Posters
AQUAPORIN-4 IS INHIBITED IN RATS WITH EAE

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Background: Aquaporin-4 (Aqp4) is a water channel that regulates the volume of cells and tissues in health and disease. Recently, several studies reported that antibodies to Aqp4 are expressed in Devic's type multiple sclerosis and therefore may serve as a diagnostic tool for neuromyelitis optica. It is not known whether these antibodies are also the cause of Devic's syndrome and whether this protein is generally involved in brain inflammation.

Methods: In our study we examined the expression of Aqp4 mRNA in samples of cerebellum and spinal cord obtained from rats with EAE. Lewis rats were immunized with a homogenate of guinea-pig spinal cord emulsified with CFA and supplemented with pertussis toxin. Rats were sacrificed before and during the expression of neurological signs of EAE. Samples of mRNA were analyzed in real-time PCR with pairs of primers to amplify cDNA of Aqp4 and many other genes related to endothelial cells and BBB functions.

Results: While several genes encoding for cytokines, metalloproteinases and tight junctions proteins were amplified at the day the clinical signs appeared, the expression of Aqp4 was deeply inhibited. The inhibition was gradually diminished and the expression returned to normal levels when animals recovered from EAE. Using immunohistochemical staining with anti-Aqp4, we found decreased expression around vessels with lymphocyte infiltrations. Furthermore, intrathecal injection of recombinant rat IFN-g caused a similar inhibition in the expression of Aqp4 mRNA in brain. Similar results were obtained with isolated rat astrocytes incubated with IFN-g.

Conclusions: We suggest that Aqp4 may play a significant role in the course of autoimmune disease in the brain and may be involved in BBB dysfunction, infiltration of cells into the tissue and edema process around leaky vessels. It is tempting to understand the mechanism of inhibition of Aqp4 in brain and elucidate its role in the pathogenesis of multiple sclerosis.
ACCUMULATION OF GAGs IN LISOSOMES DELAYS PrP\textsuperscript{Sc} DEGRADATION AND PROLONDS PRION DISEASE INCUBATION TIME

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Background: Glycosaminoglycans (GAGs) and in particular, heparan sulfate (HS), have been shown to be associated both with prion disease pathology as well as with the metabolism of the prion proteins and also to modulate prion infectivity. While addition of GAGs to scrapie infected cells increased PrP\textsuperscript{Sc} accumulation, degradation of these sulfated sugars reduces the content of PrP\textsuperscript{Sc} in cells. Interestingly, reagents such as Tilorone and Quinacrine, which are known to cause chemical mucopolysaccharidosis (MPS) by inducing accumulation of GAGs in lysosomes, reduce the accumulation of PrP\textsuperscript{Sc} in ScN2a cells. However, Quinacrine had no effect on prion disease incubation time when administered to animals after prion infection.

Objectives: In this work we investigated whether pathological accumulation of GAGs can induce de-novo conversion of PrP\textsuperscript{C} to PrP\textsuperscript{Sc} and prion infectivity. We also studied the effect of intracellular GAGs on the accumulation of PrP\textsuperscript{Sc} in cells.

Methods: We show here that PrP\textsuperscript{Sc} and prion infectivity were both absent from the brains of transgenic mice ablated for GAG degrading enzymes and thereby suffering from MPS diseases, which are known to accumulate GAGs in their lisosomes. However, addition of PrP\textsuperscript{Sc} to cells cultured in the presence of Tilorone resulted in sequestration of the prion protein in cells for a long period of time. Interestingly, when Tilorone was administrated to mice for weeks before infection with prions, incubation time for scrapie in these animals was prolonged significantly.

Conclusions: We propose that sequestration of PrP\textsuperscript{Sc}-GAGs complexes in the lysosome, while resulting in reduced degradation of PrP\textsuperscript{Sc} deoids the prion protein from its ability to convert new PrP\textsuperscript{Sc} molecules and subsequently infect cells, thereby resulting in prolonged incubation time for the disease and reduced PrP\textsuperscript{Sc} accumulation in ScN2a cells.
LONGITUDINAL NEUROCOGNITIVE ASSESSMENT OF ADULT DOWN’S SYNDROME PATIENTS

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OBJECTIVE: To assess baseline and longitudinal neurocognitive characteristics of adult Down’s Syndrome (DS) patients at risk for developing Alzheimer’s Disease (AD).

BACKGROUND: DS patients typically develop neuropathological AD in the 4th-5th decade of life. Recent studies suggest the extra copy of the amyloid precursor protein (App) present in DS causes damage to cholinergic neurons in the basal forebrain, much as occurs in clinical AD. However, no research to date has examined whether dementia in DS mimics clinical AD in its characteristic patterns of neurocognitive dysfunction, consisting of short-term verbal memory impairment, semantic impairment (naming and word generation), and constructional dyspraxia, in addition to intellectual impairment.

DESIGN/METHODS: We developed a brief, focused neurocognitive AD assessment battery appropriate for DS patients. Tasks include object naming, word generation by letter and category, 5-word list learning, clock drawing and non-verbal analytical reasoning (Color Progressive Matrices). Additional evaluations included neurological examination, MMSE, Geriatric Depression Scale, Neuropsychiatric Inventory and AD-Activities of Daily Living assessment. To date, we have obtained baseline data for 15 patients (8M/7F), whom we intend to follow up at 2-year intervals.

RESULTS: Mean age of patients was 25(8.9) at baseline (range=18-48). MMSE score mean was 18.8(4.8), with a range of 13 to 26. Mean performance was in the impaired range for all individual neurocognitive variables. However, individual scores on all variables ranged from severely impaired to normal. E.g., delayed recall from memory ranged from 0 to 5 out of 5 items. Ten-point clock drawing scores ranged from 1 to 10. Word generation (animals) ranged from 6 to 16 in 60 sec. Correlations between age (disease length) and individual cognitive variables ranged from -.242 to .563; contrary to expectations, none were statistically significant.
CLINICAL CHARACTERISTICS OF PARKINSON'S DISEASE AMONG JEWISH ETHNIC GROUPS IN ISRAEL

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Background: Differences in prevalence rates and clinical characteristics of Parkinson's diseases (PD) were reported among different ethnic groups. The Yemenite Jews are a distinctive ancient ethnic group that was separated from the Ashkenazi Jews. The LRRK2 G2019S mutation was reported to cause parkinsonism in 18% in Ashkenazi Jews in New York (NEJM 2006; 354:424-5). Our objectives were to compare the course of PD among Ashkenazi and Yemenite Jews in Israel and to investigate the prevalence of the LRRK2 G2109S mutation in the Yemenite patients.

Methods: All Yemenite (n=61) and Ashkenazi-originated countries patients (n=51) were included. Their medical records were screened for age of disease onset and duration, first clinical signs, the response to levodopa therapy and presence of response fluctuations, dyskinesias, depression and cognitive impairment. Discrete variables were compared using ANOVA. Progression of the disease was compared using linear regression, measured by the association between disease duration and the UPDRS motor scores.

Results: Age of disease onset was lower in the Yemenite compared to the Ashkenazi Jews (54.6±13.2 vs 62.1±9.5 years; p<0.001), but there was no difference in family history among groups. There was no difference in the clinical presentation, disease duration and the prevalence of fluctuations, dyskinesias, depression and psychiatric symptoms between groups. However, UPDRS motor scores were higher in the Yemenite compared to Ashkenazi Jews (34±18.8 vs 24±18; p<0.01) and disease progression was significantly faster (r=0.48, p=0.05). Albeit a small sample, the LRRK2 mutation was negative in all Yemenite patients.

Conclusions: There are no differences in the clinical characteristics of PD between Yemenite and Ashkenazi Jews, but the rate of disease progression is more rapid in the Yemenite group. These ethnic differences might be attributed to genetic and environmental factors. Surprisingly, no Yemenite patients were identified with the LRRK2 G2019S mutation. Its absence may be explained by the fact that the Yemenite ethnic division was completely separated from the Ashkenazi Jews.
Background: Carotid artery stenting (CAS) is used as an alternative to surgical endarterectomy.

Objectives: The purpose of this study was to determine the outcome of CAS in a retrospective cohort of patients, Between July 1999 and March 2003.

Patient & Methods: Fifty-six consecutive patients with carotid artery stenosis who were considered surgical risks were treated (45 male, 11 female, mean age 69). Carotid stenting was performed via the femoral artery, using long flexible femoral sheaths (WALLSTENT® or Smart Precise®).

Results: Intraprocedural complications included transient neurological findings in 5 patients (8%), cerebrovascular accident (CVA) in 2 (3%), hemodynamic changes in 11 (18%) and 4 procedural failures. Postprocedural complications included TIA in 3 patients and CVA in 6 (10%). At 30 days follow-up, 3 patients (5%) remained with signs of CVA. Two patients (3%) died during the postprocedural period and 16 (28%) died over 5-year follow-up, 1 due to recurrent CVA and the remainder due to nonneurological causes. Five-year carotid doppler follow-up was performed in 25 patients (45%). In these, normal stent flow was found in 21 patients (84%), 50-60% restenosis in 3 patients (12%) and >70% restenosis in 1 patient (4%).

Conclusions: Immediate complications were found in 18 patients (32%) - short term hemodynamic changes in 11 patients (18%), transient neurological findings in 5 (8%) and CVA in 2 (3%). At 30-day follow-up, 5 patients (9%) showed complications - minor CVA in 2 patients (3%), major stroke in 1 (1.6%) and 2 patients died (3%). These immediate complications should improve with the introduction of distal protective devices.
Objective: To compare various cognitive abilities of patients with cerebellar type of multiple system atrophy (MSA-C) to patients with parkinsonian type (MSA-P), and the cognitive profile of both MSA groups to that of Parkinson's disease (PD).

