

## Highlights of the Issue 1, 2019

Published online: 5 January 2019

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Prof. Antonio Federico

### REVIEW ARTICLES

#### Understanding multifactorial architecture of Parkinson's disease: pathophysiology to management

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(India)

<https://doi.org/10.1007/s10072-018-3585-x>

Parkinson's disease (PD) is the second most common multifactorial neurodegenerative disorder affecting 3% of population during elder age. The loss of substantia nigra, pars compacta (SNpc) neurons and deficiency of striatal dopaminergic neurons produces motor deficit. Further, increase in alpha-synuclein accumulation, mitochondrial dysfunction, oxidative stress, excitotoxicity, and neuroinflammation plays a crucial role in the pathogenesis of PD. Alpha-synuclein protein encodes for SNCA gene and disturbs the normal physiological neuronal signaling via altering mitochondrial homeostasis. The level of  $\alpha$ -synuclein is increased in both normal aging and PD brain to a greater extent and secondarily reduced clearance results in accumulation of Lewy bodies (LB). Emerging evidences indicate that mitochondrial dysfunction might be a common cause but pathological insult through protein misfolding, aggregation, and accumulation

leads to neuronal apoptosis. The observation supporting that expression of DJ-1, LLRK2, PARKIN, PINK1, and excessive excitotoxicity mediated by dysbalance between GABA and glutamate reduced mitochondrial functioning and increased neurotoxicity. Therefore, the present review summarizes the various pathological mechanisms and also explores the therapeutic strategies which could be useful to ameliorate movement disorder like Parkinsonism

#### Systematic literature review on the delays in the diagnosis and misdiagnosis of cluster headache

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(UK)

<https://doi.org/10.1007/s10072-018-3598-5>

Patients with cluster headache (CH), the most common trigeminal autonomic cephalalgia, often face delayed diagnosis, misdiagnosis and mismanagement. Objectives To identify, appraise and synthesise clinical studies on the delays in diagnosis and misdiagnosis of CH in order to determine its causes and help the management of this condition. The systematic review was prepared, conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis. It was registered with International Prospective Register of Systematic Reviews. A systematic search of different electronic databases (Medline, EMBASE, PsycINFO, PubMed, CINAHL, BNI, HMIC, AMED, HBE and Cochrane Library) was carried out in May 2017. This systematic review shows that the delays in the diagnosis of CH are a widespread problem, the time to diagnosis still vary from country to country and both patients and physicians are responsible for the delays in diagnosis

### Microbial treatment: the potential application for Parkinson's disease

Xin Fang  
(China)

<https://doi.org/10.1007/s10072-018-3641-6>

Alterations in the composition of the intestinal flora are associated with the pathophysiology of Parkinson's disease (PD). More importantly, the possible cause-effect links between gut flora and PD pathogenesis have been identified using PD animal models. Recent studies have found that probiotics improve the symptoms associated with constipation in PD patients. In addition, fecal microbiota transplantation (FMT) was recently shown to provide a protective effect against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced neurotoxicity in mice. Effective microbial therapy for PD includes probiotics and FMT. Therefore, microbial therapy may be a useful and novel approach for treatment of PD. In this review, the use of microbial treatment in PD is discussed.

### ORIGINAL ARTICLES

#### Health-related quality of life in clinically isolated syndrome and risk of conversion to multiple sclerosis

Elisa Baldin, Trond Riise, Katia Mattarozzi, Alberto Gajofatto, Franco Granella, Maurizio Leone, Alessandra Lugaresi, Susanna Malagù, Luisa Motti, Walter Neri, Ilaria Pesci, Mario Santangelo, Cinzia Scandellari, Mari Rosaria Tola, Luca Vignatelli, Corrado Zenesini, Roberto D'Alessandro on behalf of G.E.Ro.N.I.Mu. study group  
(Italy, Norway)

<https://doi.org/10.1007/s10072-018-3582-0>

The AA wanted to estimate the association between self-rated quality of life scores among patients with clinically isolated syndrome (CIS) and the risk of subsequent conversion to definite MS. One hundred sixty-two patients from the GERONIMUS cohort with a symptom or sign suggestive of MS and without a definite diagnosis of MS at the time of inclusion were asked to evaluate their health-related quality of life according to MSQoL-54 scale. They were clinically assessed and mood and depression scales were applied. The association between the scores of these scales and the risk of converting to definite MS during a 5-year follow-up was estimated using the Cox-proportional hazard regression model. Quality of life at examination was significantly lower compared to those of an age- and sex-adjusted general Italian population. During the follow-up, 116 patients (72%) converted to definite MS. No significant predictive effects were found for the summary scales of MSQoL-54 or other scales. The estimates did not change after adjusting for age, sex, BMI, education, MRI findings, Expanded Disability Status Scale (EDSS) score, and treatment at time of examination. In conclusion Persons with CIS in this cohort reported reduced self-

rated quality of life compared to the general population, but variation in these scores was not associated with subsequent conversion from CIS to clinical definite MS.

