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HIGHLIGHTS

# Highlights of the issue 7, 2019

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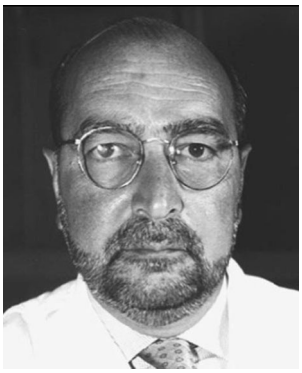

Antonio Federico
Editor-in-Chief

## REVIEW ARTICLES

### Degenerative and acquired sporadic adult onset ataxia

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https://doi.org/10.1007/s10072-019-03856-w

The diagnosis of sporadic adult onset ataxia is a challenging task since a large collection of hereditary and non-hereditary disorders should be taken into consideration. Sporadic adult onset ataxias include degenerative non-hereditary, hereditary, and acquired ataxias. Multiple system atrophy and idiopathic late cerebellar ataxia are degenerative non-hereditary ataxias. Late-onset Friedreich's ataxia, spinocerebellar ataxia type 6 and 2, and fragile X-associated tremor/ataxia syndrome account for most sporadic hereditary ataxias. Alcoholic cerebellar degeneration, paraneoplastic and other autoimmune cerebellar degeneration, vitamin deficiencies, and toxic-induced and infectious cerebellar syndrome are the main causes of acquired cerebellar degeneration. The diagnostic approach should include a history taking, disease progression, general and neurological examination, brain MRI, and laboratory and genetic tests. Novel opportunities in massive gene sequencing will increase the likelihood to define true etiologies.

### Small-fiber neuropathy definition, diagnosis, and treatment

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https://doi.org/10.1007/s10072-019-03871-x

In the last 30 years, improvement of diagnostic methods enabled routine evaluation of small A-delta and C nerve fibers impairment, which results with the clinical condition known as a small-fiber neuropathy (SFN). This syndrome develops as a result of metabolic, toxic, immune-mediated, or genetic factors. The main clinical features include neuropathic pain and autonomic disturbance, which are occasionally disclaimed due to outstanding fatigue, daily performance decline, anxiety, and depression. As clinical, neurological, nerve conduction, and electromyography studies are commonly normal, diagnosis often depends onthe finding of decreased intra-epidermal density of nerve fibers, per skin biopsy. This review highlights the etiology, clinical, diagnostic aspects, and SFN treatment.

## ORIGINAL ARTICLES

### The flavor test is a sensitive tool in identifying the flavor sensorineural dysfunction in Parkinson's disease

Anna DeRosa, Immacolata Cristina Nettore, Elena Cantone, Luigi Maione, Silvio Desiderio, Silvio Peluso, Francesco Saccà, Fiore Manganelli, Dario Bruzzese, Annamaria Colao, Giuseppe De Michele, Paolo Emidio Macchia
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https://doi.org/10.1007/s10072-019-03871-x

Gustatory perception has been poorly explored in Parkinson's disease (PD). Aim of this study was to assess the flavor ability in PD patients, using the flavor test

(FT), a new standardized and validated tool to examine the flavor perception. Thirty-eight patients (17 F and 21 M) and 36 control subjects (15F and 21 M) comparable for age and gender reenrolled. All the subjects underwent the flavor test (FT), the Sniffin' Sticks test (SST), and the gustometry test (GT), based on the basic four tastants (salty, sour, sweet, and bitter). PD patients presented a FT score significantly lower than controls($p < 0.001$). Olfaction (SST) was impaired in PD in comparison with controls ($p < 0.001$), and the patients also showed a mild reduction of basic tastant identification at the GT($p = 0.08$), with a trend toward statistical significance. There was no correlation between SST, FT, and GT. GT performance was negatively correlated with disease severity ($p = 0.004$) and stage ($p = 0.024$). The SST and FT resulted abnormal in PD in comparison with controls, independently of disease duration and severity. The ability to identify the basic four tastants was correlated with the disease severity and stage in PD patients suggesting that it might occur later in the course of the disease. FT might be a sensitive tool in identifying the sensorineural perception dysfunction in PD, even in the early stage and regardless of the disease severity.

**Efficacy and safety of deferiprone for the treatment of superficial siderosis: results from a long-term observational study**

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https://doi.org/10.1007/s10072-019-03847-x

Superficial siderosis (SS) of the central nervous system is a rare and heterogeneous condition due to deposition of hemosiderin on the surface of the brain and spinal cord. The usually progressive clinical course is characterized by a combination of hearing loss, cerebellar ataxia, and myelopathy. There is no known treatment for SS, but the iron chelator deferiprone (DFP) has been proposed as a potentially useful treatment. The AA present a long-term (average 3.7 years) evaluation of four cases of SS treated with DFP (15 mg/kg po bid). Treatment with DFP proved safe and well tolerated. Two out of the four subjects were unchanged while the other two presented a clinical improvement with reduction of postural instability and cerebellar signs. Blinded evaluation of magnetic resonance imaging (performed every 6 months during follow-up) showed a reduction of the abnormal iron deposition for all patients. This long-term observational study suggests that DFP may be effective in the management of the neurological manifestations associated with iron accumulation in SS.

