

Biomarker could indicate safety risk for the sleep deprived

Lack of sleep can be dangerous, but as sleepy individuals are often unaware of their performance impairments, there is a critical need for objective measures of deficits resulting from sleepiness to prevent accidents. New research shows that a range of eye-movement tests provides a reliable biomarker of individual acute sleep loss (<https://doi.org/10.1113/JP277779>).

The research found that a set of easily-obtainable eye-movement measures could be used to provide a sensitive and reliable tool to detect small neural deficits. Importantly, these measures could even be used to distinguish sleep-related impairment from that resulting from alcohol consumption or brain injury.

Low vitamin D levels linked to non-motor symptoms in patients with Parkinson's disease

In a study of 182 patients with Parkinson's disease and 185 healthy controls, patients with Parkinson's disease had significantly lower levels of vitamin D in their blood (<https://doi.org/10.1111/ane.13141>). Also, patients with lower vitamin D levels were more likely to fall, and to experience sleep problems, depression and anxiety.

The findings suggest that vitamin D supplementation may help to treat non-motor symptoms associated with Parkinson's disease.

'As various non-motor symptoms place a burden on individuals with Parkinson's disease and their caregivers, vitamin D might be a potential add-on therapy for improving these neglected symptoms,' said senior author Dr Chun-Feng Liu, of the Second Affiliated Hospital of Soochow University, in China.

The study also looked at whether serum vitamin D levels correlated with bone mineral density of the lumbar spine and femoral neck in patients with Parkinson's disease, but no association was found.

Oral appliances may effectively treat specific types of obstructive sleep apnoea

Researchers from Harvard Medical School and Brigham and Women's Hospital in Boston have identified five traits that appear to determine the effectiveness of an oral appliance in treating obstructive sleep apnoea (Bamagoos et al, 2019).

The researchers analysed polysomnographic data already gathered from 93 adults (average age 56 years) who were diagnosed with moderate to severe obstructive sleep apnoea, and found that patients without severe collapsibility benefitted more from the oral appliance than those with this trait. Those with a weaker reflex response of the throat muscles that act to maintain an open airway (lower muscle compensation) also benefitted more than those with a stronger reflex response. Patients with very mild collapsibility, indicating deficits in other traits, responded less well.

The researchers also found that three traits unrelated to the upper airway helped predict which patients would respond less well to an oral appliance: higher loop gain, lower arousal



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threshold and higher ventilatory response to arousal.

Senior author Dr Scott Sands, assistant professor of medicine at Harvard Medical School and Brigham and Women's Hospital in Boston, commented: 'Since oral appliances work by improving the collapsibility of the upper airway, patients without really severe collapsibility are more likely to benefit from an oral appliance, while those with sleep apnoea caused by other traits, such as exaggerated reflex responses to

drops in oxygen levels, are less likely to benefit.'

The team concluded that quantifying obstructive sleep apnoea traits using clinical polysomnography could identify an endotype-based subgroup of patients that is highly responsive to oral appliance therapy, but noted that prospective validation is warranted.

Bamagoos AA, Cistulli PA, Sutherland K et al.

Polysomnographic endotyping to select obstructive sleep apnea patients for oral appliances. *Ann Am Thorac Soc.* 2019 Aug 9. <https://doi.org/10.1513/AnnalsATS.201903-190OC>

Peripheral T helper cells may have a role in the development of type 1 diabetes

A recently described T-cell subset, peripheral T helper cells, may have a role in the development of type 1 diabetes. The frequency of circulating peripheral T helper cells was observed to be increased both in children with recently diagnosed type 1 diabetes and in healthy children who later progressed to type 1 diabetes (Ekman et al, 2019).

Earlier work demonstrated that the frequency of blood follicular helper T cells is increased in children close to the onset of type 1 diabetes. A similar ability to activate B cells was recently attributed to a novel T-cell subset. These peripheral helper T cells resemble follicular helper T cells, but express receptors that enable them to migrate to inflamed tissues.

This study suggests a role for peripheral helper T cells in the development of type 1 diabetes. The frequency of these cells was

increased in the blood of children with recently diagnosed type 1 diabetes as well as healthy, autoantibody-positive children. Importantly, the frequency was most clearly increased in autoantibody-positive children who later developed type 1 diabetes.

'Based on our results, it is possible that peripheral helper T cells may have a role in the development of type 1 diabetes. This information could be employed in the development of better methods to predict type 1 diabetes risk and new immunotherapies for the disease,' noted early stage researcher Ilse Ekman from the University of Eastern Finland.

