HIGHLIGHTS

Highlights of the issue 5, 2019

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Editor-in-Chief

REVIEW ARTICLES

Body image in multiple sclerosis patients: a descriptive review

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https://doi.org/10.1007/s10072-019-3722-1

Multiple sclerosis is a neurological disorder—may in some patients have impact on body image; this could contribute to neurological disability, psychological distress, and can reduce quality of life. This review has been conducted on studies investigating the representation of body image.
Method The AA have researched PubMed and Web of Science databases and included screening references for studies and review articles about this topic. From the initial 316 publications, we included only 9 studies that met the search criteria. Result and conclusion The results showed that this construct has been little emphasized over time and has a significant impact on the patient.

Plasma alpha-synuclein levels in patients with Parkinson's disease: a systematic review and meta-analysis

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https://doi.org/10.1007/s10072-019-03738-1

To date, there are no definitive biomarkers for diagnose Parkinson's disease (PD). The detection of α-synuclein (α-Syn) in plasma of PD patients has yielded promising but inconclusive results. To determine the performance of α-Syn as a diagnostic biomarker of PD, we used a meta-analysis.

The AA identified 173 studies through a systematic literature review. From those, only studies reporting data on total α-Syn levels were included in the meta-analysis (10 publications, 1302 participants). Quality of studies was assessed by Newcastle-Ottawa scale.

The α-Syn levels were significantly higher in PD patients than healthy controls (standardized mean difference [SMD] = 0.778, 95% confidence interval = 0.284 to 1.272, $p = 0.002$). Similar results were found after omitting any individual study from meta-analysis, with SMD ranges from 0.318 (95% CI = 0.064 to 0.572, $p = 0.014$) to 0.914 (95% CI = 0.349 to 1.480, $p = 0.002$). According to meta-regression analysis, increased mean patients age (slope = -0.232, 95% CI = -0.456 to -0.008,

$p = 0.042$), increased total number of participants (slope $= - 0.007$, 95% CI $= - 0.013$ to -0.0004, $p = 0.038$), and increased percentage of males (slope $= - 6.444$, 95% CI $= - 10.841$ to -2.047, $p = 0.004$) were associated with decreased SMD of α-Syn levels across studies. We did not find any significant association between the SMD in α-Syn levels and disease duration, disease severity, and quality of studies. Most of studies applied ELISA assays.

Total plasma α-Syn levels were higher in PD patients than controls. Analytical factors were important limitations.

ORIGINAL ARTICLES

Withdrawal from acute medication normalizes short-term cortical synaptic potentiation in medication overuse headache

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To study the effects of a standard acute medication withdrawal program on short-term cortical plasticity mechanisms in patients with medication overuse headache (MOH).

Thirteen patients with MOH and 16 healthy volunteers underwent repetitive transcranial magnetic stimulation (rTMS) over the left motor cortex; in patients with MOH, recordings were performed before and after a 3-week medication withdrawal program. Ten trains of 10 stimuli each (120%resting motor threshold) were delivered at 1 Hz or 5 Hz in two separate sessions in a randomized order. Motor evoked potential (MEP) amplitudes were measured from the right first dorsal interosseous muscle and the slope of the linear regression line from the first to the tenth stimuli was calculated for each participant.

All subjects exhibited MEP amplitude inhibition in response to 1 Hz rTMS. Alternatively, the 5-Hz trains of rTMS inhibited rather than potentiated MEP amplitudes in patients with MOH. The physiological potentiating effect of 5 Hz rTMS on MEP amplitudes was restored after drug withdrawal and in proportion with the percentage reduction in monthly headache days in patients with MOH.

The results suggest that acute medication withdrawal normalizes brain responses in patients with MOH. Clinical improvements after medication withdrawal may reflect the reversal of neurophysiological dysfunction. Accordingly, medication withdrawal should be offered to patients with MOH as early as possible in order to prevent the development of more pronounced alterations in brain plasticity.

