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A Case Report of Adult-Onset Leukoencephalopathy with Axonal Spheroids with Novel Mutation in CSFR1- Gene

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Introduction:
Adult-Onset Leukoencephalopathy with Axonal Spheroids (ALSP) is a rare genetic disorder. To the best of our knowledge, there are no reported cases in Austria. We present a clinical case of suspected ALSP with regards to clinical, radiological and laboratory findings.

Case summary:
A 50-year old female patient presentented with speech and concentration difficulties. Brain MRI showed bilateral confluent white matter lesions primarily in the frontal lobes with diffusion restriction in central parts, sparing subcortical U-fibers but involving the genu of the corpus callosum.
Blood and cerebrospinal fluid examinations were negative for pleocytosis, oligoclonal bands, kappa free light chains, MOG- and aquaporin-4-antibodies. Further investigations including vasculitis parameters, ACE, homocysteine, tumor markers, vitamin B12 and infectious serology remained negative. CADASIL and CARASIL could not be confirmed by molecular genetics.
Finally, a genetic examination for Hereditary Diffuse Leukoencephalopathy with Spheroids (HDLS) showed a c.2644_2646delCCA version on the CSF1R gene. Because of the limited data concerning pathogenicity of this variant, a clear connection from exclusively molecular genetic point of view could not be made in this case.
Our patient experienced progressive deterioration in cognitive performance within 3 months. Neurological examinations revealed an increase in tone and increased reflexes.

Conclusion:
Considering patient history, clinical and imaging findings as well as laboratory data including genetic tests, we suspect our patient of a rare genetic variant of ALSP with an underlying novel mutation.

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Fatigue, multidomain complaints, cognitive deficits and pattern of activation in severe COVID-19: behavioural and fMRI studies

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Introduction: Presence of mental fatigue and cognitive deficits in post-acute and early chronic stages of severe COVID-19 has been reported but few studies documented their occurrence in cases without prior or COVID-19-related brain damage. Aims of our studies are to determine how brain networks adapt during fMRI high-demand cognitive task and how the cognitive profile evolves in relation to the post-COVID-19 fatigue syndrome.

Methods: A fMRI pilot study has assessed in twenty-four normal subjects and in six consecutive patients with severe COVID-19 without brain damage, activation changes during a long colour-word Stroop task at 9 months. A behavioural pilot study has assessed in six consecutive patients with severe COVID-19 without brain damage, cognitive functioning, fatigue and multidomain complaints with a set of neuropsychological tests and questionnaires/scales at 12 months.

Results: Study 1: compared with controls, patients have presented different pattern of fatigue complaints, behavioural performance and/or activation networks, highlighting a trend towards two different effects: learning effect in controls and fatigue effect in patients. Study 2: a pervading mental fatigue and systematic multidomain complaints have been observed as well as association and dissociation between self-reported subjective mental fatigue, mental effort and cognitive performance.

Conclusion: In the chronic stage of severe COVID-19, even in the absence of brain damage, mental fatigue/effort, multidomain/cognitive complaints and/or cognitive dysfunction tend to be observed. Neuronal recruitment during high-demand cognitive tasks tends to be partially re-organised, with interindividual variations. Impact of this re-organisation on long-term outcome and responsiveness to rehabilitation needs to be established.

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Electromagnetic stimulation regulates blood corticosterone levels in immobilized rats: gender differences

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Introduction. A mental disorder is a condition that affects an individual`s cognition, emotional regulation, or behavior, causing distress or impairing main areas of functioning.

Methods. The effects of electromagnetic stimulation (EMS) and oxytocin (OXY) on blood corticosterone (CORT) levels in immobilized (10 days, 2 hours a day or one time, 2 hours) male and female rats while accounting for their sex hormone levels were studied. The experiments were conducted on intact and gonadectomized rats.

