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HIGHLIGHTS

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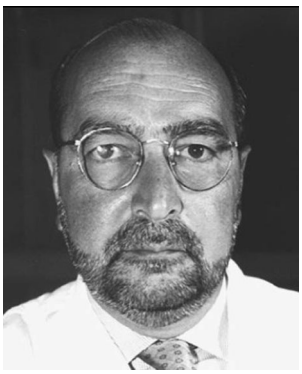

Antonio Federico
Editor-in-Chief

REVIEW ARTICLES

On the central role of mitochondria dysfunction and oxidative stress in Alzheimer's disease
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https://doi.org/10.1007/s10072-019-03863-x
Alzheimer's disease (AD) is the commonest cause of dementia, with approximately 5 million new cases occurring annually. Despite decades of research, its complex pathophysiology and etiopathogenesis presents a major hindrance to the development of an effective treatment and prevention strategy. Aging is the biggest risk factor for the development of AD, and the total number of older people in the population is going to significantly increase in the next decades, suggesting that AD incidence and prevalence is likely to increase in the future. This makes the need for a better understanding of the disease to be extremely urgent.
A search was done by accessing PubMed/Medline, EBSCO, and PsycINFO databases. The search string used was "(dementia* OR Alzheimer's) AND (pathophysiology* OR pathogenesis)". New key terms were identified (new term included "vitamin D, thyroid hormone, mitochondria dysfunction, oxidative stress, testosterone, estrogen, melatonin, progesterone, luteinizing hormone, amyloid-β (Aβ), and hyperphosphorylated tau"). The electronic databases were searched for titles or abstracts containing these terms in all published articles between January 11,965, and January 31,2019. These arch was limited to studies published in English and other languages involving both animal and human subjects.
Mitochondria dysfunction and oxidative stress play a critical role in AD etiopathogenesis and pathophysiology.
AD treatment and prevention strategies must be geared towards improving mitochondrial function and attenuating oxidative stress.

The potential roles of aquaporin 4 in amyotrophic lateral sclerosis
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https://doi.org/10.1007/s10072-019-03877-5
Aquaporin 4 (AQP4) is a primary water channel found on astrocytes in the central nervous system (CNS). Besides its function in water and ion homeostasis, AQP4 has also been documented to be involved in a myriad of acute and chronic cerebral pathologies, including autoimmune neurodegenerative diseases. AQP4 has been postulated to be associated with the incidence of a progressive neurodegenerative disorder known as amyotrophic lateral sclerosis (ALS), a disease that targets the motor neurons, causing muscle weakness and eventually paralysis. Raised AQP4 levels were noted in association with vessels surrounded with swollen astrocytic processes as well as in the brainstem, cortex, and gray matter in patients with terminal ALS. AQP4 depolarization may lead to motor neuron degeneration in ALS via GLT-1. Besides, alterations in AQP4 expression in ALS may result in the loss of blood–brain barrier (BBB) integrity. Changes in AQP4 function may also disrupt K+ homeostasis and cause connexin dysregulation, the latter of which is associated to ALS disease progression. Furthermore, AQP4 suppression augments recovery in motor function in ALS, a phenomenon thought to be associated to NGF. No therapeutic drug targeting AQP4 has been developed to date. Nevertheless, the plethora of suggestive

experimental results underscores the significance of further exploration into this area.

ORIGINAL ARTICLES

KIBRA T allele influences memory performance and progression of cognitive decline: a 7-year follow-up study in subjective cognitive decline and mild cognitive impairment

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KIBRA is a signal transducer protein, mainly expressed in the kidney and brain. A single-nucleotide polymorphism (SNP rs17070145, T → C exchange) has been linked to different cognitive function. In 2008, the AA studied 70 subjects who complained of subjective cognitive decline (SCD) and found that CT/TT carriers performed worse than CC carriers on a long-term memory test. They followed up the 70SCD subjects and also 31 subjects affected by mild cognitive impairment (MCI) for a mean follow-up time of 7 years, during which 16 SCD subjects progressed to MCI and 14 MCI subjects progressed to Alzheimer's disease (AD). Carrying the T allele was associated with MCI and with a two times-higher risk of developing MCI than CC carriers. In the SCD sample, CT/TT carriers showed a greater worsening on River mead Behavioral Memory Test (RBMT) compared to CC carriers. In the MCI sample, CT/TT carriers performed worse than CC carriers on RBMT. There is a lack of consensus on the effect of KIBRA gene variants on cognitive performances in episodic memory and on the risk of AD. The results confirm a role of T allele on progression of cognitive decline.

Clinical characteristics and factors associated with short-term prognosis in adult patients with autoimmune encephalitis of non-neoplastic etiology

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https://doi.org/10.1007/s10072-019-03883-7

Reports that autoimmune encephalitis (AE) is associated with antibodies have increased; however, little is known about the distribution of clinical symptoms, imaging changes, and prognostic factors in patients with AE of non-neoplastic etiology. Accordingly, the AA evaluated the clinical characteristics and factors associated with short-term prognosis.

From January 2016 to June 2018, 31 adult patients were diagnosed with AE of non-neoplastic etiology at Shengjing Hospital of China Medical University and their demographic and clinical characteristics were abstracted. Factors affecting disease severity and predictors of prognosis were analyzed.