Ekman I, Ihantola EL, Viisanen T et al. Circulating CXCR5-PD-1^{hi} peripheral T helper cells are associated with progression to type 1 diabetes. *Diabetologia.* 2019 Sep;62(9):1681-1688. <https://doi.org/10.1007/s00125-019-4936-8>

Report highlights the value of epilepsy specialist nurses in caring for people living with epilepsy

A new report shows the value of epilepsy specialist nurses in caring for people living with epilepsy (<https://www.epilepsy.org.uk/sites/epilepsy/files/research/The%20ESPENTE%20Study%208.7.19%20Version%201.pdf>).

Commissioned by the charity Epilepsy Action, *Epilepsy Specialist Nurses The Evidence: a Systematic Mapping Review* looks into all the evidence of the impact epilepsy specialist nurses have in the care of epilepsy patients.

Epilepsy specialist nurses provide a first point of contact for specialist advice and support to help patients – and their families and carers – manage their epilepsy. They also provide specialist nursing care focusing on seizure reduction, preparation and aftercare



Epilepsy Specialist Nurses The Evidence (ESPENTE): a Systematic Mapping Review

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for treatments, and guide patients through the referral process to specialist clinics and management of drug doses.

A key outcome to improve quality of life for epilepsy patients is 'seizure freedom' and available data suggests up to 70% of people living with epilepsy could be seizure free. However, the national average in the UK is believed to be closer to 50%. The 20% difference between those who could be seizure free and those

who actually are is known as the treatment gap.

In areas where there is little or no epilepsy specialist nurse service provision, patients rely on appointments with consultants but patients are often on long waiting lists with little support in between appointments; slowing the progress in the management of a patient's epilepsy.

Magnetic resonance imaging vs mammography for breast cancer screening in women with familial risk

Approximately 15% of all breast cancers occur in women with a family history of breast cancer, but for whom no causative hereditary gene mutation has been found. A multicentre, randomized controlled trial (FaMRIsc) carried out in the Netherlands compared magnetic resonance imaging screening with mammography in women with familial risk ([https://doi.org/10.1016/S1470-2045\(19\)30275-X](https://doi.org/10.1016/S1470-2045(19)30275-X)).

Women were eligible to participate if they were aged 30–55 years and had a cumulative lifetime breast cancer risk of at least 20% because of a familial predisposition, but were BRCA1, BRCA2 and TP53 wild-type. Participants were randomly allocated to receive either annual magnetic resonance imaging and clinical breast examination plus biennial mammography (magnetic resonance imaging group) or annual mammography and clinical breast examination (mammography group). Primary outcomes were number, size and nodal status of detected breast cancers.

A total of 1355 women provided consent for randomization, of which 675 women were

randomly allocated to the magnetic resonance imaging group and 680 to the mammography group. Of an additional 231 women opting to be in a registration group 218 were in the mammography registration group and 13 were in the magnetic resonance imaging registration group.

More breast cancers were detected in the magnetic resonance imaging group than in the mammography group (40 vs 15; $P=0.0017$). Invasive cancers were smaller in the magnetic resonance imaging group than in the mammography group and less frequently node positive. Tumour stages of the cancers detected at incident rounds were significantly earlier in the magnetic resonance imaging group and node-positive tumours were less frequent. One patient in the mammography registration group died from breast cancer during follow up.

Magnetic resonance imaging screening detected cancers at an earlier stage than mammography, although the advantages of the this screening approach might be at the cost of more false-positive results, especially at high breast density.

Last weeks before birth important for speech development

An interdisciplinary working group has found that full-term newborns can discriminate between speech and non-speech sounds the day after they are born (<https://doi.org/10.1016/j.dcn.2019.100679>). In contrast, many preterm babies still could not discriminate between speech and non-speech sounds by their expected delivery date.

Taking proton pump inhibitors and other gastric acid inhibitors could trigger allergies

Quantitative prescribing data from Austria show that drugs which block gastric acid production (especially proton pump inhibitors) correlate with subsequent prescriptions for anti-allergy medication (<https://doi.org/10.1038/s41467-019-10914-6>). This validates previous epidemiological and experimental findings that these drugs could intensify or even trigger allergies.

NHS approves app to tackle cancer-related fatigue

Untire (www.untire.me) has been approved by the NHS, and can be downloaded for free via the NHS Apps Library. The app aims to tackle cancer-related fatigue – one of the most common side effects of cancer and its treatment – by 'help[ing] users gain better control of their energy levels by getting and keeping them mentally and psychologically active.'

No benefit of faecal microbiota transplantation for diarrhoea-predominant irritable bowel syndrome

Faecal microbiota transplantation has shown promise in alleviating the symptoms of irritable bowel syndrome, but controlled data on this are scarce.

