PAW20?Saccadic correlates of cognition in progressive supranuclear palsy

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Methods We recruited symptomatic patients with suspected stroke or TIA <24 h after onset. We measured markers of inflammation, thrombosis; thrombolysis, cardiac dysfunction and cerebral damage. A panel of stroke physicians, neurologists and neuroradiologists reviewed the clinical features, brain imaging and subsequent course of each patient to make the gold standard diagnosis. We constructed multivariate logistic models to analyse the data.

Results We recruited 405 patients with suspected stroke (285 stroke or TIA, 180 mimics) at a median of 7 h (IQR 3–19 h) after symptom onset. Higher levels of Ln NT pro-BNP (OR 2.2 (95% CI 1.5 to 3.0) 75th to 25th centile) and t-tPA (OR 1.6 (1.2 to 2.2)) were associated with a diagnosis of TIA or stroke. Adjustment for neurological impairment and age attenuated these associations. The associations of higher levels of adiponectin (OR 1.8 (1.2 to 2.4)) and IL-10 (OR 1.1 (1.0 to 1.1)) with a diagnosis of mimic were robust to adjustment for neurological impairment, age and infection. A model with eight markers from systematic review had no better diagnostic performance than an emergency department clinician.

Conclusion We found no single marker or combination of markers that positively predicted a diagnosis of stroke or TIA independently of neurological impairment and age, or added usefully to the clinical diagnosis.

PAW19 CHANGES IN IRON-REGULATORY GENE EXPRESSION OCCUR IN HUMAN CELL CULTURE MODELS OF PARKINSON’S DISEASE

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Background Increase in intraneuronal iron is thought to be relevant to the pathogenesis of Parkinson’s disease (PD), although the mechanism remains elusive. Here we investigate expression of the iron importers DMT1 and the transferrin receptor (TRR1), the iron exporter ferroportin (FPN) and the receptor involved in mitochondrial iron uptake (TR2) in a human PD cell culture model.

Methods SH-SY5Y human neuroblastoma cells were differentiated and exposed to PD-relevent toxins (MPP+ (mitochondrial inhibitor), lactacystin (proteasome inhibitor), paraquat (free radical generator). Quantitative PCR was performed to assess fold change of expression levels of mRNA. Protein levels were analysed by Western blot.

Results MPP+ resulted in a significant increase in mRNA and protein levels for the iron import proteins, TRR1, TRR2 and DMT1 (+IRE) as well as the exporter FPN. Similar changes occurred with paraquat. Lactacystin resulted in a significant increase only in TRR1 mRNA.

Conclusion The finding of MPP+-induced increased expression of proteins involved in cellular and mitochondrial iron import in a human cell culture model of PD supports the hypothesis of a functional mitochondrial iron deficit driving neuronal iron uptake. Increase in FPN expression may be an adaptive response. Similar changes occur following exposure to paraquat, another inducer of oxidative stress. The response to lactacystin suggests a difference in neuronal iron handling induced by different toxins.

PAW20 SACCADIC CORRELATES OF COGNITION IN PROGRESSIVE SUPRANUCLEAR PALSY

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Introduction Oculomotor and cognitive functions are both affected by progressive supranuclear palsy (PSP). From functional-anatomical models of parallel cortico-subcortical loops, we predicted that cognition and oculomotor control would be more closely related than motor performance.

Methods 19 PSP patients and 22 controls underwent reflex saccade monitoring with a head mounted infrared saccadometer and the LATER model of reciprocal latency (Ober consulting; Carpenter et al 1995). Cognitive assessment included: the Addenbrookes Cognitive Assessment-revised (ACE-R); Hayling & Brixton Tests; frontal assessment battery (FAB) and tests of social cognition using: emotion recognition tests; TASIT and Mind in the Eyes tests. Stepwise regression analyses of cognitive function (ACE-R) included reciprocal latency, UPDRS and disease duration.

Results Saccadometry was well tolerated. PSP increased saccade latency: Reciprocal latency correlated with cognitive function (ACE-R; errors on the Hayling; FAB; face emotion recognition and TASIT). In stepwise regression analyses, reciprocal latency was the best predictor for cognition. In the presence of reciprocal latency, UPDRS and disease duration did not significantly predict cognitive function.

Conclusion PSP increased reflex saccadic latency. Critically, reciprocal latency correlated with cognitive ability, beyond UPDRS and disease duration. In the future, latencies may be able to be used as an objective correlate of cognition in this patient group.

PAW21 REWARDING VISUAL CUES INCREASE Dopamine NEUROTRANSMISSION IN PARKINSON’S PATIENTS WITH IMPULSE CONTROL DISORDERS: A PET STUDY

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Background Current evidence connects impulse control disorders (ICDs) to dopaminergic replacement therapy used for the treatment of Parkinson’s disease (PD). Common ICDs include hypersexuality, pathological gambling, compulsive shopping and binge eating. The underlying neuropathology is thought to be due to sensitisation of the dopaminergic system in the striatum and related neurocircuity.

Aim To investigate the effect of rewarding visual cues on dopamine neurotransmission in PD patients with ICDs.

Methods Ten ICD PD patients and five PD controls underwent two randomised positron emission tomography (PET) scans with 11C-raclopride (RAC) after a medication challenge with levodopa while observing neutral or rewarding (gambling, sex, food and money) images. Scans were analysed using region-of-interest approach.

Results The ICD PD group showed a significant decrease of RAC binding in ventral striatum (p=0.001) and caudate nucleus (p=0.015) in response to rewarding images (compared to neutral images), where in PD controls there was no difference.

Discussion Our PET results suggest a significant increase in the release of endogenous dopamine in ventral striatum and caudate nucleus in PD patients with ICDs and further support the role of...