Background: MSA patients and PD patients show frontal lobe dysfunction and memory deficits. We examined various cognitive functions in MSA-P and in MSA-C patients to cognitively distinguish between these groups. We also examined PD patients to cognitively weigh them against the MSA patients.

Methods: We administered neuropsychological tests to 15 MSA-P patients, 10 MSA-C patients, and 12 non-demented PD patients, matched on age and disease duration. The tests required oral outputs without motor demands. The battery evaluated verbal memory, executive functions, and information processing speed, and every subject filled out questionnaires that evaluate levels of depression (Beck, 1961) and state-trait anxiety (Spielberger, 1983). The performance of each group in the tests was compared to the expected average from their age and/or educational level. Finally, the correlation between the performances in the tests to the duration of the disease was examined.

Results: The three groups showed a significant reduction in verbal learning and memory and processing speed. However, MSA-P had greater executive dysfunction than the MSA-C that also showed executive attention deficit. No significant executive deficits were found in the PD group. In addition, as opposed to MSA-C and PD, a significant correlation was found in the MSA-P group between disease duration to the cognitive deterioration. Finally, all groups reported higher than normative levels of anxiety and depression. No significant correlations were found between the tests performance to the depression or anxiety scores in all groups.

Conclusion: Verbal learning and memory as well as processing speed are reduced in PD and in MSA patients. While MSA-C shows mainly verbal memory reduction with some executive dysfunction, MSA-P show verbal memory lost with major executive dysfunction.
I-123 MIBG CARDIAC SCINTIGRAPHY AND AUTONOMIC TEST EVALUATION IN MULTIPLE SCLEROSIS PATIENTS

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\textbf{Background:} Autonomic symptoms are common in multiple sclerosis (MS) patients and may cause significant disability. The purpose of this study is to evaluate direct cardiac sympathetic denervation in MS patients with I-123 MIBG cardiac scintigraphy compared with other parasympathetic electrophysiological examinations of autonomic dysfunction.

\textbf{Methods:} Ten patients with MS and 7 age- and sex-matched control subjects were prospectively evaluated. The neurological deficit and disability stages of the patients were rated according to the Kurtzke Expanded Disability Status Scale (EDSS). Autonomic tests included the R-R interval, Valsava ration and stand-up test. All patients and control subjects has planar and SPECT cardiac scintigraphy with I-123 MIBG injection.

\textbf{Results:} Seven (out of the 10) MS patients had relapsing-remitting (R-R) type and three had secondary progressive type (SP). A pathological MIBG cardiac washout rate was found in 3/10 MS patients, all of them with SP-MS. The other seven had normal washout rates. No correlation was found between the scan and the individual parasympathetic autonomic test results.

\textbf{Conclusion:} I-123 MIBG myocardial scintigraphy may detect direct disturbances of the sympathetic nervous system in patients with MS and is more sensitive than parasympathetic dysfunction test in patients with the SP type of disease. Determination in MS of the co-existence of autonomic dysfunction, especially the cardiac sympathetic involvement in the SP type, may aid in evaluation of disease severity, prognosis and cardiac function follow-up.
THE PULL TEST AND COGNITIVE FUNCTION: TWO UNLIKELY BEDELLFOWS

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Background: The Pull Test (PT) has been widely used to assess postural control in patients with Parkinson's disease. Less is known about its utility for identify instability in the general elderly population.

Objectives: To test the hypothesis that scores on the PT are higher (worse) among idiopathic elderly fallers and to identify the factors that are associated with performance on this test.

Methods: 313 community living adults (age 68 ± 7 yrs) participated in a self-referred neurological survey. 125 reported at least one fall during the previous year and 188 were non-fallers that served as an age- and sex-matched control group. Subjects underwent balance and gait evaluations and completed a computerized neuropsychological assessment battery.

Results: PT scores were significantly higher (worse) (p=0.006) among fallers (1.4+/- 0.8) compared to non-fallers (0.9+/-0.9). For the non-fallers, high scores on the Pull test were positively correlated with fear of falling (p=0.035), but were not correlated with measures of cognitive function, affect, or motor function. In contrast, among the fallers, worse scores on the PT were not correlated with fear of falling (p=0.435). Instead, they showed, on average, significant cognitive impairment: global cognitive scores, memory and attention scores were significantly lower, compared to those with better PT performance.

Conclusions: Among older adults, the Pull Test is different in fallers and non-fallers and its performance is apparently related to cognitive function. Fear of falling may serve as an early defense mechanism that protects healthy adults from falling but it might disappear when dementia emerge.
Background: In the setting of an acute stroke, anemia has the potential to worsen brain ischemia, however, data relating hemoglobin levels to long-term clinical outcomes in acute stroke remain limited.

Methods: We examined the association between baseline hemoglobin values and one year mortality and outcome in 863 consecutive patients with acute stroke (ischemic or hemorrhagic).

Results: After adjustment for differences in baseline characteristics, patients with anemia at baseline (hemoglobin<13 in males, <12g/dL in women) had after 1-year an OR for death of 1.73 (95%CI, 1.07-2.82), for death or disability (Barthel Index<75) 1.81 (1.08-3.04) and for death or long-term nursing care 1.56 (0.90-2.68). A reverse J-shaped relationship between hemoglobin levels and clinical outcomes was observed by examining hemoglobin levels in categories of <11 (n=47), 11-12 (n=74), 12-13 (n=127), 13-14 (n=193), 14-15 (n=224), 15-16 (n=125), and >16g/dL (n=73). Using hemoglobin levels 14-15g/dL as the reference, the OR for 1-year mortality adjusted for potential confounders rose as hemoglobin levels fell below 12g/dL, with an OR of 1.56 (0.71-3.38) for 11-12g/dL and 3.05 (1.28-7.25) for <11g/dL, while at the other end of the range, patients with levels >16g/dL had an OR of 1.63 (0.69-3.78). The adjusted OR for death or long-term nursing care after 1-year were 2.04 (1.01-4.11) for hemoglobin level of 12-13g/dL, 1.70 (0.71-4.05) for 11-12g/dL and 3.47 (1.30-9.47) for <11g/dL, while at the other end of the range, patients with levels >16 g/dL had an OR of 1.55 (0.63-3.76).

Conclusions: Anemia is a strong predictor of poor outcome in patients with acute stroke. Findings suggest a reverse J-shaped association between hemoglobin level and long-term outcome after acute stroke.
AGE-RELATED COGNITIVE DECLINE MEASURED BY COMPUTERIZED ASSESSMENT CORRELATES WITH REGIONAL BRAIN CHANGES MEASURED BY Q-SPACE MRI

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Objective: To investigate the relationship between age-related changes in brain structures and cognitive performance in multiple domains under the hypothesis that age-related cognitive decline is a multi-regional process.

Background: Aging is a complex heterogeneous process accompanied by cognitive decline. Although defined as a natural condition, neurodegenerative processes are involved in aging, manifest by reduced memory, executive function, motor abilities, and processing speed that may be associated with multi-regional structural brain changes.

Design/Methods: In the present study we used Q-space imaging (QSI), a highly sensitive MRI method for detection of structural brain changes. QSI was performed on 50 subjects, age 25-82y who also completed a battery of computerized tests (Mindstreams®, NeuroTrax Corp., NY) assessing memory, executive function, motor abilities, and verbal function outside the scanner. Test performance and age served as covariate correlation inputs for voxel based morphometry (VBM). Region of interest (ROI) analysis was guided by the VBM results and correlation coefficients computed for age and test performance per ROI. The ROIs included the thalamus, hippocampus, fusiform, cingulum, inferior longitudinal fasciculus (ILF), corpus-callosum, and medial frontal gyrus (MFG).

Results: Age was highly correlated with QSI indices in all ROIs, but cognitive performance was correlated in a task- and ROI-specific fashion. For example, correlations with accuracy on the non-verbal memory test were 0.48 in the ILF (p<0.0001) and 0.43 in the hippocampus (p<0.002) but <0.3 in other ROIs. The correlations with reaction time on the information processing speed task were 0.48 (p<0.001) in the MFG (bilateral) and <0.35 in all other regions.

Conclusions/Relevance: Although brain changes with age are multi-regional, brain changes associated with performance in particular cognitive domains are region-specific, as revealed by VBM. Using advanced MRI methodologies (e.g. QSI), investigation of heterogeneous aging process can be focused by specific relationships between structural changes and cognitive decline.

Disclosures: Efrat Sasson and Yaniv Assaf have nothing to disclose. Ely Simon and Glen Doniger are employees of Neurotrax.
OBJECTIVE: To determine whether demographic, mood or neurocognitive variables predict the development of major depression after successful deep-brain stimulation (DBS) surgery for severe Parkinson’s disease (PD).

BACKGROUND: Major depression is a known sequela of DBS for severe PD. Screening for pre-existing depression as well as dementia is an essential part of the patient selection process. However, no studies have heretofore examined retrospectively whether demographic, mood or neurocognitive variables can predict the development of post-DBS major depression.

DESIGN/METHODS: Sixty-three PD patient candidates for DBS underwent mood and dementia assessment. Forty-eight patients were deemed suitable and 15 unsuitable based on both mood and cognitive criteria. Thirty-five suitable patients underwent DBS surgery of the sub-thalamic nucleus (STN) and follow-up mood assessment for at least one year.

RESULTS: Average patient age was 59.1 (8.5); average disease length was 11.7 years. Three patients (8.6%) developed major depression as measured by Hamilton Depression Rating Scale (HDRS) scores and subjective self-report. All were male. Patients developing depression were significantly younger (52.7 vs. 59.7 yrs, p<.05) and had significantly lower pre-surgery HDRS scores (10 vs. 14, p<.05). No neurocognitive variables predicted post-DBS depression.

