



PRACTICE-CHANGING UPDATES

ARTICLES

1 [Safety and efficacy of midazolam nasal spray in the outpatient treatment of patients with seizure clusters: An open-label extension trial.](#)

Wheless JW, Meng TC, Van Ess PJ, Detyniecki K, Sequeira DJ, Pullman WE.

Epilepsia. 2019 Sep;60(9):1809-1819.

PMID: 31353457

The safety and efficacy of intranasal midazolam (MDZ-NS) has been shown in a previous phase 3, randomised, double-blind, placebo-controlled trial. This open-label extension trial evaluated safety and seizure-related outcomes with repeated intermittent use of single-dose MDZ-NS in the group of patients who completed the aforementioned trial. Caregivers administered MDZ-NS 5mg when patients experienced SCs and a 2nd dose could be given if seizures did not terminate within 10 minutes or recurred within 10 minutes-6 hours. Main outcome of treatment success (defined as seizure termination within 10mins and no recurrence 10mins-6hours after drug administration) was achieved in 55% and 80% of patients receiving 1 and 2 doses of MDZ-NS, respectively, regardless of treated episode number. Treatment-emergent adverse events (TEAEs) were reported in 57.1% of patients and mostly nasal discomfort and somnolence. None reported treatment-related respiratory depression, drug abuse or dependence. Results show repeated, intermittent, acute treatment of patients experiencing SCs with MDZ-NS in the outpatient setting is well tolerated over an extended period, with maintenance of efficacy suggesting no development of tolerance.

TECHNOLOGY AND MEDICINE

ARTICLES

1 [Does Use of Electronic Alerts for Systemic Inflammatory Response Syndrome \(SIRS\) to Identify Patients With Sepsis Improve Mortality?](#)

Seetharaman S, Wilson C, Landrum M, Qasba S, Katz M, Ladikos N, Harris JE, Galiatsatos P, Yousem DM, Knight AM et. al

Am J Med. 2019 Jul;132(7):862-868.

PMID: 30831065

A retrospective, observational, cohort study to determine if use of automated electronic alerts for earlier identification (and therefore antibiotic administration) of patients with Systemic Inflammatory Response Syndrome (SIRS) and evidence of organ dysfunction, would improve mortality. Results showed no significant association between time from BPA (Best Practice Alert) to antibiotic administration or mortality, and that BPAs may not only misclassify patients with SIRS as having sepsis, but time to antibiotic administration in patients identified by it as meeting SIRS criteria with evidence of end-organ dysfunction, did not affect 30-day mortality. Patients with BPA alerts had in fact higher rates of antibiotic use and Clostridium Difficile infection.



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NEUROLOGY

ARTICLES

- 1 [Recent developments in drug-induced movement disorders: a mixed picture](#)
Stewart A Factor, Pierre R Burkhard, Stanley Caroff, Joseph H Friedman, Connie Marras, Michele Tinazzi, Cynthia L Comella
Lancet Neurol. 2019 Sep; 18(9):880-890
PMID: 31297947

A large and ever-growing number of medications (including the second-generation antipsychotics) are associated with debilitating side-effects ranging from tardive syndromes and parkinsonism to potentially fatal acute syndromes. This review highlights recent developments in the diagnosis and treatment of drug-induced movement disorders- from the use of dopamine transporter imaging for drug-induced parkinsonism, to the approval of the first drugs indicated for tardive syndromes (valbenazine and deutetrebazine which have demonstrated improved patient outcomes), for example.
- 2 [Volitional Suppression of Parkinsonian Resting Tremor.](#)
Blakemore RL, MacAskill MR, Myall DJ, Anderson TJ.
Mov Disord Clin Pract. 2019 Jul 1;6(6):470-478.
PMID: 31392248

It has been clinically observed that some patients with Parkinson's disease (PD) are able to suppress their tremor at will for brief periods through conscious mental processes. This study is the first detailed, systematic investigation of voluntary tremor suppression in PD. Tremor characteristics were assessed via triaxis accelerometry of the index finger of the more-affected hand and surface EMG measuring neuromuscular activity of select forearm muscles. It was found that attempted voluntary tremor suppression reduced tremor amplitude and relative EMG power, with increased tremor frequency of the acceleration and EMG signals. The data suggest exertion of significant conscious control over Parkinsonian resting tremor is possible.
- 3 [Associations between cerebrovascular risk factors and parkinson disease.](#)
Kummer BR, Diaz I, Wu X, Aaroe AE, Chen ML, Iadecola C, Kamel H, Navi BB.
Ann Neurol. 2019 Aug 29. doi: 10.1002/ana.25564.
PMID: 31464350

A retrospective study of 1,035,536 patients, to determine whether cerebrovascular risk factors (CVRF) are associated with subsequent diagnosis of Parkinson's disease (PD) and whether these associations are similar in magnitude to those with subsequent diagnosis of Alzheimer's disease (AD). Marginal structural Cox models adjusting for time-dependent confounding were used to characterise the association between exposures and outcomes of- a new diagnosis of idiopathic PD (primary) and a new diagnosis of AD (secondary). Results indicate that CVRFs are associated with PD, with the strength of this association being comparable to that with AD.



4 [PET-detectable tau pathology correlates with long-term neuropsychiatric outcomes in patients with traumatic brain injury](#) FULL ARTICLE ACCESS

Keisuke Takahata, Yasuyuki Kimura, Naruhiko Sahara, Shunsuke Koga, Hitoshi Shimada, et. al

Brain, 2019 Sep 02. pii: awz238.