A double-blind, randomized, placebo-controlled crossover trial was carried out in patients aged 18–65 years with moderate-to-severe diarrhoea-predominant irritable bowel syndrome ([https://doi.org/10.1016/S2468-1253\(19\)30198-0](https://doi.org/10.1016/S2468-1253(19)30198-0)). Patients were randomly assigned to receive faecal microbiota transplantation capsules followed by identical-appearing placebo capsules, or placebo capsules followed by faecal microbiota transplantation capsules over 3 days. The trial was terminated during recruitment because results from an interim analysis revealed futility.

Faecal microbiota transplantation was safe, but did not induce symptom relief at 12 weeks compared with placebo. Further studies are needed to determine the efficacy of faecal microbiota transplantation for diarrhoea-predominant irritable bowel syndrome.

Small association between major surgical admissions and the age-related cognitive trajectory

A prospective longitudinal cohort study was carried out in the UK to quantify the association between major surgery and the age-related cognitive trajectory (Krause et al, 2019).

The study included 7532 adults with as many as five cognitive assessments between 1997 and 2016 in the Whitehall II study, with linkage to hospital episode statistics. Exposures of interest included any major hospital admission, defined as requiring more than one overnight stay during follow up.

The primary outcome was the global cognitive score established from a battery of cognitive tests encompassing reasoning, memory, and phonemic and semantic fluency. The odds of substantial cognitive decline induced by surgery defined as more than 1.96 standard deviations from a predicted trajectory (based on the first three cognitive waves of data) was also calculated.

After accounting for the age-related cognitive trajectory, major surgery was associated with a small additional cognitive decline, equivalent on average to less than 5 months of aging (95% credible interval 0.01–0.73 years). In comparison, admissions for medical conditions and stroke were associated with 1.4 (1.0–1.8) and 13 (9.6–16) years of aging respectively. Substantial cognitive decline occurred in 2.5% of participants with no admissions, 5.5% of surgical admissions and 12.7% of medical

admissions. Compared with participants with no major hospital admissions, those with surgical or medical events were more likely to have substantial decline from their predicted trajectory (surgical admissions odds ratio 2.3, 95% credible interval 1.4–3.9; medical admissions 6.2, 3.4–11.0).

The authors emphasised the robustness of these findings, as the sample size is larger and had longer follow-up than previous studies, providing greater power to estimate the association between surgery and the cognitive trajectory. The study also examined admissions for medical conditions separately from surgical admissions, as considering them together could exaggerate any association with surgery.

Major surgery is associated with a small, long-term change in the average cognitive trajectory that is less profound than for major medical admissions. The odds of substantial cognitive decline after surgery was about doubled, although this was lower than that for medical admissions. This information should be conveyed to patients and be weighed against the potential health and quality of life benefits of surgery during informed consent discussions with patients.

Krause BM, Sabia S, Manning HJ, Singh-Manoux A, Sanders RD. Association between major surgical admissions and the cognitive trajectory: 19 year follow-up of Whitehall II cohort study. *BMJ*. 2019 Aug 7;366:l4466. <https://doi.org/10.1136/bmj.l4466>

Methotrexate persistence and adverse drug reactions in patients with juvenile idiopathic arthritis

An analysis aimed to calculate methotrexate monotherapy persistence and describe the occurrence of and factors associated with the development of adverse drug reactions with methotrexate (<https://doi.org/10.1093/rheumatology/kez048>).

Patients with juvenile idiopathic arthritis starting methotrexate monotherapy were included. Patient characteristics, treatment details and adverse drug reaction occurrence were collected at treatment start, 6 months, 1 year and annually. Treatment exposure was calculated from methotrexate start

until methotrexate monotherapy cessation, last follow up or the cut-off, whichever came first. Survival analysis assessed the time on methotrexate monotherapy and the time to the first adverse drug reaction on methotrexate monotherapy within 2 years. Multivariable logistic regression assessed characteristics associated with any adverse drug reaction and specifically with gastrointestinal adverse drug reactions.

A total of 577 patients started methotrexate. At 2 years, 310 (54%) were no longer on methotrexate monotherapy. Over this time, 212 (37%) patients

experienced one or more adverse drug reaction; commonly gastrointestinal or elevated liver enzymes. Lower physician global assessment and older age predicted any and gastrointestinal adverse drug reactions respectively. Patients with polyarticular rheumatoid factor and juvenile idiopathic arthritis had reduced odds of both any adverse drug reaction and a gastrointestinal adverse drug reaction.

Research to identify which children will respond and/or experience adverse drug reactions is crucial to inform treatment decisions and management planning.