CONCLUSIONS: 1. Male gender, younger age and lower pre-DBS depression scores are risk factors for post-DBS depression requiring pharmacologic treatment. 2. Levodopa may selectively or preferentially elevate mood and mask depression in younger and/or male PD patients. 3. Post-DBS mood assessment follow-up is essential, due to the high (8.6%) rate of post-surgical major depression.
MODULATION OF PROTEOLYTIC PROCESSING OF THE P75 NEUROTROPHIN RECEPTOR BY ITS CO-RECEPTORS: TRKS, SORTILIN, AND NGR

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Background: The p75 neurotrophin receptor (p75NTR) emerges as a multifaceted neurotrophin receptor that mediates diverse and sometimes opposing events in neuronal survival, growth, apoptosis, and synaptic modulation. It has been previously shown that p75NTR undergoes shedding of its extracellular domain (ectodomain) via a TNF-converting enzyme (TACE)-like metalloprotease, which is enhanced by treatment with phorbol esters (Jung et al., JBC 278:42161-9, 2003; Weskamp et al., JBC 279:4241-9, 2004). Further experiments have demonstrated that co-expression of p75NTR with TrkA leads to release of a distinct ectodomain fragment by a different, serine protease-like activity. Interestingly, NGF induces this p75NTR ectodomain cleavage only when p75NTR and TrkA are co-expressed, suggesting a novel, neurotrophin-dependent mechanism of p75NTR regulation via differential proteolysis.

Objectives: To investigate the effects of other known co-receptors, including other Trk family members, Sortilin, and the Nogo receptor (NgR), on p75NTR processing.

Methods: p75NTR constructs were co-expressed in heterologous HEK 293 cells with several known p75NTR co-receptors. p75NTR cleavage products were assayed via immunoprecipitation and western blotting.

Results: Co-expression of TrkB and TrkC with p75NTR resulted in increased p75NTR processing, similar to that observed with TrkA. Sortilin, a putative co-receptor for pro-neurotrophins, also enhanced p75NTR ectodomain shedding and p75NTR processing in a TACE-independent manner. Experiments with both endogenous and engineered truncation mutants suggest that the C-terminal intracellular domains of both TrkB and Sortilin are necessary for enhanced p75NTR processing. In contrast, co-expression of NgR was found to be inhibitory in p75NTR processing.

Conclusions: Our observations raise the possibility that proteolytic processing of p75NTR can be differentially modulated by its co-receptors. These results further suggest that co-receptor regulation of p75NTR proteolysis may provide a mechanism by which the multiple and diverse functional outcomes associated with p75NTR are achieved.
THE IMPACT OF MULTIPLE RESECTIONS FOR GLIOBLASTOMA MULTIFORME

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Introduction: The role of multiple resections in the management and prognosis of glioblastoma multiforme (GBM) is unclear. Data on re-operation for resection for recurrent GBM are sparse.

Methods: We retrospectively searched our prospectively collected data base for primary (de novo) glioblastoma multiforme patients who underwent three or more resections from 1995 until present by our Neurosurgical team. From a total of 633 patients in our data base with a diagnosis of GBM, we excluded patients with a prior diagnosis of lower grade tumor which transformed to glioblastoma. We only considered tumor resection and did not consider diagnostic biopsy, shunting for hydrocephalus, or wound revision as one of the three or more surgeries.

Results: We identified 24 patients from our data base with 3 or more operations for primary glioblastoma. Of the 24 patients, 3 had diagnosis of gliosarcoma. 19 of these patients underwent 3 tumor-resective operations; 4 underwent 4 operations; and 1 patient underwent 5 operations for tumor resection. 18 patients were male, and 6 were female. Ages ranged from 32-69, with median age 53. Twelve tumors were right-sided and 12 were left sided. The temporal and frontal lobes were most frequently represented, with several tumors spanning adjacent lobes. Range of survival for patients with 3+ surgeries, from date of diagnosis to date of death, was 9 (a case with 4 resections) to 45 months (m) (also 4 resections). Median survival times for biopsy only, one surgery, two surgeries, and three or more surgeries were respectively: 3.6 m, 8.1 m, 14.3 m, and 18.8 m. As a group, younger patients (<60) benefited more from multiple resections.

Conclusions: Increased survival progressively correlated with an increasing number of tumor resections. Age was inversely correlated with survival.
THE LONG-TERM EFFECT OF BOTULINUM-TOXIN FOR POST-WH IPLASH PAIN SYNDROME

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Background: Myofascial pain syndrome characterized by local pain and stiffness, trigger points may evolve after whiplash injury. Some patients will develop a chronic, pain syndrome. Botulinum neurotoxin type A has shown controversial results in term of its effectiveness for post whiplash chronic neck pain.

Objective: The aim of study is to test the long-term efficacy of early on trigger point injection of botulinum neurotoxin type A, in relieving Myofascial neck pain in patients with post-whiplash injury.

Methods: 20 patients with cervical Myofascial pain, 2-48 weeks after whiplash injury, were randomly assigned to receive either 200U of Botox or placebo group into 4 trigger points (10 patients/group). Eighteen patients (9 in each group) completed a six-month follow-up. Outcome measures included intensity of pain evaluated by a 0-10 VAS Scale, 0-4 Numerical Pain Scale (NPS) of maximal and average pain intensities during the preceding week, and “pain diaries” using VAS 0-10. Quality of life evaluated by the SF-36 questionnaire and global assessment of the treatment efficacy completed by the physician and the patients, the intensity of unpleasantness and pain in response to pressure algometer, range of cervical motion, adverse effects and consumption of other therapies. All parameters were recorded in each visit (baseline and 3,6,9, 12 and 24 weeks after the injection).

Results: A time dependant improvement in all tested parameters was found in both groups. All parameters showed a consistently larger improvement in the botulinum treated group compared in the placebo, but not at a significant level.

Conclusions: The results are consistent with those of earlier small trials indicating a greater effect in the treatment group without statistical significance. It is difficult to determine whether the lack of significant effect is a result of the small sample size and several other limitations of the studies or from lack of therapeutic effect, the use of botulinum neurotoxin remains an optional therapy for selected patients.
COMPARISON OF THE SCOPA-Cog, MMSE AND MATTIS DEMENTIA RATING SCALE IN PARKINSON’S DISEASE PATIENTS (PDpts) AND AGE MATCHED CONTROLS

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Background: In Parkinson Disease cognitive disturbances are diagnosed in about 39% of subjects (Cummings, 1988). Evaluation of cognitive performances in a routine clinical setting is quite difficult and time consumer. The MMSE is not quite sensitive.

By the other hand Mattis score has been used in PD with good results although is time consumer.

Recently the SCOPA-Cog (SCales for Outcome in PArkinson’s disease Cognition) which consists of 10 items with a maximum score of 43 has been developed and its validation and reliability in PD patients was established (Marinus et al, Neurology, 2003).

Objectives: In this study we have applied the MMSE, Mattis and SCOPA-Cog in order to evaluate the effectivity of this novel test compared with the others. In addition we correlated the mental decline of patients (as evaluated with the three tests) with their motor severity according with Yahr scale (I and II=1mild; III=2 moderate and IV + V=3 severe).

Patients and Methods: Thirty healthy controls (CONT; mean age 65+9.7) and 59 PD pts (mean age 66.5±9.8 y; disease duration 8.1±5.6y, motor severity 1: 21 pts; 2: 22 pts; 3: 16pts) were included. PDpts were classified as non demented (PDNDEM) (n=50) and demented (PDDem) 9 of them according with Clinical Dementia Rating [CDR] [1 and more) and 8 according with MMSE (25 scoring and less).

Statistics: Anova test with repeated measures was applied for analysis of data.

Results: No significant difference was found between CONT and PDNDEM in comparing MMSE (p= 0.007), Scopa-Cog (p=0.007) Mattis (p= 0.23) although a trend of differentiation among both groups was evident. Mental deterioration according with MMSE results did not correlate with motor decline (p=0.12). The SCOPA-Cog (p=0.031) and Mattis (p=0.039) by the contrary showed similar correlation with lower cognition score for patients with advanced PD. SCOPA-COG was usually performed within 20 minutes (+3); Mattis usually took 40 minutes (+6 minutes).

Conclusions: SCOPA-Cog is a simple, sensitive, validated test, which in our understanding should be incorporated in the battery of cognitive tests for the evaluation of PD patient.
AUTOSOMAL DOMINANT PARTIAL EPILEPSY WITH AUDITORY FEATURES: DESCRIPTION OF A TUNISIAN JEWISH FAMILY NOT LINKED TO LGI1 GENE

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Background and Objectives: Autosomal dominant partial epilepsy with auditory features (ADPEAF) is a rare familial epilepsy with onset in adolescence or early adulthood. In some families mutations in Leucine-rich glioma inactivated (LGI1) gene have been identified. We describe a new Israeli Tunisian Jewish family with ADPEAF.

Methods: Clinical characteristics and results of EEG, computed tomography (CT), and magnetic resonance imaging (MRI) were evaluated in four affected members of the family. Genetic counseling was performed and a four generation pedigree drawn. Sequencing of the LGI1 gene was performed on one affected individual.

Results: Four affected members from two generations had a rare and drug-responsive adult onset tonic-clonic seizures constantly preceded by an auditory aura. The most common auditory symptoms were simple; talking, buzzing, ringing and loss of hearing bilateral. Routine and sleep electroencephalograms were normal. MRIs of brain were normal. Sequencing of the LGI1 gene did not reveal the causative mutation in the affected individual tested.

