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HIGHLIGHTS

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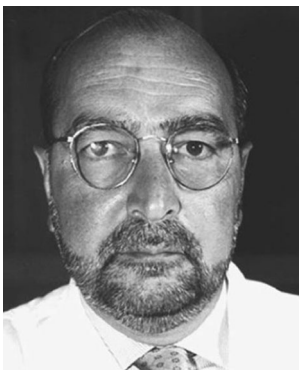

Antonio Federico
Editor-in-Chief

REVIEW ARTICLES

Influences of genetic variants on stroke recovery: a meta-analysis of the 31,895 cases

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The influences of genetic variants on functional clinical outcomes following stroke are unclear. In order to reliably quantify these influences, the AA undertook a comprehensive meta-analysis of outcomes after acute intracerebral haemorrhage (ICH) or ischaemic stroke (AIS) in relation to different genetic variants. PubMed, PsycInfo Embase and Medline electronic database s were searched up to January 2019. Outcomes, defined as favourable or poor, were assessed by validated scales (Barthel index, modified Rankin scale, Glasgow outcome scale and National Institutes of Health stroke scale). Results Ninety-two publications comprising 31,895 cases met our inclusion criteria. Poor outcome was observed in patients with ICH who possessed the APOE4 allele: OR=2.60 (95% CI=1.25–5.41, p=0.01) and in AIS patients with the GA or AA variant at the BDNF-196 locus: OR=2.60 (95% CI=1.25–5.41, p=0.01) or a loss of function allele of CYP2C19: OR=2.36 (95% CI=1.56–3.55, p<0.0001). Poor outcome was not associated with APOE4: OR=1.02 (95% CI=0.81–1.27, p=0.90) or IL6-174 G/C: OR=2.21 (95% CI=0.55–8.86, p=0.26) in patients with AIS. Conclusions It was demonstrated that recovery of AIS was unfavourably associated with variants of BDNF and CYP2C19 genes whilst recovery of ICH was unfavourably associated with APOE4 gen

Optic nerve sheath diameter: present and future perspectives for neurologists and critical care physicians

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Estimation of intracranial pressure (ICP) may be helpful in the management of neurological critically ill patients. It has been shown that ultrasonography of the optic nerve sheath diameter(ONSD) is a reliable tool for non-invasive estimation of increased intracranial pressure (ICP) at hospital admission or in intensive care. Less is known about the estimation of increased ICP and usefulness of ONSD in the prehospital setting. The aim of this review was to elucidate both prevailing and novel applications of ONSD for neurologists and critical care physicians. In this review, the AA discuss the technique and the novel approach of ONSD measurement, the clinical applications of ONSD in neurology and critical care patients. Results ONSD measurement is simple, easy to learn, and has diverse applications. ONSD has utility for ICP measurement in intracranial hemorrhage and ischemic stroke, meningitis and encephalitis, and idiopathic intracranial hypertension (IIH). It is also valuable for lesser known syndromes, where an increase of ICP is postulated, such as acute mountain sickness and posterior reversible encephalopathy syndrome. ONSD changes develop in inflammatory or ischemic optic neuropathies. Some papers demonstrate the usefulness of ONSD studies in symptomatic intracranial hypotension.

Conclusions ONSD is a safe and low-cost bedside tool with the potential of screening patients who need other neuroimaging and those who may need an invasive measurement of ICP.

Vitamin D in migraine headache: a comprehensive review on literature

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As a primary headache, migraine has been established as the first leading disability cause world wide in the subjects who aged less than 50 years. A variety of dietary supplements have been introduced for migraine complementary treatment. As an anti-inflammatory and antioxidant agent, vitamin D is one of these agents which has been of interest in recent years. Although higher prevalence of vitamin D deficiency/insufficiency has been highlighted among migraineurs compared to controls, there is not any consensus in prescribing vitamin D in clinical practice. Therefore, in the current review, in addition to observational and case-control studies, the AA also included clinical trials concerning the effects of vitamin D supplementation on migraine/headache. Based on a PubMed/MEDLINE and Science Direct database search, this review study includes published articles up to June 2019 concerning the association between migraine/headache and vitamin D status or supplementation. Results The percentage of subjects with vitamin D deficiency and insufficiency among migraineurs and headache patients has been reported to vary between 45 and 100%. In a number of studies, vitamin D level was negatively correlated with frequency of headaches. The present findings show that supplementation with this vitamin in a dose of 1000–4000 IU/d could reduce the frequency of attacks in migraineurs. Conclusion It seems a high proportion of migraine patients might suffer from vitamin D deficiency/insufficiency. Further, the current evidences show that in addition to routine drug therapy, vitamin D administration might reduce the frequency of attacks in migraineurs. However, these results have yet to be confirmed.