Septoplasty vs non-surgical management for nasal obstruction in adults with a deviated septum

An open, multicentre, pragmatic, randomized controlled trial was performed in 16 secondary and two tertiary referral hospitals in the Netherlands (van Egmond et al, 2019). Adults with nasal obstruction, a deviated septum and an indication for septoplasty were randomly allocated to receive either septoplasty with or without concurrent turbinate surgery or non-surgical management. Patients were stratified by sex, age and deviation severity. The primary outcome was health-related quality of life at 12 months.

Over 3 years, 203 participants were randomly assigned to receive either septoplasty with or without concurrent turbinate surgery ($n=102$) or non-surgical management ($n=101$), and 189 participants were analysed at 12 months. At 12 months, the mean score on the Glasgow Health Status Inventory of patients assigned to septoplasty was 72.2 (standard deviation 12.2) and for those assigned to non-surgical management was 63.9 (standard deviation 14.5, mean difference 8.3, 95% confidence interval 4.5–12.1), favouring septoplasty. Septal abscess occurred



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in one surgical patient and septal perforation in two surgical patients.

The authors concluded that septoplasty is more effective than non-surgical management for nasal obstruction in adults with a deviated septum. This effect was sustained up to 24 months of follow up.

Commenting on the findings, Dr Niels van Heerbeek, Department of Otorhinolaryngology, Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, Netherlands,

said: ‘Patients with a deviated septum breathe more easily after this operation and their quality of life improves, but the effects of this procedure have never been systematically investigated. We are delighted to have demonstrated that the most frequently performed ear, nose, and throat operation in adults is effective.’

van Egmond MMHT, Rovers MM, Hannink G, Hendriks CTM, van Heerbeek N. Septoplasty with or without concurrent turbinate surgery versus non-surgical management for nasal obstruction in adults with a deviated septum: a pragmatic, randomised controlled trial. *Lancet*. 2019 Jul 27;394(10195):314–321. [https://doi.org/10.1016/S0140-6736\(19\)30354-X](https://doi.org/10.1016/S0140-6736(19)30354-X)

Increased risk of cardiovascular disease for healthy 75-year-olds who stop taking statins

A nationwide study of 120 173 people in France, who were aged 75 years between 2012 and 2014 and had been taking statins continuously for 2 years, has found that those who stopped taking their statins had a 33% increased risk of being admitted to hospital with heart or blood vessel problems during an average follow-up period of 2.4 years (Giral et al, 2019).

The study is the first to evaluate the impact of discontinuing statins taken for primary prevention in older people. Dr Philippe Giral, an endocrinologist specialist in prevention of cardiovascular disease at Pitié-Salpêtrière Hospital, Paris, France, who led the research said that although further, randomized studies

are needed before guidelines can be updated, he would advise elderly people who are taking statins to prevent cardiovascular disease to continue taking them.

‘To patients, we would say that if you are regularly take statins for high cholesterol, we would recommend you don’t stop the treatment when you are 75. To doctors, we would recommend not stopping statin treatment given for primary prevention of cardiovascular diseases in your patients aged 75,’ he said.

Giral P, Neumann A, Weill A, Coste J. Cardiovascular effect of discontinuing statins for primary prevention at the age of 75 years: a nationwide population-based cohort study in France. *Eur Heart J*. 2019 Jul 30. pii: ehz458. <https://doi.org/10.1093/eurheartj/ehz458>

More colorectal cancer cases being diagnosed in younger patients

A new study has found that the proportion of adults diagnosed with colorectal cancer under the age of 50 years in the United States has continued to increase over the past decade, and that younger adults are diagnosed with more advanced disease (<https://doi.org/10.1002/cncr.32347>).

To determine recent trends in colorectal cancer rates, Dr Boone Goodgame, of The University of Texas at Austin, and colleagues examined information from the National Cancer Database registry. From 2004 to 2015, 130 165 patients under 50 years of age and 1 055 598 patients over 50 years of age were diagnosed with colorectal cancer.

- Among the major findings were:
- The proportion of patients diagnosed with colorectal cancer under 50 years of age rose from 10% in 2004 to 12.2% in 2015
 - 51.6% of younger adults were diagnosed with more advanced stages of cancer (stage III/IV) vs 40% in those older than 50 years
 - Rates of colorectal cancer diagnosis in young adults increased over time regardless of income level, with the highest proportion of young adult diagnoses in the top income category
 - The proportion of colorectal cancers diagnosed in younger individuals rose in urban areas, but not in rural areas.

‘Several studies have shown that the rates of colorectal cancer in younger adults have risen slowly in the US since the 1970s, but for practicing physicians, it feels like we are seeing more and more young people with colorectal cancer now than we were even 10 years ago,’ said Dr Goodgame.

He noted that the cause of increasing rates of colorectal cancer in younger patients is unclear, but research suggests that it may be a combination of increases in body weight and changes in gastrointestinal bacteria.