Conclusions: ADPEAF is a distinct condition with homogeneous clinical features but genetic heterogeneity. LGI1 is not responsible for the disease in the family presented here. Further genetic investigations will follow to hopefully identify a possible novel causative gene and mutation responsible for ADPEAF in this family.
ACTIVATION AT THE TEMPORO-PARIETAL JUNCTION IN
POSITIVE SCHIZOTYPY

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Background: Impaired self- and own body-processing in patients with schizophrenia and individuals along the schizophrenia spectrum might relate to relative dysfunctional cortical activation at the temporo-parietal junction. Here we investigated whether strength or duration of temporo-parietal junction activation during an own-body processing task correlates with level of abnormal self-processing in healthy subjects as measured by the frequency of spontaneously experienced schizotypal body schema alterations (perceptual aberrations) and dissociative experiences.

Methods: Participants carried out a mental imagery task with respect to their own body. Behavioral data and high density EEG were measured. EEG data were analyzed using evoked potential mapping and electrical neuroimaging. Participants completed two validated self-report questionnaires, one asking about perceptual aberration and one about dissociative experiences.

Results: The own body transformation task activated the right temporo-parietal junction at 310-390ms. Participants' reaction times and duration of activation at the right temporo-parietal junction, but not its strength, were found to correlate positively with perceptual aberration scores. No relationship was found with dissociative experiences scores. Brain activations proceeding and following activation of the right temporo-parietal junction did not correlate with scores on either scale.

Conclusions: The positive correlation between performance and right temporo-parietal activation in an own body transformation task with perceptual aberrations scores in our healthy population suggests that disturbances in self- and body-processing in individuals along the schizophrenia spectrum might be due to prolonged, rather than stronger activation of the right temporo-parietal junction. We argue that this might reflect pathologies in cortico-cortical connections and/or re-entry of top-down dynamics.
Objective: We describe a central vestibular syndrome in the roll plane composed of contraversive body tilt (CBT), contralateral deviated gait, contralateral ocular cyclorotation (OC) and contralateral deviation of the static subjective visual vertical (SVV) with altered perception of verticality.

Methods: We studied eight consecutive patients with acute unilateral vascular internuclear ophthalmoplegia (INO), examining the eyes torsion by fundus photos, clinical bedside exam of posture, gait, ocular motility, and we measured the static subjective visual vertical (SVV). All patients had imaging by brain CT.

Results: All the patients had contralateral (to the side of the INO) body tilt and an oblique gait, in addition, in six there was an OC of the contralateral eye, with the upper pole rotating away from the INO. In 4 patients in whom the SVV was measured, it was deviated also away from the clinical INO, away from the medial fasciculus lesion (MLF).

Interpretation: Vascular, unilateral, ischemic, acute pontine or pontomesencephalic INO is in many cases accompanied by a central vestibular syndrome in the roll plane.
ANXIETY, DEPRESSION AND SWALLOWING DISORDERS IN PATIENTS WITH PARKINSON’S DISEASE

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Background: Swallowing disturbances (SD) are associated with affective responses such as anxiety and depression. SD, anxiety and depression are common in patients with Parkinson’s disease (PD). The relationships between these affective symptoms and SD in patients with PD are unclear.

Objective: To characterize the relationships between level of anxiety, depression and the patients’ subjective report as well as objective assessment of SD in patients with PD.

Method: Sixty-six PD patients, non-demented by MMSE, answered if experiences any SD, completed SD questionnaire, and underwent evaluation for anxiety and depression. All patients underwent detailed clinical swallowing evaluations and those diagnosed with SD by the speech language pathologist (SLP) also had fiberoptic endoscopic evaluation of swallowing to determine aspiration.

Results: Thirty-seven PD patients (24 males) with SD, diagnosed by the SLP (mean age 69.1 ± 10.1 years, disease duration 8.5 ± 6.1 years and H&Y stage 2.3 ± 1.2) and 29 PD patients (24 males) without SD (mean age 64.5 ± 13.2 years, disease duration 7.5 ± 6.1 years and H&Y stage 1.8 ± 1.0) participated in the study. The SD patients group reported significantly higher anxiety and depression than patients without SD (t (66) =3.116, p=0.003, and t(67)=2.056, p=0.044, respectively). The clinical characteristics of the two groups were similar. Among the patients with SD, 50% exhibited aspiration. No significant difference was found in anxiety and depression level between patients with and without aspiration.

Conclusion: Patients with PD with SD exhibit more depression and anxiety than PD patients without SD. The contributing role of anxiety or depression to the development or worsening of SD and as a result, their place in the treatment strategy needs farther investigation.
CLINICAL FEATURES OF LATE-ONSET IDIOPATHIC INTRACRANIAL HYPERTENSION

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Background: Idiopathic intracranial hypertension (IIH) formerly referred to as pseudotumor cerebri, is typically a disorder of obese females of childbearing age, who are otherwise healthy. The aim of the study is to review the clinical features, risk factors and visual outcome in patients who were diagnosed with IIH after the age of 40 years.

Methods: We retrospectively reviewed the medical records of consecutive patients with IIH, who fulfilled the modified Dandy criteria, during 1998 - 2005.

Results: Seventeen patients who were 40 years of age or older at the time of diagnosis, were recognized and consisted our study population. Follow up period was 21.7 months (between 3 and 58 months). Fifteen patients were women and 2 were men. The mean age upon diagnosis was 50.2 years, with a range of 42 to 61 years. Eleven patients were considered significantly overweight, 64.7% patients had systemic arterial hypertension. Visual symptoms, mainly blurred vision and transient visual obscuration (TVO), were the most common presenting symptom, reported by 70.5% patients. Upon last follow up examination, all patients had corrected visual acuity. Fourteen patients had normal visual field, and the visual field defect remained stable in 3 patients.

Conclusions: Our results suggest that the IIH should be considered in the differential diagnosis of adult patients with visual symptoms, especially when associated with headache. The frequent association of systemic hypertension may indicate a possible risk factor for IIH other than obesity.
MENINGISMUS IS A COMMONLY OVERLOOKED FINDING IN TENSION-TYPE HEADACHE IN CHILDREN AND ADOLESCENTS

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Background: In many cases of Tension Headaches in children, no attention is paid to meningeal symptoms, consequently the results of neurological examination are considered normal. This is the first study to focus on the presence of meningeal signs in children with chronic headaches.

Methods: The patient population comprised 887 patients aged 5-17 years who were examined by a pediatric neurologist in a routine outpatient practice over a 8-year period. Their complaints and anamnesis could possibly be diagnosed as Tension-Type Headache. During a neurological examination particular attention was paid to meningeal symptoms, including nuchal rigidity, Kernig's sign, Brudzinski's three signs (upper, middle and lower), and the "tripod" sign.

Results: The syndrome of meningismus (meaning meningeal signs without symptoms of meningitis) was present in 97% of the patients. Meningismus consisted of positive Kernig's sign, Brudzinski's lower sign and the "tripod" sign. In this group of children (the 97%), when bending the head forward there was noted rigidity of occiput muscles or they complained of pain in the head, neck and epigastrium. According to anamnestic data, up to 80% of children, prior to beginning of headaches had any illness, commonly - infectious diseases in otolaryngological region, mostly Streptococcal infection.11% of the children mentioned minor head or back trauma prior to the period of the headache. For treatment we used a recommended method that is applied also in “post lumbar puncture headaches”: namely, rest in a recumbent position. This method proved to be successful during a course of 7 to 10 days, bringing relief from the headache. In addition, the meningeal signs had disappeared.

Conclusion: We conclude that the major clinical syndrome of so-called Tension Type Headaches in children and adolescents is Meningismus Syndrome. The origin of this syndrome is possibly chronic, sterile, mild pachymeningitis, possible autoimmune. The cause of pachymeningitis is most likely one of various infections of otolaryngological region, or a minor trauma of the head or/and back.
Background: Ocular lateropulsion is a common finding in lateral medullary infarcts. It is probably due to damage to fibers that project from the contralateral inferior olivary nucleus via the inferior cerebellar peduncle to the Purkinje cells and via the fastigial nuclei to the opposite PPRF. We present a patient with a right homonymous hemianopia who reported improved vision after a recent left lateral medullary infarction that caused left ocular lateropulsion.

Case report: A 49-year-old man was admitted because of sudden onset of vertigo, dysphagia, vertical diplopia and loss of coordination in the left limbs. Two years previously he suffered a left temporo-occipital infarct with a congruous right homonymous hemianopia. On examination his eyes deviated to the left. There was a skew deviation with the right eye hypertropic. A gaze evoked nystagmus was observed. His speech was dysarthric. Signs of severe left cerebellar dysfunction and a crossed sensory loss were found. A brain MRI revealed a recent ischemic lesion in the left dorsolateral medulla oblongata and a chronic left occipitotemporal mediocaudal infarct. The patient reported that his vision had improved. Since the previous stroke his vision was blurred, he used to bump into objects on the right and had difficulty reading. He became now able to see clearly, to observe better moving objects and to read more fluently.

Discussion: Ocular search of a patient with hemianopia would be expected to occur towards the blind hemifield in order to bring the objects onto the retina of the healthy side. Therefore the principal question is why eye deviation towards the healthy hemifield would improve vision? Firstly, gazing in the direction opposite the blind hemifields could enhance an alternative visual system, possibly by activation of the superior colliculus-pulvinar system and the uncrossed retino-geniculate fibres. Secondly, the direction of gaze opposite the hemianopic side may have corrected a visual defect that was due to dysfunction of cells that function upon hemispheric rather than retinotopic coordinates. Finally, the possibility of changes in the modality-specific attention will be discussed.
Background: There are a very limited data about the dynamics of TCD parameters in patients who underwent carotid angioplasty and stenting (CAS).