Recumbent stepping aerobic exercise in amyotrophic lateral sclerosis: a pilot study

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Aerobic exercise can promote neuroplastic responses in the healthy and injured brain. Although the role of exercise in amyotrophic lateral sclerosis (ALS) is debated, new evidence suggests that exercise may reduce disease progression. While common exercise modalities such as the treadmill and cycle ergometer have been explored in ALS, the safety and feasibility of a total body recumbent stepper have not been investigated. Additionally, the functional and neurophysiological effects of recumbent stepping in ALS are still unknown. Here, we investigated the safety and feasibility of a 4-week recumbent stepping program to slow disease progression in ALS and possibly facilitate neuroplasticity.

Nine individuals with ALS performed moderate intensity recumbent stepping for four weeks. Outcomes included participation satisfaction questionnaire, ALS Functional Rating Scale Revised (ALSFRS-R), clinical tests of walking and endurance, fatigue severity scale, Beck depression inventory, SF-12, and transcranial magnetic stimulation-induced motor evoked potentials (MEPs). All measurements were collected at baseline, post-intervention, and at the 1-month follow-up.

Eight participants completed the study without any adverse events. The ALSFRS-R scores were similar at the end of the study and at follow-up. No significant differences were noted for any of the clinical outcomes. MEPs were present only in two participants and changes in corticomotor excitability after exercise were minimal.

Results from this preliminary study support the safety and feasibility of 12 sessions of total body recumbent stepping in individuals with ALS.

Mutations in the SPAST gene causing hereditary spastic paraplegia are related to global topological alterations in brain functional networks

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The AA's aim was to describe the rearrangements of the brain activity related to genetic mutations in the SPAST gene.

Ten SPG4 patients and ten controls underwent a 5 min resting state magnetoencephalography recording and neurological examination. A beam former algorithm reconstructed the activity of 90 brain areas. The phase lag index was used to estimate synchrony between brain

areas. The minimum spanning tree was used to estimate topological metrics such as the leaf fraction (a measure of network integration) and the degree divergence (a measure of the resilience of the network against pathological events). The betweenness centrality (a measure to estimate the centrality of the brain areas) was used to estimate the centrality of each brain area.

The results showed topological rearrangements in the beta band. Specifically, the degree divergence was lower in patients as compared to controls and this parameter related to clinical disability. No differences appeared in leaf fraction nor in betweenness centrality.

Mutations in the SPAST gene are related to a reorganization of the brain topology.

Stroke during sleep and obstructive sleep apnea: there is a link

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The onset of ischemic stroke symptoms has been established to have a diurnal variation, with a sizeable proportion (8–28%) occurring during sleep. Obstructive sleep apnea (OSA) has been established as an important risk factor for ischemic stroke. However, data on the relationship between OSA and wake-up stroke (WUS) has been scarce. The aim of our study is to determine the relationship between OSA and WUS.

This is a case-control study conducted on acute stroke patients who presented to one of two major medical centers in Riyadh of Saudi Arabia. Those who woke up with the symptoms were labeled as WUS, and those whose stroke occurred while awake were labeled as non wake-up stroke (NWUS). The Berlin Questionnaire, which was submitted to either the patient or his/her partner, was used to determine the frequency of OSA in the two groups.

One hundred seven patients (60% males) with acute stroke were admitted between March 2016 and March 2017. Of the 40 patients with WUS, 29 (72.5%) had underlying OSA based on the Berlin Questionnaire, whereas only 30 (45%) of the 67 patients with NWUS have underlying OSA. Logistic regression analysis showed OSA is highly prevalent in the patients with WUS (OR = 3.25; 95% CI = 1.397–8.38; $p = 0.0053$).

OSA is an important risk factor for ischemic stroke during sleep. Health care providers must be vigilant in inquiring about symptoms suggestive of OSA in every ischemic stroke patient, especially the patient whose stroke occurred during sleep.