The diagnostic value of SNpc using NM-MRI in Parkinson's disease: meta-analysis

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The main purpose of this study was to systematically evaluate the accuracy of neuromelanin-sensitive magnetic resonance imaging (NM-MRI) in Parkinson's disease (PD) diagnosis using a meta-analysis method. In PubMed, Web of Science, Embase, and Google Scholar, the literatures were searched for the diagnostic value of neuromelanin-sensitive magnetic resonance imaging in PD. The literatures were screened in the light of Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA). Data analysis was processed by Stata 12.0 software to obtain meta-analysis, heterogeneity analysis, and publication bias. Meta-analysis results showed by using NM-MRI observed substantia nigra pars compacta (SNpc) on PD, the pooled diagnostic sensitivity and specificity were 0.82(95%CI,0.74–0.87)and0.82(95%CI,0.73–0.89), respectively. And the pooled positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were 4.58 (95% CI, 3.08–6.82) and 0.22 (95% CI, 0.16–0.31), respectively. Moreover, subgroup analysis according to the measurement criteria of SNpc showed the SNpc volume should be used as good marker for diagnosing PD. Finally, Fagan test demonstrated that when PLR was equal to 5, the posterior probability is significantly enhanced to 53%, compared with prior probability (20%). As for NLR (0.22), the prior probability is 20%, while the posterior probability remarkably dropped to 5%. In conclusion, SNpc signal detected by NM-MRI exhibited high sensitivity and specificity for diagnosis of PD, which was a high-performance imaging diagnostic method for PD. We recommend NM-MRI imaging technology to be widely used in Parkinson's diagnosis.

ORIGINAL ARTICLES

Association between rs10046, rs1143704, rs767199, rs727479, rs1065778, rs1062033, rs1008805, and rs700519 polymorphisms in aromatase (CYP19A1) gene and Alzheimer's disease risk: a systematic review and meta-analysis involving 11,051 subjects

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CYP19A1 enzyme (aromatase) encoded by CYP19A1 (cytochrome p450 family 19 subfamily a member 1) gene plays a key role in the biosynthesis of estrogen, which has been significantly associated with Alzheimer's disease (AD). To ascertain whether CYP19A1 gene polymorphisms are correlated with the susceptibility to AD, we performed this systematic review and meta-analysis of currently available studies. Materials and methods A comprehensive literature search was conducted by using PubMed, Embase, and Web of Science databases and the Cochrane Library. The association was evaluated by using odds ratios (ORs) and 95% confidence intervals (CIs) through Stata software (version 12.0). Results A total of eight articles including 39 case–control studies with 11,051 subjects including 3215 AD cases and 7836 controls were involved in this meta-analysis. By pooling all eligible studies, the

AA detected that rs10046, rs1143704, rs767199, and rs727479 polymorphisms in CYP19A1 gene were significantly associated with AD risk. A significant association between rs10046 polymorphism and AD risk was found under allele contrast, homozygous (TT vs CC: OR=1.17, 95%CI=1.02– 1.34, I2 =0.0%,P=0.026), and dominant genetic models. In addition, they observed an association between with rs1143704 polymorphism under heterozygous and dominant genetic models (TT+TA vs AA: OR=1.36, 95%CI=1.03–1.79, I2 =0.0%, P=0.033). Similar results were found in rs767199 and rs727479 polymorphisms, while null results were found for other polymorphisms. Conclusions This systematic review and meta-analysis suggested that the rs10046, rs1143704, rs767199, and rs727479 polymorphisms in CYP19A1 gene significantly increase AD susceptibility. In addition, the results demonstrated that homozygous TT genotype in rs10046, dominant AA and AG genotypes in rs767199, homozygous TT genotype in rs727479, and dominant TT and TA genotypes in rs1143704 might be the susceptibility genotypes for AD, while no associations were observed between rs1065778, rs1062033, rs1008805, and rs700519 polymorphisms and AD susceptibility

The association of low levels of nesfatin-1 and glucagon-like peptide-1 with oxidative stress in Parkinson's disease