Objective: To compare parameters of cerebral hemodynamics by CTD before and after CAS.

Patients and Methods: Sixty eight patients (mean age 69±9.5 years, 76.5%-males) with severe carotid stenosis (83.4±10.2%) were examined by TCD before and one to three months after CAS. Thirty two patients were referred to CAS due to primary carotid stenosis and 36 due to restenosis after carotid endarterectomy (CEA). A broad TCD protocol was applied including the following indexes: asymmetry of cerebral blood flow velocity (CBFV) in middle and anterior cerebral arteries (MCA and ACA), CBFV in basilar artery, pulsability index (PI) and flow acceleration (FA) index.

Results: The difference in TCD parameters between the groups with primary stenosis and with restenosis, before CAS, was statistically significant for asymmetry of CBFV in ACAs only. The index was higher in patients with primary stenosis. All examined TCD parameters after CAS in primary stenosis as in restenosis as well as in the whole group of patients showed significant and similar improvement.

Conclusions: Carotid angioplasty and stenting effectively restore cerebral hemodynamics in patients with primary severe carotid stenosis as well as in patients with restenosis after CEA.
EVIDENCE FOR SYSTEMIC MICROINFLAMMATION IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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Background: Amyotrophic lateral sclerosis (ALS) is a progressive neuromuscular disease, the exact etiology of which is still unknown. Recent evidence suggests that neuro-inflammation may influence onset and/or progression of the disease.

Aim: to determine the intensity of systemic inflammation in clinically asymptomatic (without overt infection and/or inflammation) ALS patients, in order to determine whether the existence of ALS itself is associated with a heightened inflammatory activity, and whether it has prognostic significance.

Patients and Methods: The study group consisted of ALS patients from the ALS out-patient clinic at the Tel Aviv Medical Center. The control group was selected from the database of the Tel Aviv Medical Center Inflammation Survey. The following inflammatory parameters were compared between the groups: the erythrocyte sedimentation rate (ESR), fibrinogen and C-reactive protein concentrations, leukocytes count, and the neutrophils to lymphocytes ratio. Moreover, the correlation between inflammatory parameters and the disability status of the patients, as expressed by the ALS Functional Rating Scale (ALSFRS-R), was evaluated.

Results: 62 patients (21 women, 34%) were included. Their mean age was 58.7±13.9 years. For each patient we found a perfectly matched control from the database. CRP, fibrinogen and the neutrophils to lymphocytes ratio were significantly (p<0.001, 0.01, 0.01 respectively) elevated in the patients group. A statistically significant inverse correlation was found between ALSFRS-R and CRP, ESR, and fibrinogen levels (p=0.026, 0.034, <0.001 respectively).

Conclusions: Our findings suggest that ALS patients harbor a heightened systemic microinflammation, that is possibly related to their pathogenesis, and is correlated to their disease stage.
DISTAL MEDIAL PLANTAR NEUROPATHY IN INFANTRY RECRUITS

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Background: Physicians in basic military training units of the Israeli defense forces (IDF) frequently encounter soldiers with forefoot sensory symptoms. In this study we prospectively evaluated the clinical characteristics and prevalence of distal forefoot sensory disturbances among infantry recruits.

Methods: All the soldiers of an infantry unit (4 to 6 weeks into their basic training) were asked to report sensory disturbances in their feet. All subjects who reported plantar sensory symptomatology were evaluated by a neurologist (G.I.). During the study period, nerve conduction studies were conducted in infantry recruits referred to our electrodiagnostic laboratory due to similar symptoms.

Results: We studied 269 trainees, 178 men and 91 women. Average age was 19 years (SD 0.69, range 18 to 22). Plantar sensory disturbances were reported by 19 soldiers (7.1%). Affected individuals described loss of sensation, numbness, tingling, and disturbances in temperature sensation. Burning sensation, increased pain sensitivity, and muscle cramps were reported by 20 to 30%. One third of the patients reported nocturnal exacerbation of the symptoms. The sensory loss (for pain, light touch, and thermal sensation but not for vibration or proprioception) was limited to the fronto-medial aspect of the plantar region, the region innervated by a distal branch of the medial plantar nerve. On distal MPN stimulation, absent or markedly reduced distal branch sensory potentials were found in four of the eight patients.

Conclusions: Distal medial plantar neuropathy (DMPN) is a common disorder among infantry trainees. Further study is indicated to assess the natural history of the disease.
Objective: To study the effects of Constraint Induced Movement Therapy (CIMT) on cortical motor activation patterns in sub-acute sub-cortical stroke patients.

Background: CIMT is a well established technique to improve the function of a paretic limb in stroke patients. It is based on the theory of "learned non-use" of the injured limb. Although many studies using this method have shown that CIMT leads to a long lasting behavioral improvement in the affected limb, the neural basis of this improvement is not yet clear.

Methods: 3 patients suffering from left sub-cortical strokes 3 to 6 months after the event participated in the study. Patients were treated with classical CIMT methods including constraining of the left arm for 90% of awaking hours and participating in 6 hours/day rehabilitation program for 2 weeks. Clinical evaluation included: upper-extremity portion of the Fugl-Meyer Assessment (FMA), the Wolf Motor Function Test (WMFT), Motor Activity Log (MAL) and other functional examinations. Additionally, 4 consecutive functional magnetic resonance imaging (fMRI) scans were conducted, before and after CIMT treatment. During fMRI scans, subjects performed isotonic ankle, knee, wrist or elbow movements of either body side separately, in a constant frequency.

Results: All 3 patients exhibited improvement on FMA, MAL and WMFT scores immediately after the treatment, representing increased use and better function of the affected arm. However, the only patient, so far, that was examined 6 months post treatment exhibited deterioration on the MAL. In this patient, the abnormal ipsilateral representation of the paretic hand which appeared pre-treatment disappeared in the fMRI scan immediately post treatment, returning to a normal activation pattern. This effect was short lasting: In the long term follow up, activation patterns elicited by the injured limb returned to their abnormal pre-treatment appearance, thus correlating to the MAL deterioration. The 2nd patient also showed abnormal ipsilateral representation of the paretic hand pre-treatment, which returned to the normal pattern 3 months post-CIMT. The 3rd patient showed no change between the pre and post treatment scans.

Conclusions: Reorganization of cortical motor patterns occurs in response to CIMT treatment in some patients. This effect is thought to be relatively short lasting.
BILATERAL COORDINATION OFGAIT AND ITS RELATION TO
FREEZING OF GAIT IN PARKINSON’S DISEASE

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Background: Among patients with Parkinson’s disease (PD), freezing of gait (FOG) episodes often occur when the patient starts walking and turns, two tasks that likely demand a high degree of coordination between the two legs.

Objective: To test the hypothesis that impairments in the bilateral coordination of stepping are related to FOG in PD.

Methods: We compared the gait of PD patients that experience FOG (PD+FOG; n=21) with the gait of those who do not (PD-FOG; n=13) with regards to the relationship of FOG to the bilateral coordination of stepping during an 80 m walk. Specifically, we quantified the stride duration of one foot as a gait cycle or 360°, determined the relative timing of contra-lateral heel-strikes, and defined this as the phase, \( \phi \) (ideally, \( \phi = 180^\circ \) for every step). The sum of the coefficient of variation of \( \phi \) and the mean absolute difference between \( \phi \) and 180° was defined as the Phase Coordination Index (PCI), representing variability and inaccuracy, respectively, in phase generation. Subjects were studied in an "Off" and again in an "On" state.

Results: During "Off", PCI values were higher (poorer coordination) in PD+FOG compared to PD-FOG, \( p<0.024 \). Stride-to-stride phase adjustments, \( \Delta \phi \), were also studied. For both patient groups, the number of 'converging' \( \Delta \phi \), i.e., shifting \( \phi \) values towards 180°, was significantly higher than the number of 'diverging' \( \Delta \phi \), i.e., shifting \( \phi \) values away from 180° (\( p<0.0001 \)). We found that both groups scale their 'converging' adjustments to the same extent, but when generating diverging \( \Delta \phi \), PD+FOG patients exhibit far less control (\( p<0.006 \)). Asymmetry in clinical symptoms and the measures of bilateral coordination were not associated.

Conclusions: This study demonstrates that distinctive impairments in the bilateral coordination of gait, in particular timing of the heel-strike of one foot with respect to the other, are associated with FOG. We speculate that in PD, poor left/ right coordination in walking makes the locomotor system more vulnerable and freezing episodes can occur more easily in challenging situations.
IMPACT OF DIETARY VITAMIN B12 DEFICIENCY ON ACADEMIC ACHIEVEMENTS IN SCHOOL CHILDREN

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Objective: To determine the impact of vitamin B12 or folic acid deficiency and anemia on academic achievements of elementary school children in a low socioeconomic population.

Background: Deficiency of certain nutrients such as vitamin B12, folic acid and iron is often associated with impairment of memory, concentration and learning abilities. Dietary deficiency of these micronutrients is uncommon in western countries, particularly among non vegetarian young subjects while it is common in developing countries. This study was conducted among the Bedouin population in the south of Israel, where extremely high rates of selective malnutrition were previously found.

Methods: 67 elementary school children aged 9-11 years were randomly tested. Serum levels of vitamin B12, folic acid and blood hemoglobin were measured. Individual data regarding number of family members, father’s employment status and weekly meat consumption was collected for each student. The school achievements were obtained in comparison to the average marks achieved by all during the last two semesters of the school year.

