There was also decreased connectivity between the anterior cingulate and right lateral occipital cortex, and between the left anterior insula to the cerebellum and precuneus cortex. Conclusions: The process of effort discounting is correlated to functional connectivity changes involving the precuneus, anterior cingulate, and left anterior insula in healthy older adults.

P.002

Saccade parameters reveal cognitive impairment and differentially associate with cognitive domains across neurodegenerative diseases

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Background: Eye movements reveal neurodegenerative disease processes due to overlap between oculomotor circuitry and disease-affected areas. Characterizing oculomotor behaviour in context of cognitive function may enhance disease diagnosis and monitoring. We therefore aimed to quantify cognitive impairment in neurodegenerative disease using saccade behaviour and neuropsychology. Methods: The Ontario Neurodegenerative Disease Research Initiative recruited individuals with neurodegenerative disease: one of Alzheimer's disease, mild cognitive impairment, amyotrophic lateral sclerosis, frontotemporal dementia, Parkinson's disease, or cerebrovascular disease. Patients (n=450, age 40-87) and healthy controls (n=149, age 42-87) completed a randomly interleaved pro- and anti-saccade task (IPAST) while their eyes were tracked. We explored the relationships of saccade parameters (e.g. task errors, reaction times) to one another and to cognitive domain-specific neuropsychological test scores (e.g. executive function, memory). Results: Task performance worsened with cognitive impairment across multiple diseases. Subsets of saccade parameters were interrelated and also differentially related to neuropsychology-based cognitive domain scores (e.g. antisaccade errors and reaction time associated with executive function). Conclusions: IPAST detects global cognitive impairment across neurodegenerative diseases. Subsets of parameters associate with one another, suggesting disparate underlying circuitry, and with different cognitive domains. This may have implications for use of IPAST as a cognitive screening tool in neurodegenerative disease.

P.003

CJD in the modern era: The value of clinical features and diagnostic tests

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Background: The advent of real-time quaking-induced conversion (RT-QuIC) assays has transformed the diagnostic approach to sporadic Creutzfeldt-Jakob disease (CJD) facilitating earlier recognition of affected patients. Recognizing this, we evaluated the performance of clinical features and diagnostic tests for CJD in the modern era. Methods: Clinical data were extracted from the electronic medical records of 115 patients with probable or definite CJD assessed at Mayo Clinic from 2014-2021. Clinical features and diagnostic tests were evaluated at presentation, and associations with diagnosis and prognosis determined. Results: Mean age-at-symptom onset was 64.8 ±9.4 years; 68 patients were female (59%). The sensitivity of clinical markers (myoclonus) and tests historically considered in patients with suspected CJD was poor (stereotyped EEG abnormalities, 16%; CSF 14-3-3, 60%). Conversely, RT-QuIC (93%), t-tau >1149 pg/mL (88%), and characteristic signal abnormalities on MRI (77%) identified most patients. Multivariable linear regression confirmed shorter days-to-death in patients with myoclonus (125.9, $CI_{95\%}$ 23.3-15.5, p=0.026), visual/cerebellar signs (180.19, $CI_{95\%}$ 282.2-78.2, p<0.001), positive 14-3-3 (193, $CI_{95\%}$ 304.9-82.9; p<0.001), and elevated t-tau (9.0, $CI_{95\%}$ 1.0-18.0, for every 1000 pg/ml elevation; p=0.041). Conclusions: CSF RT-QuIC and elevated t-tau, and stereotyped MRI abnormalities were consistently detected in CJD patients. Myoclonus, EEG findings, and CSF protein 14-3-3 were less useful in the modern era.

P.004

Dissecting the neuropathological causes of rapidly progressive dementia

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Background: A clear understanding of the neuropathological causes of RPD is needed to inform the diagnosis and treatment of patients with rapidly progressive dementia (RPD). Methods: Patients with <4.0 years from symptom onset to death were identified within the Mayo Clinic Neurodegenerative Brain Bank (1998-2020). Relevant clinical details were extracted from available records. Neuropathological diagnoses were assigned following standard protocols. Results: 310/8586 (3.6%) cases met RPD criteria. Relative to typically progressive cases, prion disease most commonly presented as RPD (74%, 32/43), followed by progressive supranuclear palsy/corticobasal degeneration (PSP/