Results. As a result of immobilization, the content of CORT in the blood increased in both groups of rats. Chronic immobilization stress dysregulates HPA axis function in rats of both sexes. Gender differences are related to circulating gonadal hormones. Repeated EMS and OXY intranasal (IN OXY) (18 IU) (after each session of immobilization) or intracerebroventricular (1 μl/animal) returned the blood CORT level to normal. The effects of EMS and IN OXY were significant in intact rats compared with gonadectomized rats. Therefore, sex hormones play an essential role in maintaining the activity of the HPA axis and regulating negative feedback.

OXY released from the hypothalamus and adenohypophysis can inhibit CRF and ACTH secretion. Therefore, circulating OXY may inhibit CORT secretion directly from the adrenal glands (P0.01). Our results provide significant evidence to support the existence of a relationship between these two hormones.

Conclusion. EMS- and IN OXY -induced down-regulation of corticosterone levels may improve stress-induced impairment of hypothalamic-pituitary-adrenal axis activity.

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Case report: A patient with Parkinson`s disease and Syringomyelia or why every meeting with the patient should be like the first. S. Bozhinov, P. Bozhinov Neurology clinic, Heart and Brain Hospital, Pleven, Bulgaria

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Syringomyelia is a rare neurological disease associated with the formation of a cavity filled with cerebrospinal fluid within the spinal cord. The growth of this cavity gradually compresses various anatomical structures and leads to certain neurological symptoms. In the early stages of the disease, the clinical presentation can be concealed and misinterpreted as symptoms of other diseases.

We present a clinical case of a patient admited to the our neurology clinic with reduced muscle strength and atrophy of the muscles of the right hand, Parkinson’s syndrome for the right limbs, and dissociated sensory loss in the lower cervical and upper thoracic segments. We performed an EMG study as well as MRI with contrast matter of the whole spinal cord and discovered an elongated high signal (on T2W) tubule-like lesion in the myelon with characteristics of Hydro/Syringomyelia. Due to the lack of therapeutic effect with levodopa and dopamine agonists in the past we performed a SPECT/CT with I123 DaTSCAN demonstrating bilateral dopaminergic degeneration in the striatum, more pronounced in the left one, corresponding to Parkinson’s desease.

Conclusion: The presented clincial case demonstrates the importantance of conducting a detailed patient evaluation upon every clinical examination, including history, detailed neurological status, and advanced neuroimaging techniques, if appropriate, in order to make early diagnosis and discuss the following therapeutic options.

Key words: Syringomyelia, Parkinson`s desease, MRI, Chiari malformation type 1.

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Electromagnetic stimulation improves chronic restraint stress-induced spatial memory impairment in rats of both sexes

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Introduction. Electric magnetic stimulation (EMS) is a noninvasive treatment method that is used in many neurodegenerative diseases. The study aimed to investigate the correlates of cognitive function in the chronic restraint stress model of rats of both sexes on the background of EMS.

Methods. Experiments were conducted on intact and gonadectomized rats both gender (n=32, 4–6 months old, 190- 220 g). Parameters of EMS were detected in experiments. Chronic restraint stress (CRS) performed 2 hours, during 10 days. The process of learning was studied using an elevated multi-branch maze. The learning ability was tested 7, 14, and 30 days after the learning test. Data reliability was assessed using ANOVA.

Results. After immobilization, the learning ability was impaired in rats of both sexes ($P \leq 0.01$) compared to unstressed rats. Stressed rats did not remember the correct trajectory of the maze ($P \leq 0.01$). The number of mistakes was higher than in unstressed rats. The immobilized rats could not complete the task even on the 5th day of the train. The EMS improves learning time only in intact stressed rats. In gonadectomized rats, the EMS had minimal effects. EMS might affect the imbalances of neurotransmitter systems and hyperactivity of the HPA axis, which are essentially responsible for the expression of depressive-like behavior and fear responses only in the presence of sex hormones.

Conclusion. EMS has an anxiolytic effect in immobilized rats. This treatment improves learning and retention of information in stressed rats of both sexes.

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Adverse childhood experiences impair spatial memory in adulthood

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Introduction. Adverse Childhood Experiences (ACE) in adulthood are associated with neurodegenerative diseases and impairment of cognitive function. ACE causes hippocampal neurodevelopmental dysfunction and alters hypothalamic-pituitary-adrenal (HPA) axis activity, although there is still no complete understanding of these effects.