Methylation of cation–chloride cotransporters NKCC1 and KCC2 in patients with juvenile myoclonic epilepsy

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The etiology of juvenile myoclonic epilepsy (JME) is still unknown and the process of elaboration of multiple genetic mechanisms is ongoing. The aim of this study was to investigate the potential role of NKCC1 (SCL12A2) and KCC2 (SCL12A5) in JME by comparing their DNA methylation status in patients with JME versus healthy controls. Forty-nine patients with JME and 39 healthy individuals were compared for DNA methylation at the 5CpG islands. A total of 71 (81%) samples were found to have methylation in the NKCC1 gene, 36 (73%) from patients and 35 (90%) from healthy individuals. Out of the KCC2 samples, 50 (57%) were found to have methylation, 33 (67%) from patients and 17 (44%) from healthy individuals. In patients with JME, methylation of NKCC1 (73%) was lower than its methylation in the controls (90%) ($p = 0.047$). On the other hand, methylation of KCC2 in patients with JME (67%) was greater than the methylation in the controls (44%) ($p = 0.022$). Twenty-eight patients were treated with VPA and ongoing medications were not found to be associated with methylation ($p > 0.05$). In the present study, we determined significantly lower NKCC1 DNA methylation and significantly higher KCC2 DNA methylation levels in patients with JME compared with the healthy controls. This implies that NKCC1 expression can be higher and KCC2 expression can be reduced in affected people. Further studies that investigate the potential effect of DNA methylation mechanisms regulating gene expression on seizure activity and how they change JME network activity will be helpful.

Assessing seasonal dynamics of Guillain-Barré syndrome with search engine query data

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(Italy)

In previous studies, data deriving from Google Trends showed promising correlation with disease incidence trends assessed with public health control systems. The aim of this work is to use search engine query data to investigate seasonal dynamics in Guillain-Barré syndrome (GBS) in the USA.

Average Google monthly search volumes for GBS from 2008 to 2017 were analyzed for the USA overall and on regional base with generalized estimating equation models. Association with monthly historical temperature variations was tested.

Monthly search volume for GBS displayed the greatest positive anomaly for October, clustering with September and November. Region-wide analysis confirmed this pattern and showed secondary spring (Feb/Apr) subpeaks in Pacific and Midwest. Association of GBS search volume with month-to-month temperature variations showed J-shaped relationship, with the highest peak occurring in months with greatest temperature falls, and subpeak in months with sharpest temperature rises

This study represents the first approach in investigating digital epidemiology of GBS and establishing possible links with traditional epidemiology. Cold season GBS peak has been observed by some traditional studies; hypothetical pathogenic relationship with infectious antecedents is supported from finding GBS peaks clustering with greatest temperature change. Further studies are needed to compare these findings to traditional public health approaches.

BRIEF COMMUNICATION

Inflammatory cytokines expression in Wilson's disease

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Wilson's disease (WD) is an autosomal recessive inherited disorder of copper (Cu) metabolism. Inflammation is a self-defensive reaction aimed at eliminating or neutralizing injurious stimuli, and restoring tissue integrity. Copper deposition may lead to inflammation in the organs and tissues of WD patients.

The aim of this study was to compare the plasma levels of inflammatory cytokines in patients with WD and healthy group, and also to assess whether inflammatory cytokines affects the clinical manifestation of WD.

Ninety-nine patients with WD and 32 controls were recruited for this study. Ray Biotech antibody microarray was used to detect the levels of plasma inflammatory cytokines.

The results showed significant increase in T helper (Th) 1 cells (IL-2, TNF-α, and TNF-β), Th2 cells (IL-5, IL-10, and IL-13), and Th17 (IL-23) ($p < 0.05$). Higher plasma Th 1 cells (IL-2, TNF-α, and TNF-β), Th 2 cells (IL-13), and Th 17 (TGF-β1, IL-23) levels were found in neurological patients compared with control groups ($p < 0.01$). Besides, the AAs found Th 1 cells (TNF-α and TNF-β), Th 3 (TGF-β1), and Th 17 (IL-23) levels were significantly higher in hepatic and neurological patients ($p < 0.05$). In addition, the higher Th1 cells (IL-2, TNF-α, and TNF-β), Th2 cells (IL-13), and Th17 (TGF-β1, IL-23) and the course of WD were associated with the severity of the neurological symptoms for WD patients. Altogether, the results indicated that dysregulation of cytokines, mainly increased expression of cytokines and chemokines, occurred in WD patients.