity and mortality, and existing therapies fail 20%-30% of patients. Deep brain stimulation (DBS) is an emerging treatment for refractory mood disorders, but its success depends critically on target selection. DBS focused on known targets within mood-related frontostriatal and limbic circuits has been variably efficacious. Here, we examine the effects of stimulation in orbitofrontal cortex (OFC), a key hub for mood-related circuitry that has not been well characterized as a stimulation target. We studied 25 subjects with epilepsy who were implanted with intracranial electrodes for seizure localization. Baseline depression traits ranged from mild to severe. We serially assayed mood state over several days using a validated questionnaire. Continuous electrocorticography enabled investigation of neurophysiological correlates of mood-state changes. We used implanted electrodes to stimulate OFC and other brain regions while collecting verbal mood reports and questionnaire scores. We found that unilateral stimulation of the lateral OFC produced acute, dose-dependent mood-state improvement in subjects with moderate-to-severe baseline depression. Stimulation suppressed low-frequency power in OFC, mirroring neurophysiological features that were associated with positive mood states during natural mood fluctuation. Stimulation potentiated single-pulse-evoked responses in OFC and modulated activity within distributed structures implicated in mood regulation. Behavioral responses to stimulation did not include hypomania and indicated an acute restoration to non-depressed mood state. Together, these findings indicate that lateral OFC stimulation broadly modulates mood-related circuitry to improve mood state in depressed patients, revealing lateral OFC as a promising new target for therapeutic brain stimulation in mood disorders.

Cortical control of a tablet computer by people with paralysis.

Nuyujukian P[1,2,3,4,5,6], Albites Sanabria J[7,8], Saab J[7,8,9], Pandarinath C[1,2,10,11], Jarosiewicz B[1,2,8,12], Blabe CH[1], Franco B[13], Mernoff ST[9,14], Eskandar EN[15,16], Simeral JD[7,8,9,13], Hochberg LR[7,8,9,13,17], Shenoy KV[2,3,4,5,6,18,19], Henderson JM[2,4,5].

PLoS One. **2018 Nov 21**;13(11):e0204566. doi: 10.1371/journal.pone.0204566. PMCID: PMC6248919. PMID: 30462658. eCollection 2018.

General-purpose computers have become ubiquitous and important for everyday life, but they are difficult for people with paralysis to use. Specialized software and personalized input devices can improve access, but often provide only limited functionality. In this study, three research participants with tetraplegia who had multielectrode arrays implanted in motor cortex as part of the BrainGate2 clinical trial used an intracortical brain-computer interface (iBCI) to control an unmodified commercial tablet computer. Neural activity was decoded in real time as a point-and-click wireless Bluetooth mouse, allowing participants to use common and recreational applications (web browsing, email, chatting, playing music on a piano application, sending text messages, etc.). Two of the participants also used the iBCI to "chat" with each other in real time. This study demonstrates, for the first time, high-performance iBCI control of an unmodified, commercially available, general-purpose mobile computing device by people with tetraplegia.

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