Methods. For the formation of moderate stress in the early postnatal (PN) age, the Chronic Immobilization Stress (CIS) model (immobilization from PN0 to PN20 for 2 hours for 20 days) was chosen. The impact of CIS on cognitive function and behavioral manifestations in adult female rats was studied. To determine the possible therapeutic effects of electric magnetic stimulation (EMS), stressed rats received EMS additionally. In this group of rats, the behavioral and cognitive functions in adulthood (PN80) were established. Data reliability was assessed by ANOVA.

Results. ACE has been shown to cause cognitive impairment in adulthood. Stressed adolescents took longer to complete the correct trajectory in the elevated maze test. They made more errors than unstressed rats. EMS improved the time pass in the maze ($P \leq 0.01$). These data were similar to those of non-stressed female rats. The EMS had positive effects on hippocampal-dependent memory (elevated maze test) in stressed rats depending on sex hormone levels. Also, EMS enhanced the negative feedback of glucocorticoids on glucocorticoid receptors in adult rats.

Conclusion: EMS is a non-invasive treatment method that might be used as a complementary drug for the treatment of different neurodegenerative diseases caused by ACE.

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FOG score is an effective tool to assess freezing of gait in Parkinson’s disease patients

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Background: Freezing of gait (FOG) is an episodic phenomenon, which limits mobility in advanced Parkinson’s disease (PD). FOG can be overlooked during routine examination and may not always respond to treatment, including levodopa and deep brain stimulation (DBS).OBJECTIVE: To evaluate the most suitable clinical test to detect FOG in PD patients treated with DBS.

Patients and Methods: FOG was assessed in 32 PD patients (5 F, 27 M, average age of 59.9±6.5 years), treated with dopaminergic medication and DBS (lasting 4.9±3.3 years). Patients filled Freezing of Gait Questionnaire (FOGQ) as a screening tool and underwent tests of gait: Timed Up and Go test (TUG), 10m Speed walk test (SWT), Short step test (SST) and FOG score according to Ziegler.

Results: Twenty-seven patients reported FOG in FOGQ. FOG score revealed FOG in 22 patients (total score 8.3±SD 9.7), TUG in 10, SST in 8 and SWT in 2. The total FOG score showed significant correlation with FOGQ (r=0.50, p=0.003), even higher in single task subscore (r = 0.56, p 0.001) and dual motor task (r = 0.65, p 0.001). Two patients with negative screening performed FOG in SST and FOG score – dual motor/mental task.

Conclusion: Majority (84%) of our patients with advanced-stage Parkinson`s disease on DBS therapy referred FOG according to FOGQ. The Ziegler test seems to be the most sensitive clinical tool, single motor and dual motor tasks show good correlation with referred FOG, dual motor/mental task can reveal FOG even in patients with negative screening.

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Transcranial Sonography Characteristics Of Cerebellar Neurodegenerative Ataxias

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Introduction: Cerebellar neurodegenerative ataxias encompass disorders affecting the cerebellum and its pathways. Transcranial sonography (TCS) has been used for the evaluation of brain parenchymal structures in various diseases especially in neuropsychiatric and neurodegenerative diseases. The aim was to investigate TCS characteristics of patients with neurodegenerative cerebellar ataxias.

Materials and methods: We included a total of 74 patients with cerebellar degenerative ataxia, 36.5 had autosomal dominant, while 33.8% had sporadic onset. Standardised ultrasonographic planes were used for the identification of brain structures of interest. All patients were clinically evaluated using SARA, INAS, neuropsychological and psychiatric scales.