#### Expert recommendations for diagnosing cervical, oromandibular, and limb dystonia

Giovanni Defazio, Alberto Albanese, Roberta Pellicciari, Cesa L. Scaglione, Marcello Esposito, Francesca Morgante, Giovanni Abbruzzese, Anna R. Bentivoglio, Francesco Bono, Mario Coletti Moja, Giovanni Fabbrini, Paolo Girlanda, Leonardo Lopiano, Claudio Pacchetti, Marcello Romano, Laura Fadda, Alfredo Berardelli  
(Italy)

<https://doi.org/10.1007/s10072-018-3586-9>

Diagnosis of focal dystonia is based on clinical grounds and is therefore open to bias. To date, diagnostic guidelines have been only proposed for blepharospasm and laryngeal dystonia. To provide practical guidance for clinicians with less expertise in dystonia, a group of Italian Movement Disorder experts formulated clinical diagnostic recommendations for cervical, oromandibular, and limb dystonias and a list of clinical features characterizing neurological/non-neurological conditions mimicking dystonia. The clinical features reaching a content validity ratio >0.5 contributed to the final recommendations. The recommendations retained patterned and repetitive movements/postures as the core feature of dystonia in different body parts. If present, a sensory trick confirmed diagnosis of dystonia. In the patients who did not manifest sensory trick, active exclusion of clinical features related to conditions mimicking dystonia (features that would be expected to be absent in dystonia) would be necessary for dystonia to be diagnosed. Although reliability, sensitivity, and specificity of the recommendations are yet to be demonstrated, information from the present study would hopefully facilitate diagnostic approach to focal dystonias in the clinical practice and would be the basis for future validated diagnostic guidelines.

#### Olfactory bulb atrophy in migraine patients

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<https://doi.org/10.1007/s10072-018-3597-6>

Osmophobia and headache triggered by odors are commonly seen in migraine, and these are symptoms that differentiate migraine from other primary headaches. Since these odor-related symptoms are disease-specific, we aimed to measure the volume of olfactory bulb and depth of olfactory sulcus in migraine patients. Patients and method A total of 93 subjects, consisting of 62 episodic migraine (32 with osmophobia, 30 without osmophobia) patient

sand 31 healthy controls, were included in this study. Diagnosis and classification of migraine were performed according to the beta version criteria of International Classification of Headache Disorders (ICHD-3 Beta version). More significantly in the left OBV, low OBV has been determined in migraine patients compared to the control group ( $p < 0.001$ ,  $p = 0.020$ ). When migraine patients with or without osmophobia were compared to the control group; OBV was determined to be the lowest in migraine group with osmophobia, and left-weighted bilateral OBV was determined to be low ( $p < 0.001$ ,  $p = 0.046$ ). No statistically significant difference was determined between groups in OSD measurements ( $p = 0.646$ ,  $p = 0.490$ ). In conclusion Left weighted bilateral OBV atrophy determined in migraine patients may be guiding for the clarification of migraine pathophysiology and enlightening of the relation between migraine and odor.

### **Boosting and consolidating the proprioceptive cortical aftereffect by combining tendon vibration and repetitive TMS over primary motor cortex**

Luisa Perasso, Laura Avanzino, Giovanna Lagravinese, Alessandro Giannini, Emanuela Luisa Faelli, Ambra Bisio, Angelo Quartarone, Vincenzo Rizzo, Piero Ruggeri, Marco Bove  
(Italy)

<https://doi.org/10.1007/s10072-018-3606-9>

Tendon vibration of a limb elicits illusory movements in the direction that the vibrated muscle would be stretched, followed by a transient perception of movement in the opposite direction, that was demonstrated to correspond to a B cortical after effect (Goodwin et al. *Science* 175:1382–1384, 1972). Primary motor cortex (M1) excitability of the non-vibrated antagonist muscle of the vibrated muscle increased during vibration and decreased thereafter. The cortical after effect is of interest when considering the possibility to use tendon vibration in rehabilitation for restoring unbalance activity between antagonistic muscles but, due to its short-lasting duration, has not been explored so far. The AA investigated the possibility to consolidate the cortical aftereffect by combining tendon vibration with a concomitant high-frequency 5-Hz repetitive transcranial magnetic stimulation (rTMS) protocol. The distal tendon of the flexor carpi radialis muscle (FCR)

was vibrated and concomitantly a 2-min 5-Hz rTMS protocol was administered on the left hemi-scalph hotspot of the vibrated FCR or its antagonist muscle (extensor carpi radialis (ECR)). The AA found that this protocol induced a pattern of unbalanced M1 excitability between vibrated muscle and its antagonist with increased excitability of the FCR and decreased excitability of ECR cortical areas, which persisted up to 30 min.

### **HISTORY OF NEUROLOGY**

#### **Ernst Trömner: beyond the reflex hammer**

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(Brazil, Germany)

<https://doi.org/10.1007/s10072-018-3571-3>

Ernst Trömner (1868–1930) was a German neurologist and psychiatrist at the St. Georg Hospital in Hamburg. As clinician and researcher, he contributed to our understanding of various fields within neurology including language and speech disorders, hypnosis and suggestion, sleep physiology and diseases, leukemia with nervous system involvement, gait disorders, metabolic myelopathy, Parkinson's disease, organic psychosis, and schizophrenia. However, his main interest was muscle reflexes. De facto, Trömner described a variant of the Achilles tendon reflex, a modification of the Oppenheim's and Babinski's reflexes, Bredis covered the corneo mandibular reflex and described the joint reflexes of the lower extremities as well as a muscle stretch reflex of the diaphragm. Moreover, Trömner has developed the first sedimentation chamber to assess the cerebrospinal fluid as well as the muscle plessimeter and, probably most considerable, the reflex hammer which is widely used by neurologists around the globe to date and is commonly referred to as the Trömner hammer. His name has also become inextricably linked with the finger flexor reflex, which is commonly known as the Trömner reflex. This article briefly summarizes Professor Ernst Trömner's life and his contributions to clinical neurology and psychiatry beyond his most famous eponyms, the hammer and the finger flexor reflex.

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