Results: Vitamin B12 deficiency was found in 30% of the study population, more commonly among females (40%), whereas anemia was found in 12% and none of the subjects had folic acid deficiency. Poor school performance was recorded in 100% of students with vitamin B12 deficiency compared to 26% of children with B12 levels above 200 pg/ml (p=0.023). A positive correlation between low serum vitamin B12 and number of weekly meat meal, and a negative correlation with the total number of family members was found. There was no correlation between anemia and school performance.

Conclusion: Despite the small number of school children enrolled in this study, our results demonstrate a high prevalence of vitamin B12 deficiency among Bedouin elementary school children and a positive correlation between low vitamin levels and low academic achievement. These findings further underscore the need to supplement the diet of low socioeconomic populations with essential micronutrients.
Background: Mental practice refers to a training technique, widely used in the field of neurological rehabilitation, whereby the procedures required to perform a given task are mentally rehearsed in the absence of physical movement. We studied the gains in performance in practice on a higher-level cognitive skill – solving a modified version of the Tower of London (ToL) task in either actual or mental practice. The ToL is considered a planning task, in which the participant must rearrange, using a minimum number of moves, a set of three colored discs arranged on three pegs, so that the final configuration matches a specified goal state.

Objectives: To compare, in terms of effectiveness and transferability of the acquired knowledge, between two different training modes - actual vs. mental practice.

Methods: A modified version of the ToL, with an additional peg and an additional disc to the original three-peg three-disc version was used. The task included 3 levels of difficulty. Transfer tasks (conditions) included: switching from actual to mental performance or vice versa and performance with a different hand. Participants (N=52; in three main groups: actual, mental and combined practice) were trained in 3 consecutive daily sessions on the ToL task.

Results: Both training conditions resulted in large significant gains in terms of both speed and accuracy. While both conditions resulted in 'within-session' improvements, mainly during the initial session, only participants who underwent actual training showed 'between-sessions' gains – additional gains evolving after the termination of the training experience. Mental practice resulted in less effective transfer. However, a limited experience with actual performance added to a mainly mental practice schedule ("combined practice") resulted in robust performance gains in both mental and actual performance. Actual practice resulted in some hand specificity.

Conclusions: Although mental practice was effective, actual training on the ToL task resulted in robust learning reflecting many of the characteristics of procedural learning in simple perceptual and motor tasks.
IN Volvement of NF-KB in Regulating O(6)-Methylguanine-DNA-Methyltransferase: New Mechanism Whereby NF-KB Mediates DNA Damage Repair

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Background: O(6)-methylguanine-DNA-methyltransferase (MGMT) and nuclear factor kappa-B (NF-B) are two key effectors associated with the development of resistance to alkylating agent-based chemotherapy.

Objective: This prompted us to hypothesize that NF-B might be involved in MGMT regulation.

Results: Consistent with this hypothesis, we have discovered two putative NF-B binding sites within the MGMT promoter region, and have demonstrated by an electrophoretic mobility shift assay the specific and direct interaction of NF-B at each of these sites. Transfection of HEK293 cells with the NF-B subunit p65 induced a 55-fold increase in MGMT expression while addition of the NF-B super repressor \textsuperscript{\Delta}NI B completely abrogated the induction. We also found a significant correlation between the extent of NF-B activation and MGMT expression in the glioma cell lines and the human glial tumors tested. Furthermore, the extent of NF-B activation in the gliomas was correlated with MGMT expression and independent of MGMT promoter methylation. These findings are of potential clinical significance as we show that cell lines with forced expression of p65 or high constitutive NF-B activity are less sensitive to nitrosourea treatment regardless of MGMT promoter methylation status.

Conclusion: The findings of our study strongly suggest that NF-B plays a major role in MGMT regulation, and may shed light on the novel role of NF-B in regulating the DNA damage repair mechanism, and acquisition of chemoresistance.
Background: Recurrent falls in the elderly are commonly associated with extrapyramidal syndromes, but also in abnormalities that involve other parts of the central nervous system. It is difficult to differentiate between the various causes of recurrent falls, especially if extrapyramidal symptoms are part of the clinical presentation. We investigate the integrity of the striatal dopamine transporters using \(^{123}\text{I}\)-FP-CIT single-photon emission computed tomography (SPECT) imaging in patients with recurrent falls.

Patients and Methods: 21 patients who were referred to the Movement Disorders Unit for evaluation of sudden recurrent falls, without a definite neurological diagnosis, were included in a prospective cohort study. A thorough evaluation of the neurological signs and postural responses was performed. SPECT with the dopamine transporter (DaT) ligand was performed 180 min after injection of 185 MBq \(^{123}\text{I}\)-FP-CIT using a dual-head gamma-camera.

Results: DaT SPECT was normal in 15/21 patients (71%). Of those 73% had abnormal MRI imaging suggestive of artherosclerosis lesions. Eleven patients with a normal DaT SPECT had mild parkinsonian symptoms. Two patients with no parkinsonian symptoms had abnormal SPECT values. There was no correlation of the SPECT results with patient age, fall duration, or fall frequency, and no significant difference in the relative distribution of SPECT findings among patients with and without extrapyramidal symptoms or vascular risk factors.

Conclusions: The diagnosis of recurrent falls cannot be accurately confirmed on the basis of clinical features alone. \(^{123}\text{I}\)-FP-CIT SPECT imaging may be useful for determining whether or not recurrent falls in individual patients, regardless of the presence or absence of extrapyramidal symptoms, are due to degeneration of the nigrostratial system.
SUDDEN ONSET OF FOCAL NEUROLOGICAL SYMPTOMS IN PREGNANCY:
MIGRAINE IS MORE COMMON THAN ISCHEMIA.

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Background: Sudden onset of focal neurological symptoms in young healthy pregnant women is not infrequent and usually leads to extensive and costly evaluations. While in some patients the symptoms may be attributed to true ischemia, the pathogenesis remains unclear for others.

Objective: To determine the pathogenesis of focal neurological symptoms in previously healthy pregnant women and to set up prognostic variables for target screening in appropriate patients.

Methods: Previously healthy pregnant women, presenting to our hospital with acute neurological symptoms, were recruited. Those with prior history of migraine or cerebrovascular disease were excluded. Their evaluation included an MRI/ MRV protocol, complete cardiovascular evaluation (echocardiography, duplex ultrasonography and hypercoagulability tests). The outpatient follow-up was estimated at 12 months further on.

Results: Nine patients were enrolled, mean age of 32.6 (range- 24-41). The mean pregnancy age at the symptoms onset was 35 weeks (range 17-44). Presenting symptoms included dysphasia (5) with hemisensory (4) or hemimotor (4) syndrome. Detailed history revealed that in 4 of the 9 patients the symptoms were preceded by scintillating scotomas and in 6 patients were followed by throbbing headache (first-ever in the lifetime). Only one patient had evidence of frank infarction on MRI, another two had single bright focus on FLAIR , and 6 patients had completely normal scans. Echocardiography was normal in all except one patient, which showed a mobile cardiac mass interpreted as a thrombus, with normal MRI and no evidence for stroke on follow up. Carotid duplex and hypercoagulability tests were negative in all patients. None of our patients had true ischemic event during follow-up. Three of them developed migraine with aura during this period.

Conclusions: The occurrence of focal neurological symptoms in pregnancy is frequently preceded by aural visual phenomena and may be attributed to a first-ever migraine attack. Frank ischemia appears to be less common than migraine, therefore a brain MRI and extensive evaluations may not be warranted in such patients.
DOLICHOECTASIA OF THE VERTEBRAL ARTERY PRESENTING AS ACUTE VESTIBULAR SYNDROMES

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Background: Dolichoectasia of the vertebral artery (DVA) may cause a variety of brainstem and cranial nerve syndromes due to compression or ischemia. Transient vestibular dysfunction associated with DVA has rarely been described.

Objectives: To describe two patients with acute vestibular syndromes and DVA diagnosed by TCD and MRI.

Case reports: Two patients presented with repeated short episodes of acute vertigo, oscillopsia, nystagmus and loss of balance. Peripheral vestibular dysfunction was initially suspected, however, a history of a brief diplopia in one patient, and a non-rotatory horizontal nystagmus without latency or fatigability in the other, pointed to a central origin. Computerized tomography did not show any brain lesions. TCD demonstrated reduced blood flow velocities in both VA’s and in the basilar artery in both patients. Brain MRI showed dolichoectasia of one VA with some compression of the medulla oblongata on the symptomatic side, and hypoplasia of the other VA.

Conclusions: Dolichoectasia of the VA is a rare but important cause of some vestibular syndromes, and should be considered in the differential diagnosis of transient acute vertigo. MRI is helpful in the diagnosis of such anomalies of the cerebral blood vessels, however, not always available for any case with vestibular dysfunction. The role of TCD in the evaluation of dolichoectasia of intracranial vessels has not yet been established. However, the demonstration of reduced BFV in the posterior circulation in our cases, combined with similar findings in the literature, may indicate some abnormality in these vessels, and the need for further workup. Accurate diagnosis of such anomalies is important in choosing the appropriate treatment and determining the need for a long-term follow-up. TCD may prove to be a useful tool in the evaluation of intracranial dolichoectasia. Further studies are needed in order to determine a specific abnormal blood flow pattern in such cases.
BEHAVIORAL AND PSYCHIATRIC MANIFESTATIONS FOLLOWING DEEP BRAIN STIMULATION OF THE SUBTHALAMIC NUCLEUS IN PARKINSON’S DISEASE: CAN WE IDENTIFY PREDISPPOSING FACTORS?