Results: The brainstem raphe was discontinued in 33.8% of patients. The substantia nigra (SN) hyperechogenicity was identified in 79.7%. Third and fourth ventricle enlargement had 79.7% and 45.9% of patients, respectively. A positive and statistically significant correlation was found between SN hyperechogenicity with dystonia (p0.01), rigidity and dyskinesia (p0.05). Higher SARA total score statistically significantly correlated with the larger diameter of III (r=0.373; p=0.001) and IV ventricle (r=0.324; p=0.005). In such patients echogenicity of substantia nigra has been linked to extrapyramidal signs and raphe discontinuity to depression. Furthermore, ataxia and its clinical subtypes have positively correlated with IV ventricle diameter indicating brain atrophy and brain mass reduction.

Conclusion: In our study we have shown the main TCS characteristics of patients with neurodegenerative ataxias. Our results have shown that TCS is an effective, dependent and reproducible technique in monitoring patients with neurodegenerative ataxias.

Keywords: neurodegenerative cerebellar ataxias; transcranial sonography; hyperechogenicity, ventricle enlargement, raphe discontinuity

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Autoimmune Involvement in CANVAS: Exploring the Association with Vitiligo and Implications for Ganglionopathy and Vestibular Failure. A Case Report and Literature Review.

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Objective: To report a case of CANVAS with vitiligo and its autoimmune implications for ganglionopathy and vestibular failure.

Background: CANVAS, a recently described neurological syndrome, presents as adult-onset ataxia with potential inheritance patterns of autosomal dominant or recessive origin. However, the precise pathophysiological mechanism underlying CANVAS remains elusive. Particularly, speculation has arisen regarding a possible autoimmune component in its etiology.

Methodology/Design: Case Report and Literature Review.

Results/Case Presentation: A 51-year-old woman came for incoordination. Previous MRI revealed cerebellar atrophy and electrodiagnostic studies were consistent with sensory axonal polyneuropathy. There was no chronic exposure to alcohol, heavy metals/toxins, and a negative FHx of neuropathy. The exam revealed vitiligo in her upper extremities, variable portions of her face, and lower extremities, and no organomegaly. There was hypotonia in all extremities, normal muscle power, and absent knee and ankle reflexes. There was limb ataxia on finger-to-nose testing, and rapid alternating movements were slowed. Gait was broad-based and ataxic, with swaying and incoordination. Sensory examination showed intact light touch and positional sense. Vestibular testing showed a marked reduction of the VOR function in horizontal canals consistent with vestibular areflexia. Routine blood work, including Sjogren's, heavy metals, serum B12/folate, thyroid function testing, and genetics all were negative.

Conclusion: While vitiligo is not part of CANVAS diagnostic criteria, there`s an emerging association between autoimmunity and CANVAS. Genetic factors are implicated in some cases. The presence of autoimmunity (vitiligo) in a CANVAS-like presentation suggests a potential autoimmune mechanism, urging further investigation for this subset of patients.

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Time perception in Alzheimer’s disease and Parkinson’s disease

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Time perception is one of the most important functions of the brain, necessary for a person in everyday life for independent functioning, which undergoes significant pathological changes in patients with neurodegenerative diseases.

We aimed to investigate time perception in patients with Alzheimer’s disease (AD) and Parkinson’s disease (PD).

We examined 20 patients with PD (10 right-onset and 10 left-onset) and 15 patients with AD. All the patients underwent examination on MoCA, MMSE, The Apathy Scale, Plutchik’s Impulsivity Scale. We conducted tests for implicit and explicit time perception. Implicit time perception tests included video test where patient should determine the duration of symbol appearance and question after 20 minutes of entering room how long time passed from the beginning to now. The explicit test was performed with a stopwatch indicating intervals of 5 seconds 4 times. Parkinsonism severity in patients with PD was assessed with UPDRS-III.

In AD, implicit time perception was more impaired, in both test of 20 minutes and video-test. It was associated with cognitive impairment (p0,05), time was lost in memory. In PD, there was a tendency toward changes in both implicit and explicit time perception, in the absence of other cognitive impairments, impulsive disorders, and regardless of the severity of motor disturbances. Patients with right-onset had more impaired time perception compared to left-onset patients (p0,05).

Our findings suggest time perception disturbances in patients with both PD and AD. Further continuation and expansion of this research will allow us to detail the characteristics and pathoanatomy of these changes.