PMID: pending

The link between tau deposition and neurodegenerative disorder following traumatic brain injury (TBI) has been confirmed by post-mortem studies. However, the possibility of an association between tau lesion topology with late-onset psychiatric symptoms in patients with TBI has not been explored. This study assessed tau deposits in long-term survivors of TBI by PET with 11C-PBB3, and evaluated those associations with late-life neuropsychiatric outcomes. Results showed that increased 11C-PBB3 binding capacity was associated with late-onset neuropsychiatric symptoms following TBI. In particular, a close correlation was found between psychosis and 11C-PBB3 binding capacity in the white matter.

5 [Predictors of Acute, Rehabilitation and Total Length of Stay in Acute Stroke: A Prospective Cohort Study](#). FULL ARTICLE ACCESS

Ng YS, Tan KH, Chen C, Senolos GC, Chew E, Koh GC.

Ann Acad Med Singapore. 2016 Sep;45(9):394-403.

PMID: 27748786

A prospective, cohort study of 1277 patients to identify predictors of post-stroke acute as well as rehabilitation length of stays (LOS). Patients were classified as having a short LOS if < 7 days, and long if > 7 days. It was found that patients with haemorrhagic strokes and anterior circulation infarcts had significantly longer acute, rehabilitation and total LOS. Patients with short acute LOS had fewer medical complications while achieving similar functional independence measure (FIM) scores, compared to those with longer acute LOS - suggesting earlier transfer of patients (where appropriate) from acute care to rehabilitation units allows for rehabilitation efficacy while minimising development of medical complications.

6 [Self-managed, computerised speech and language therapy for patients with chronic aphasia post-stroke compared with usual care or attention control \(Big CACTUS\): a multicentre, single-blinded, randomised controlled trial](#) FULL ARTICLE ACCESS

Rebecca Palmer, Munyaradzi Dimairo, Cindy Cooper, Pam Enderby, Marian Brady, Audrey Bowen, Nicholas Latimer et. al

Lancet Neurol. 2019 Sep; 18(9):821-833

PMID: 31397288

Post-stroke aphasia may improve over many years with speech and language therapy, but the latter is often less readily available from a few months after stroke. The study assessed the clinical efficacy of self-managed, computerised speech and language therapy (CSLT) as a potentially more sustainable and cost-effective therapeutic strategy in the long-term. It was found that CSLT in addition to usual care resulted in clinically significant improvement in personally-relevant word finding but not an improvement in conversation.



- 7 [Opening of ATP-sensitive potassium channels causes migraine attacks: a new target for the treatment of migraine.](#)
Al-Karagholi MA, Hansen JM, Guo S, Olesen J, Ashina M
Brain. 2019 Jul 10. pii: awz199.
PMID: 31292608
- A randomised, double-blind, placebo-controlled study investigated the opening of ATP-sensitive potassium channels (KATP) as a possible mechanism causing migraine attacks, with potential for exploring a new therapeutic target. Patients were given KATP channel opener Levromakalim, before incidence and severity of migraine attacks and headaches compared with that of placebo. All patients given Levromakalim developed migraine attacks- 94% more than placebo- suggesting a key role of KATP channels in migraine pathophysiology and the therapeutic potential of KATP channel-blockers in migraine treatment.
- 8 [High dose vitamin D exacerbates central nervous system autoimmunity by raising T-cell excitatory calcium.](#) FULL ARTICLE ACCESS
Darius Häusler, Sebastian Torke, Evelyn Peelen, Thomas Bertsch, Marija Djukic, Roland Nau, Catherine Larochelle et. al
Brain. 2019 Jul 13. pii: awz190.
PMID: 31302671
- Poor vitamin D status is linked to higher relapse rate and earlier disability in multiple sclerosis (MS) patients, who are therefore often prescribed cholecalciferol. This study examined the correlation between vitamin D status and central nervous system (CNS) autoimmunity. Mice were fed varying doses of cholecalciferol to represent deficiency, modest and excessive supplementing of vitamin D in MS patients. Compared to vitamin D-deprived mice, those given moderate supplementation had reduced severity of subsequent autoimmune encephalomyelitis. Mice with vitamin D levels >200nm/l however, developed fulminant autoimmune encephalomyelitis. Findings suggest moderate vitamin D levels have a regulatory effect, but continuous high dose vitamin D could trigger MS disease activity by raising mean levels of T-cell excitatory calcium.
- 9 [Chronic dengue virus encephalitis in a patient with progressive dementia with extrapyramidal features](#)
Johnson TP, Larman HB, Lee MH, Whitehead SS, Kowalak J, Toro C, Lau CC, Kim J, Johnson KR, Reoma LB, Faustin A et. al
Ann Neurol. 2019 Aug 28. doi: 10.1002/ana.25588.
PMID: 31461177
- A case report of a patient presenting with progressive dementia, extrapyramidal signs and chronic inflammation. Dengue virus was not detected in the serum or cerebrospinal fluid (CSF), but found in brain tissue post-mortem. PCR and sequencing of the brain biopsy sample taken 33 months ante-mortem was positive for dengue virus, indicating chronic infection despite robust immune response and no evidence of immunodeficiency. Chronic dengue viral infections have not been reported, but findings suggest dengue viral infections may persist in the CNS and should be considered in patients with progressive dementia and extrapyramidal features.

SELF-LEARNING MODULES

Check out the Neurology [Self-Learning Modules](#) on the AMS website!

Unlimited attempts, with 5 CME points awarded on successful completion of each module.