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Background: Behavioral and psychiatric complications following deep brain stimulation of the subthalamic nucleus (STN-DBS) for Parkinson’s disease (PD) are not uncommon.

Objective: To identify predisposing factors for behavioral and psychiatric worsening following STN DBS.

Methods: 22 patients (16 males) and caregivers were interviewed retrospectively concerning aspects of behavior during three months preceding the DBS operation and three months before the study. We used the Neurobehavioral Rating Scale (NRS), the Beck Depression Inventory (BDI), the Neuropsychiatric Inventory (NPI), the Brief psychiatric rating scale (BPRS - partial), the Work and social Adjustment Scale (WSAS) and three questions addressing the hedonistic homeostatic dysregulation syndrome (HHD). According to a clinician’s global impression of change for the motor (CGIC-M) and behavioral (CGIC-B) status patients were divided into two groups, those who remained stable or improved behaviorally and those who had worsened. The groups were compared using the Fisher exact test and the Mann-Whitney test.

Results: The two groups (11 patients each) did not differ in terms of gender, age at operation, time from PD onset to DBS, length of follow-up since operation, extent of medication reduction following DBS or the motor outcome. Patients in group 1 had a longer disease duration [18 (13-21) vs. 11 (11-14.5); median, IQR; p=0.047] and a longer time to surgery (p=0.151). A comparison of the NPI, NRS and HHD scores revealed no significant differences between the groups. Analysis of individual items of the NPI and BPRS scales revealed that agitation or aggression were higher before DBS in group 1 compared group 2 (mean ± SD) (0.73 ± 0.79 vs. 0.27± 0.9; p=0.032).

Conclusions: In this study preoperative behavioral scores did not predict behavioral complications. Shorter disease duration and a lower degree of agitation were the only factors found to be in association with psychiatric worsening.
Background: When acute vertigo with vertical diplopia is accompanied by positive neurological findings such as nystagmus and skew deviation, a clinical diagnosis of a brainstem or cerebellar lesion is usually highly suspected. However, these symptoms and signs can be sometimes of peripheral origin.

Objectives: To report three cases of acute vertigo with skew deviation and vertical diplopia due to vestibular neuritis and to present the bedside neurological tests which readily support the diagnosis and exclude a brainstem or cerebellar lesion.

Methods: Two women and one man (58, 60 and 50 years old respectively) with sudden severe vertigo, nausea, vomiting, disequilibrium and vertical diplopia were examined and videotaped.

Results: Bedside neuro-otological examination disclosed in all the patients head tilt with skew deviation and jerky nystagmus beating to the opposite direction of the head tilt. All had also a positive head thrust test to the side of the head tilt and some instability that did not constrain ambulation. The rest of their neurological examination was normal. All had normal brain and temporal bone MRI. Caloric irrigation of the ears showed unilateral loss of response. Diplopia and skew deviation resolved within three weeks. On follow-up examination eight months to 2 years, the only complaint was a transient sensation of dizziness and disequilibrium when turning suddenly to the side of the lesion. On detailed neuro-otological examination the only sign was a unilateral positive head thrust test.

Conclusions: Vestibular neuritis can mimic an acute brainstem or cerebellar lesion causing vertigo and skew deviation. The characteristics of the nystagmus and skew deviation, a positive head thrust test and the possibility of ambulation with otherwise normal neurological examination, strongly support the peripheral origin of the disorder without any need to conduct urgent additional tests. Interruption of otolith input to central vestibular and ocular-motor pathways is responsible for the skew deviation in vestibular neuritis.
THE CJD RATING SCALE: A NEW TOOL FOR EVALUATION OF NEUROLOGIC SYMPTOMATOLOGY IN EARLY CJD PATIENTS


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Background: There is no standardized method to rate severity of disease in CJD.

Objectives: To evaluate sensitivity and specificity of a new scale in CJD patients and their relatives, both positive and negative for the E200K mutation.

Methods: 16 CJD patients (12 E200K, 4 sporadic), 23 healthy carriers of the E200K mutation (C+) and 25 subjects from the same family without the mutation (C-) underwent a detailed neurological examination by neurologists blind to genotype and rated the symptoms. The C- subjects are extremely unlikely to develop the disease; the C+ subjects, while currently healthy, are expected to begin deterioration in the future. The new scale includes 29 items thought to reflect progression of disease in CJD. It screens for the presence of positive neurological signs in the visual and oculomotor systems, the brainstem, the cerebellum, the pyramidal and the extrapyramidal systems. Each item is scored as 0= the abnormal sign is not present 1= the abnormal sign is equivocal/present and 2= the abnormal sign is definite/severe.

Results: There was a highly significant difference in the scale total score between the groups (F2,59=80, p<.0001). The patients scored 12.64±6.6, the C+ 0.48±1 and the C- 0.36±.6. There was no overlap between the scores of patients (range 4-23) and the C- group (range 0-2). The two C+ subjects that demonstrated slightly elevated total scores also had slightly lower MMS (26 and 25), and may represent a possible conversion to symptomatic status.

Conclusions: The scale total score showed excellent sensitivity and specificity in this study, and correlations with age and MMS as expected. The snout reflex may be excluded for low specificity, and other items for low sensitivity. While the current data are preliminary, the scale may also have the potential of detecting preclinical disease in subjects at risk.

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Background: The activity of the immune system displays a circadian rhythm. In diseases characterized by aberrant immune activity, chronotherapy – treatment regimen tailored to diurnal body rhythms – may increase medication efficiency, safety, and tolerability. The goal of this study was to compare the outcomes of intravenous corticosteroid administration during the day or night, for treatment of acute multiple sclerosis (MS) relapses.

Methods: Seventeen MS patients were included in the study. Clinical assessment of disability was performed at trial entry, and at days 7 and 30 from therapy initiation. Adverse events and preference of nighttime versus daytime therapy were assessed at the end of the treatment course.

Results: After nighttime treatment, clinical recovery was significantly enhanced and the mean number of side effects was significantly lower. Furthermore, the majority of patients expressed a preference for nighttime versus daytime treatment.

Conclusions: The study suggests a potential benefit for implementation of chronotherapy using steroid treatment for acute MS relapse, with implications for other immune-mediated disorders.
COMPUTERIZED COGNITIVE ASSESSMENT PREDICTS CONVERSION TO DEMENTIA WITHIN TWO YEARS: INTERIM ANALYSIS OF A PROSPECTIVE STUDY OF MCI

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Objective: To predict conversion from MCI to dementia over a two-year follow-up period using baseline cognitive and clinical data.

Background: Only 10-15% of individuals diagnosed with MCI convert to dementia each year, and it is challenging for the clinician to predict risk. The present report is an interim analysis of a study for prospective identification of elderly at high risk for dementia in a multiethnic cohort.

Design/Methods: Two-year follow-up data was available for 38 individuals with MCI (Petersen’s criteria; age: 74.5±8.4; education: 13.5±4.2) who had completed computerized cognitive assessment (Mindstreams, NeuroTrax, Corp. NY) at baseline. Baseline data for these MCIs was compared with that of controls (N=58; age: 74.8±7.9; education: 13.5±3.8) by independent groups t-test. Logistic regression was used to predict probability of conversion to dementia among the MCIs. Candidate predictors included memory, executive function, visual spatial, verbal function, attention, and motor skills age- and education-stratified summary scores as well as cognitive complaint and Lawton iADL data.

Results: MCIs at baseline performed more poorly than controls in memory, executive function, verbal function, and attention (p<0.001) but not in visual spatial or motor skills. Univariate regression models indicated that an MCI converting to dementia was most likely to have an abnormal memory (odds ratio: 11.7) or executive function (odds ratio: 4.5) score at baseline. A multivariate model with memory, executive function, visual spatial, verbal function, cognitive complaint, and Lawton iADL score as predictors correctly classified 89% of MCIs as converters or non-converters (sensitivity: 79%; specificity: 95%). iADL deficit was associated with poor executive function and attention performance at baseline (p=0.02).

Conclusions/Relevance: Computerized cognitive assessment of multiple domains can assist clinicians in identifying MCI patients at high risk for dementia who would benefit most from early treatment.

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EFFECTS OF MOTOR AND COGNITIVE TASKS ON HEMODYNAMIC PARAMETERS IN ORTHOSTATIC HYPOTENSION

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Background: Orthostatic hypotension (OH) is a frequent and often underdiagnosed disorder that is known to affect cognitive and motor performance. The effects of OH on cognitive function while walking have not yet been studied.

Objectives: To assess the relationships between hemodynamic changes (mainly blood pressure), gait, and cognitive performance under single or dual tasking.

Methods: The study group included 10 subjects with OH (age 71.5 ± 10.6 years, 3 females) and a group of 16 age and gender-matched controls. Blood pressure (BP) and heart rate (HR) were monitored continuously during the entire investigation using a pulse plethysmograph (Finapres Medical Systems), and gait parameters were measured using force-sensitive insoles (Infotronic Ultraflex).

Results: In the OH group, on tilt table examination, systolic blood pressure (SBP) declined by a mean of 31.2±10.4 mmHg (range 20-46 mmHg), and diastolic BP (DBP) declined by 8.2 ± 8.4 mmHg. During baseline walking, mean SBP in the OH group was similar to levels measured during the supine condition, while in controls SBP increased by 11.3±17.8 mmHg (p<0.03). HR significantly increased in both the control and OH groups. Cognitive challenge while walking caused significant increase by 16±17 and 10±6 mm Hg respectively in mean SBP and DBP measures in the control group, as compared to baseline walking (p<0.05). In the OH group, mean DBP increased by 8±7 mm Hg, while mean SBP was essentially unchanged, rising by 4±17 mm Hg. HR was unchanged in both groups. The effects of dual tasking on gait parameters included a reduction in speed and an increase in gait variability, which were similar in both groups.