**Clinical, laboratory features, and prognostic factors in adult acute transverse myelitis: an Italian multicenter study**

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The AA compared the clinical, laboratory, and radiological features of different subgroups of acute transverse myelitis (ATM) diagnosed according to the criteria established by the Transverse Myelitis Consortium Working Group (TMCWG) as well as of non-inflammatory acute transverse myelopathies (NIATM) to identify possible short- and long-term prognostic factors. A multicenter and retrospective study comprising 110 patients with ATM and 15 NIATM admitted to five Italian neurological units between January 2010 and December 2014 was carried out. A significantly higher frequency of isolated sensory disturbances at onset in ATM than in NIATM patients (chi-square = 14.7; $P = 0.005$) and a significantly higher frequency of motor symptoms in NIATM than ATM (chi-square = 12.4; $P = 0.014$) was found. ATM patients with high disability at discharge had more motor-sensory symptoms without (OR = 3.87; $P = 0.04$) and with sphincter dysfunction at onset (OR = 7.4; $P = 0.0009$) compared to those with low disability. Higher age (OR = 1.08; $P = 0.001$) and motor-sensory-sphincter involvement at onset (OR = 9.52; $P = 0.002$) were significantly associated with a high disability score at discharge and after a median 1-year follow-up. The diagnosis of ATM may prevail respect to that of NIATM when a sensory symptomatology at onset occurs. In ATM, patients older and with motor-sensory involvement with or without sphincter impairment at admission could experience a major risk of poor prognosis both at discharge and at longer time requiring a timely and more appropriate treatment.

**Emotional consciousness preserved in patients with disorders of consciousness?**

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https://doi.org/10.1007/s10072-019-03848-w

Increasing evidence from studies of brain responses to subject's own name (SON) indicates that residual consciousness is preserved in patients with disorders of consciousness (DOC) and that specific network activation might provide evidence of consciousness. However, it remains unclear whether SON is suitable for detection of emotional

consciousness; moreover, the particular aspects of brain network organization that are critical for consciousness are unknown. The present study used an innovative approach to explore affective consciousness inpatients with DOC during emotional stimuli. EEG data were acquired from 15 patients and 15 healthy volunteers. We analyzed brain potentials and functional network connectivity with a passive emotional paradigm based on graph theoretical methods. Larger N1 or P3a was detected in patients uponexposure to emotional sound, relative to neutral stimuli. Brain topology revealed that emotional sound evoked significantly stronger network linkages in healthy controls; additionally, it evoked several connectivity changes in patients with DOC. In conclusion, emotional consciousness might be partially preserved in patients with DOC; moreover, EEG network patterns could provide new insights into the neural activity of emotional perception in these patients.

**A Delphi consensus statement of the Neuropathic Pain Special Interest Group of the Italian Neurological Society on pharmacoresistant neuropathic pain**

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https://doi.org/10.1007/s10072-019-03870-y

To improve patient care and help clinical research, the Neuropathic Pain Special Interest Group of the Italian Neurological Society appointed a task force to elaborate a consensus statement on pharmacoresistant neuropathic pain. The task force included 19 experts in neuropathic pain. These experts participated in a Delphi survey consisting of three consecutive rounds of questions and a face-to-face meeting, designed to achieve a consensus definition of pharmacoresistant neuropathic pain. In the three rounds of questions, the participants identified and described the main distinguishing features of pharmacoresistance. In the face-to-face meeting the participants discussed the clinical features determining pharmacoresistance. They finally agreed that neuropathic pain is pharmacoresistant when "the patient does not reach the 50% reduction of pain or an improvement of at least 2 points in the Patient Global Impression of Change, having used all drug classes indicated as first, second, or third line in the most recent and widely agreed international guidelines, for at least 1 month after titration to the highest tolerable dose. The consensus statement might be useful for identifying eligible patients for invasive treatments, and selecting patients in pharmacological trials, thus improving patient care and helping clinical research.

## BRIEF COMMUNICATION

**PON1 is a disease modifier gene in amyotrophic lateral sclerosis: association of the Q192R polymorphism with bulbar onset and reduced survival**

Federico Verde, Cinzia Tiloca, Claudia Morelli, Alberto Doretti, Barbara Poletti, Luca Maderna, Stefano Messina, Davide Gentilini, Isabella Fogh, Antonia Ratti, Vincenzo Silani, Nicola Ticozzi
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https://doi.org/10.1007/s10072-019-03834-2

Previous studies have associated single-nucleotide polymorphisms (SNPs) in the gene encoding the detoxifying enzyme paraoxonase 1(PON1) to the risk of sporadic ALS. Here, the AA aimed to assess the role of the coding rs662 (Q192R) SNP as a modifier of ALS phenotype. They genotyped a cohort of 409 patients diagnosed with ALS at their Center between 2002 and 2009 (269 males and 140 females; mean age at onset, $58.3 \pm 37.5$ years). They found PON1 to be a disease modifier gene in ALS, with the minor allele G associated both with bulbar onset (30.9% vs. 24.6%, $p = 0.013$) and independently with reduced survival (OR = 1.38, $p = 0.012$) under a dominant model. No association was found with gender or age at onset. As this SNP is known to modify the detoxifying activity of paraoxonase 1 with respect to different substrates as well as other activities of the protein, the AA hypothesize that the identified association might reflect specific motor neuron vulnerability to certain exogenous toxic substances metabolized less efficiently by the 192R alloenzyme, or to detrimental endogenous pathophysiological processes such as oxidative stress. Further exploration of this possible metabolic susceptibility could deepen our knowledge of ALS pathomechanisms.