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Oxidative stress plays a substantial role in degeneration of dopaminergic neurons at the substantia nigra. Recent reports describe nesfatin-1 and glucagon-like peptide-1 (GLP-1) as molecules with neuroprotective property that relieve oxidative stress. In this study, the AA aimed to determine the blood levels of nesfatin-1, GLP-1 and oxidative stress status in patients with PD. Material and method Forty patients with PD, followed-up at the Department of Neurology of Mugla Sitki Kocman University Training and Research Hospital, were enrolled, as well as 40 age- and sex-matched participants as a control group. They determined and comparednesfatin-1, GLP-1, total antioxidant status (TAS), and total oxidant status (TOS) levels in patients with PD and control group. Results The mean GLP-1 and nesfatin-1 values of patients with PD were lower than those of the control group, whereas their mean TOS value was higher. The mean TAS values, on the other hand, did not reveal any significant difference between the patient and the control groups. Conclusion The lower nesfatin-1 and GLP-1 levels, in addition to higher TOS levels, in patients with PD compared to those of control group suggest that the neuroprotective effects of these molecules might be related to the oxidative processes. Further studies are required to search for the impact of above named molecules on the treatment option and the likelihood that they may slow down disease progression

Analysis of the GCG repeat length in NIPA1 gene in C9orf72-mediated ALS in a large Italian ALS cohort

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Amyotrophic lateral sclerosis (ALS) is characterized by degeneration of upper and lower motor neurons. The hexanucleotide repeat expansion in C9orf72gene (C9orf72-HRE) is the most frequent genetic cause of ALS. Since many ALS pedigrees showed incomplete penetrance, several genes have been analyzed as possible modifiers. Length of the GCG repeat tract in NIPA1 (non imprinted in Prader-Willi/Angelman syndrome 1) gene has been recently investigated as a possible modifier factor for C9orf72HRE patients with contrasting findings. To disclose the possible role ofNIPA1GCG repeat length as modifier of the disease risk in C9orf72-HRE carriers, the AA analyzed a large cohort of 532 Italian ALS cases enriched in C9orf72-HRE carriers (172 cases) and 483 Italian controls. This sample size is powered (92%power,p=0.05) to replicate the modifier effect observed in literature. They did not observe higher frequency of NIPA1 long alleles (>8GCG) in C9orf72-HRE carriers (3.5%) compared with C9orf72-HRE negative patients (4.1%) and healthy controls (5%). For the latter comparison, we meta-analyzed the data with currently available literature data, and no statistically significant effect was observed (p=0.118). In conclusion, they did not confirm a role ofNIPA1 repeat length as a modifier of the C9orf72 ALS disease risk

Validation of clinical criteria for referral to head imaging in the neurologic emergency setting

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In recent decades, diagnostic imaging became an important generator of large increases in medical spending. Inappropriate head CT referrals also increase population irradiation and unnecessarily burden and frighten patients. Objective To validate previously proposed clinical criteria for referral to head imaging (age>55years, focal neurological deficit, changed mental state, nausea or vomiting, coagulation disorder, cancer) in a setting of emergency neurological service. Methods We retrospectively analyzed electronic records

of 500 consecutive referrals to neurological emergency and 500 referrals to emergency head imaging. In patients with several referrals, only results of the first evaluation were further analyzed. Thr AA calculated relations between clinical predictors, referrals, and findings of head imaging. Results Of 486 first referrals of consecutive patients, 216 (44%) were referred to the emergency, and 100 (21%) to nonemergency head imaging. Remaining 170 (35%) were not referred to head imaging. Clinical predictors of pathologic head imaging fulfilled 77%, 41%, and 43% of patients, respectively. Pathologic head imaging had 153 of 490 (31%) referred patients. Referral criteria fulfilled 146 (sensitivity 95%) of them. Intracranial pathology was found in 7 of 125 patients not fulfilling referral criteria (negative predictive value 94%): 3 reported transient neurological symptoms, 2 sudden headache, and 2 headache with nausea and vomiting. Conclusion It was confirmed utility of previously proposed clinical criteria for referral to head CT in emergency neurological setting. In addition, and was found transient neurological symptoms, sudden severe headache, and headache with nausea or vomiting as additional independent indications for emergency head imaging.