Conclusion: Subjects with OH respond differently than controls to a 2-minute walk with regard to BP and HR. The dual tasking condition further separated OH subjects from age matched controls. Patients with documented OH on tilt-table testing, have reduced hemodynamic adaptation to continuous motor and cognitive demands. This observation may have important clinical implications.
OUTCOME OF DEEP BRAIN STIMULATION (DBS) PROCEDURE IN PARKINSON’S DISEASE PATIENTS (PDPTS) AFTER 1 YEAR: THE ASSAF HAROFE EXPERIENCE

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Background: In the last years many publications have reported DBS as a useful procedure to treat PDpts with motor fluctuations and dyskinesias.

Objectives: To analyze patients who underwent DBS in the Subthalamic Nucleus (STN) before and 1 year after the procedure.

Patients and methods: Six patients (mean age 64±8.6 y; 4males; mean disease duration 13.8 ± 9.3 y; Yahr stage II 2pts; III 3pts; IV 1pts) were evaluated. Each patient was evaluated 12 hours after stopping medication (OFF) and 60 minutes after Levodopa (LD) ingestion (ON). After the operation all the evaluations were done while the stimulator was on. Motor evaluation included motor part of UPDRS, Total Short Parkinson Evaluation Scale (SPES), Time walking 6meter; ADL of SPES. Cognitive evaluation included MMSE, MATTIS, Hamilton test for depression.

Results: Motor status improved while OFF medication (UPDRS before 34.75 ± 11.4 and after DBS 21± 7.53 (n=5). Also while ON the motor symptoms improved but in a lower proportion (UPDRS before 19.6 ±15.2 and after DBS 8.6±6.7 (n=5). The SPES and 6 meter walk showed similar results (A more robust positive effect while patients were off medication). Dyaskinesias almost abated. MMSE, MATTIS and Hamilton did not change significantly. One patient committed suicide 7 months after the procedure. Retrospectively we were notified by the family that the patient had been treated in the past for severe depression. Treatment: Daily LD before DBS 1195.8 ± 485.8 mg. After DBS LD 512.5+ 329.3 mg. Dopa agonists (converted to pergolide) : before 1.275 (+1.02)mg after DBS 0.835(±0.23) mg.

Conclusions: DBS seems to be a very effective tool when PDpts are carefully selected. Depression even in the past may be a serious contraindication for the procedure. Dyskinesias after DBS in the STN may decrease mainly due to less consumption of LD.
MOTOR-MOOD DISSOCIATION IN PARKINSON DISEASE PATIENTS (PDPTs) AFTER DEEP BRAIN STIMULATION (DBS) IN THE SUBTHALAMIC NUCLEUS (STN). ONE YEAR FOLLOW-UP

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Background: One of the serious adverse events observed after DBS in PDpts with motor fluctuations and dyskinesias is the occurrence of behavioral changes difficult to deal with.

Objectives: In order to avoid frustrations and increase the confidence of the patients who underwent the procedure we adopted and "open door policy" in the follow-up of patients

Patients and Methods: Five PD pts who underwent DBS STN (intraoperative macroelectrode stimulation) were regularly examined for 1 year. The pts were "switched on" during admission between 2-4 weeks after surgery. They were initially admitted for 3-4 days for optimal setting and monitoring Thereafter they were discharged and advised to come whenever they feel they need. We also asked them to fill a diary of motor fluctuations, dyskinesias or other symptom as applicable. At visits motor functions and mood were assessed and setting changed as required. In addition we asked pts to evaluate the results of the operation applying the Clinical Global Impression scoring.

Results: Average of visits at 1-3 months: 5/month; at 4-6 months 3/month; at 7-9 1/month; at 10-12months 0.5/month. One patient of the group committed suicide at seven months. This patient did not come to follow –up and latter were notified that he has committed suicide.

Discussion: There was a marked improvement in motor functions in all patients without motor fluctuations (see another presentation of the group). Two patients reported improvement in the sense of well being. Three patients reported feeling "not-good ON" even when fully mobile. This dichotomy between motor ON and lack of emotional ON has not been previously described. We overcome this by changing the setting to a less "optimal" motor setting but to a setting that improved their sense of well being.

Conclusions: Both motor and mood responses need to be considered in determining the optimal DBS setting.
Background: Botulinum toxin type A (BTX-A) injections are effective for patients with cervical dystonia (CD). However the efficacy is usually assessed by clinical scales and questionnaires.

Objectives: to suggest a newly developed series of objective quantitative functional measures that might be helpful in assessing the involved muscles, planning the injection sites and evaluating the efficacy of BTX-A treatment.

Methods: Consecutive CD patients were tested immediately before and 6 weeks following EMG-guided injections of BTX-A (Dysport; mean dose 700±240 IU, range 500-1050 IU). Clinical outcome measures included the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and the Tsui CD Impairment Scale. In addition, patients were assessed for several functional quantitative outcome measures consisting of cervical range of motion (CROM) and the extent of change from the maximal excursion of the head (CV) using the Zebris three-dimensional Motion Capture System; pressure-pain threshold (PPT) using the Somedic Algometer; isometric strength of the cervical muscles using a dedicated wall-mounted dynamometer.

Results: Preliminary data of 4 patients (4 women, mean age of 53.5±6.6 years, range 46-60) are presented. Following treatment there was a marked clinical improvement with a mean reduction of 61.25% (29%, range 25-90%) and 39% (31%, range 4-76) in Tsui and TWSTRS scales respectively. The total CROM increased significantly (p=0.014) from 233 to 244º and the consistency of performing the motion has profoundly improved, indicated by a mean CV of 11.3% and 3.5% prior to and following injection, respectively. Neither the PPT nor the isometric strength evidenced change.

Conclusions: CD patients, treated with BTX-A exhibited, in accordance with their clinical improvement, a higher consistency of CROM performance, and a slight increase in total CROM. No objective weakness was evident in the neck muscles following injections. The CROM and CV are objectively measured functional outcomes that may be useful for the quantification of the therapeutic response.
LEFT UPPER LIMB ALLESTHESIA: A SUPRAMODAL HEMI CORPOREAL REPRESENTATIONAL DEFICIT OR A MULTICOMPONENTAL DEFICIT?

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Objective: To investigate whether allesthesia of the left upper limb, in a patient with a right parietal lesion, is supramodal or dependent upon posture and body part stimulated.

Background: When patients with allesthesia are touched on the contralesional side they report that they where touched on the ipsilesional side. This phenomenon has been interpreted to be a result of a degraded contralesional body representation. Clinical and experimental observations, however, suggest that allesthesia might result from impairments to specific components of the body representation. We investigated whether the left allesthesia is supramodal (both sensory and motor-allokinetic), posture dependent (palm up or down) and body part specific.

Methods: Experimental subject was a patient with left hemiparesis (without right-left confusion or asomatognosia), left hemispatial neglect, and allesthesia of his left arm after right CVA and 5 people without brain injury were controls. The subjective localization of tactile stimuli was investigated with subjects palm up (palm touched) versus palm down (dorsum touched), as well as trunk being touched (intersection of anterior axillary line and lowest rib). Also allokinesia was tested, raising an arm in response to command.

Results: Controls preformed perfectly correct in all conditions. The patient made left-sided allesthetic errors with palm down on 44.4% of trials. This rate did not differ from the rate of allokinetic errors (41.7%), but these rates did significantly differ from rate of allesthesic errors when the palm was up (22.2%, p<0.002) and from allesthesic error in response to stimuli place on the trunk (8.3%, p<0.04). All these error rates of the patient were different from the control subjects except body stimulation.

Conclusions: The parallel involvement of both sensory and motor modalities suggests supramodal deficit in a body representation. This representation is influenced by posture and does not appear to include all body structures suggesting that this representation is both hierarchical and multicomponental.
CENTRAL NERVOUS SYSTEM TUBERCULOSIS: A CLINICO – PATHOLOGICAL PRESENTATION

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Background: Central nervous system (CNS) tuberculosis (TB) remains a public health problem, particularly in developing countries. The clinical spectrum is broad and may be non-specific making early diagnosis difficult. This increases the incidence of mortality.

Patient and Methods: We present a 55-year-old woman that was admitted to our hospital because of headaches, somnolence and mild left hemiparesis with subacute worsening without fever or meningeal signs. The brain CT revealed hydrocephalus and RT basal ganglia ischemic findings. A Ventriculostomy was performed without clinical improvement. Cerebrospinal fluid findings showed elevated protein levels, mononuclear pleocytosis and normal sugar level. Ziehl Nielsen, serum and CSF test for cytomegalovirus, Epstein–Barr virus, herpes simplex virus, herpes zoster virus, and enteroviruses, antibodies to the West Nile Virus were negative. Multiple lesions of increased signal intensity in T1, Ischemic findings and localized leptomeningeal enhancement were also detected on Brain MRI. Isoniazid, rifampin, pyrazinamide, ethambutol, pyridoxine and full corticosteroid treatment was started. A brain biopsy showed acute and chronic inflammatory infiltrate with scattered epithelioid granulomata predominantly in the meninges compatible with angiitis of the CNS. 10 days later mycobacterium tuberculosis was cultured from 2 separated CSF samples. The patient did not respond to treatment and remained comatose. She was transferred to a unit for chronic patients at Tel – Hashomer Hospital.

Conclusions: We will discuss the clinical and pathological findings of this challenging diagnosis. The atypical presentation of our patient with only mild focal signs, headaches and somnolence without fever, neck rigidity or other symptoms highlights the importance of considering TB in the differential diagnosis also in regions of low incidence.