Among 31 patients, 19 had anti-NMDAR, 5 had anti-GABABR, and 7 had anti-LGI1 antibody encephalitis. Status epilepticus, ataxia, and cognitive dysfunction were the most common neurological symptoms. Deep white matter (DWM) abnormalities were the most common changes observed on MRI. Logistic regression analysis indicated that conscious disturbance (odds ratio = 11.67, 95%, confidence interval 2.13–64.04; $p = 0.005$) is an independent factor associated with poor prognosis in AE.

The clinical manifestations of AE are diverse; status epilepticus, ataxia, and cognitive dysfunction are most common. The DWM of the brain, rather than the limbic lobe system, was most prone to MR signal abnormalities. Conscious disturbance may be an important predictor of poor short-term prognosis in patients with AE of non-neoplastic etiology.

Cerebrospinal fluid vitamin D-binding protein as a new biomarker for the diagnosis of meningitis

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https://doi.org/10.1007/s10072-019-03873-9

Meningitis is an inflammatory process involving meninges. It is difficult to diagnose because of the absence of a diagnostic biomarker. The AA first report here the possibility of cerebrospinal fluid (CSF) vitamin D-binding protein (VDBP) as a new biomarker for the diagnosis of meningitis.

This prospective study enrolled a total of 102 subjects (58 patients with non-neurologic disease, 17 patients with meningitis, and 27 patients with other neurologic diseases) from 2017 to 2018. CSF and blood samples were collected in pairs. Total 25(OH)D in CSF and serum and VDBP levels in serum were measured. GC genotyping was also performed to determine polymorphisms of rs4588 and rs7041. CSF total 25(OH)D and VDBP levels were compared with serum total 25(OH)D and VDBP levels according to disease (meningitis vs. non-meningitis). Receiver operating characteristic (ROC) analysis for the diagnosis of meningitis using CSF VDBP level was performed.

Mean CSF VDBP and serum VDBP levels of all patients were 1.48 ± 1.32 and 181.28 ± 56.90 μg/mL, respectively. CSF VDBP level in the meningitis disease group (3.20 ± 1.49 μg/mL) was significantly ($P < 0.001$) higher than that in other disease groups. According to ROC curve analysis, the appropriate cut-off value for CSFVDBP was 1.96 μg/mL, showing sensitivity of 82.4% and specificity of 85.9%. AUC of CSF VDBP was 0.879 (95% CI: 0.789–0.962).

CSF VDBP level showed very good diagnostic performance. It could be used as a potential biomarker for the diagnosis of meningitis.

Causes of chronic neuropathies: a single-center experience

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Chronic neuropathies are a common cause of neurological disability worldwide. However, few reports have evaluated, in real life, the prevalence of the several conditions which can cause it.

The authors reviewed informatic database for outpatient office to confirm identification of chronic neuropathy in a 3-year interval period.

Among the 100 selected patients with chronic neuropathies, almost one fifth (19%) remained idiopathic. The most common etiologies were diabetes (17%), dysimmune neuropathies (38%), and vitamin B12 deficiency (9%). In the dysimmune neuropathies group, we distinguished various etiologies, including dysimmune neuropathies associated or not with systemic autoimmune diseases (7 and 3%, respectively), chronic inflammatory polyneuropathy (CIDP) (8%), multifocal motorneuropathy (MMN) (3%), paraproteinemic (8%), celiac disease-related (6%), and paraneoplastic (3%) neuropathies.

In this report from a single neurological center, treatable causes of chronic neuropathies, such as dysimmune neuropathies, including CIDP, and celiac disease-associated neuropathy, were common. These findings suggest the utility of routine screening with blood testing for dysimmune neuropathy and celiac disease for all patients presenting with idiopathic chronic polyneuropathy in whom primary diagnostic testings had failed to identify an etiology for the disease. Significance The results indicate that patients with peripheral neuropathy could receive a benefit from being evaluated routinely in a specialized neurological center, as many of the conditions that were discovered represented potentially treatable causes of neuropathy.

The predictive dysphagia score (PreDyScore) in the short and medium-term post-stroke: a putative tool in PEG indication

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The AA performed an evaluation of dysphagia in an unselected series of strokes to identify factors causing persisting dysphagia at 1 month after onset and to formulate a predictive score.

The AA evaluated the association between dysphagia and clinical aspects (univariate analysis) at the 7th and 30th days after admission. They performed a multivariate logistic regression at the 30th day on the factors that were significant. The AA computed a simple score for predicting persistent dysphagia.

The AA recruited 249 patients. At the 7th day, 94 patients were dysphagic (37.75%). Factors associated with dysphagia included TACI (OR 3.85), mRS ≥3 (OR 4.45), malnutrition (OR 2.69), and BMI ≥20 (OR 0.52). At the 30th day, 217 patients remained in the study, and dysphagia persisted in 75 (36.76%). The factors that were associated with dysphagia were age > 74 years (OR 1.99), TACI (OR 5.82), mRS score ≥ 3 (OR 4.31), malnutrition (OR 3.27), and BMI ≥20 (OR 0.45). The multivariate analysis indicated that mRS ≥3 (OR 1.80) and BMI ≥20 (OR 0.45) remained significantly associated with dysphagia. The best correlation with dysphagia was the sum of mRS and the reciprocal of the BMI multiplied by 100 ((mRS+ 1 BMI) × 100). Using <6and> 8 as cut offs, the sensitivity was 67.03%, and the specificity 95.65%.

BMI <20 and mRS ≥3 are easily measurable bedside predictive factors of persistent dysphagia. PreDyScore showed good sensitivity and very good specificity and enables the prediction of persistent dysphagia with great accuracy in any clinical setting.