Genetic and lifestyle predictors of ischemic stroke severity and outcome

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Different models that include clinical variables and blood markers have been investigated to predict acute ischemic stroke treatment course and recovery. Aim The aim of the study was to investigate associations between lipid levels, lifestyle factors, hemostatic (F5, F2, SERPINE1, F13A1, and FGB), and atherogenic (APOA5 and ACE) gene variants and acute ischemic stroke (AIS) severity. Materials and methods This study included 250 patients with AIS in which F5, F2, SERPINE1, F13A1, FGB, APOA5, and ACE genotypes were determined. Total cholesterol (TC), high-density cholesterol, low-density cholesterol, and triglycerides concentrations were measured within 24 h of the AIS onset. Examination of the neurological deficit was done using National Institutes of Health Stroke Scale/Score (NIHSS). Results APOA5 genotype [TC+CC] was more frequent (P=0.026) in patients with the NIHSSscore ≥21. Univariateregression analysis has shown that triglycerides (OR 0.55, 95% CI 0.34–0.91; P = 0.019), obesity(0.28,95%CI0.10–0.73;P=0.010), age (OR 1.08, 95% CI 1.04–1.13; P<0.001), and APOA5 genotype (TC + CC) (OR 2.40, 95% CI 1.10–5.25; P=0.034) are significantly associated with a severe stroke. When all variables were included in model age (OR 1.06, 95% CI 1.01–1.11; P=0.018), obesity(OR0.25,95%CI0.08–0.77;P=0.016) and APOA5 genotype (TC+CC) (OR3.26,95%CI1.29–8.23;P= 0.012) remained significant for the risk of severe AIS. Conclusion APOA5 genotype (TC + CC), age, and obesity could be used as prognostic risk factors for a very severe stroke (NIHSS≥21).

Dementia trajectory for patients with logopenic variant primary progressive aphasia

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The timing of progression of logopenic variant primary progressive aphasia (lvPPA) to severe dementia has not been elucidated. To address this shortcoming, 10 patients with lvPPA were continuously followed. Patients were assessed with the annual rate of change in the Clinical Dementia Rating(CDR) sum of boxes and period from lvPPA onset to the onset of benchmark signs, including mild, moderate, or severe dementia, episodic memory deficits, topographical disorientation, difficulties with using controls for electronic appliances, and conceptual apraxia. When severe dementia was evident, we also investigated the incidence of severe cognitive and behavioral signs such as neologistic jargon, difficulties in recognizing family members, pica, and mirror sign. Results The mean time for patients to reach a particular CDR was as follows: CDRof1,4.1±1.3years post-onset; CDR2,5.7± 1.6 years; CDR 3,7.3±1.6 years. The annual rate of change in the CDR sum of boxes was3.4±1.1, corresponding to1.7 years for the CDR to increase by 1.0. Difficulties with using electronic controls began at 3.3±1.6 years, episodic memory deficits at 4.0±2.0 years, topographical disorientation at 5.2±2.1 years, and conceptual apraxia at 5.5±2.1 years. For patients who progressed to severe dementia, six could not recognize family members, five exhibited pica, three experienced mirror sign, and one developed neologistic jargon. Conclusions The results suggest that patients with lvPPA progress rapidly to dementia and develop conceptual apraxia, episodic memory deficits, visuospatial deficits, and semantic memory deficits.

Genetic variants within Ninjurin 2 gene are associated with risk of ischemic stroke in Iranian population

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Previous genetic and epidemiological studies have shown the contribution of genetic factors in conferring the risk of ischemic stroke. Among the acknowledged risk factors of stroke are the single nucleotide polymorphisms (SNPs) near Ninjurin2 (NINJ2) gene which encodes a surface adhesion protein. In the current study, the AA investigated the role of two SNPs near this gene in ischemic stroke in Iranian

population. The frequency of the Aallele of the rs11833579 was significantly lower in cases compared with controls (OR(95%CI)=0.68(0.54–0.86), adjusted Pvalue=0.002). The rs11833579 was significantly associated with risk of stroke in co-dominant (AAvs.GG:OR(95%CI)=0.39(0.23–0.66), adjusted Pvalue=0.003) and recessive (OR(95%CI)= 0.44 (0.27–0.72), adjusted P value=0.001) models. The rs3809263 was associated with risk of stroke in dominant model (OR (95% CI)=1.5 (1.09–2.06), adjusted P value=0.02). The A C haplotype (rs11833579 and rs3809263) decreased the risk of stroke(OR(95%CI)=0.72(0.57–0.91), adjustedPvalue=0.03), while the GT haplotype conferred susceptibility to stroke (OR (95%CI)=1.42(1.11–1.82), adjustedPvalue=0.02). Consequently, the present case-control study supports the role of NINJ2 as a risk locus for ischemic stroke in Iranian population.