001 ALTERED INTERVAL TIMING AS A NOVEL MARKER OF COGNITIVE FLUCTUATIONS IN LEWY BODY DEMENTIA

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Introduction Cognitive fluctuations are a core clinical feature of Dementia with Lewy Bodies(DLB), characterized by marked spontaneous variations in cognitive abilities and alertness. There is a paucity of objective measurements of fluctuations in the clinical setting. Altered time awareness represents a potential clinical marker of fluctuations and/or their severity. In this study we aimed to investigate qualities of interval timing in patients with DLB.

Methods 25 patients with probable DLB and 14 older controls underwent testing using a simple time perception paradigm testing probing different aspects of interval timing including time estimation(retrospective estimation of interval length),time production(prospective determination of an interval) and time pacing(explicit timing of an interval).Intervals of 10 to 90s were randomized between trials.Self/carer-reporting of fluctuations were measured using the clinician assessment of fluctuation(CAF) and one-day fluctuation(OFS) scales.

Results We found significant differences in interval timing between controls and DLB for time estimation and time production. Overall, DLB patients estimated less time which was significant at 90 seconds(proportion of interval=0.92 vs 0.69; p=0.03). DLB produced less time(proportion of 90s interval 0.58 vs 1.0; p<0.001). Errors in time estimation at 90 seconds correlated with fluctuation presence according to the CAF(r=0.47;p=0.009) whilst errors in time pacing at 90s correlated strongest with fluctuation severity according to the OFS(r=0.65,p<0.001). ROC analysis identified time production(90s) as a good test to distinguish DLB from controls (AUC=0.8;95%CI:0.75–0.98).

Conclusion We demonstrate objective evidence for altered temporal processing in DLB and suggest abnormal interval timing as a novel and clinically useful bedside marker of cognitive fluctuations.

002 THERAPEUTIC LAG IN RELAPSING MULTIPLE SCLEROSIS

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Introduction In multiple sclerosis (MS), treatment start or switch is prompted disease activity, often represented by relapses. Immunomodulatory therapies have potent effects on relapse rates but the time required to attain maximal effect is unclear. We aim to develop a method that allows identification of the time to full clinically manifest effect of treatment on relapses.

Methods Data from MSBase, a multinational MS registry, were used. Inclusion criteria consisted of patients with remitting relapsing MS or clinically isolated syndrome (CIS), minimum 3-year pre-treatment follow up, 1-year treatment persistence, yearly review and availability of the minimum dataset. Stratified by therapy, density curves representing relapses occurrence were created. The first local minimum of the first derivative after treatment start was identified, representing stabilisation of treatment effect. Similar method was utilised to calculate the last pre-treatment point of stabilisation. Annualised relapse rates (ARR) were compared in the pre-treatment pre stabilisation and post-treatment post stabilisation periods.

Results 4979 eligible patients with 6218 treatment epochs were identified for analysis. Time, in years, to treatment effect was shortest for interferon beta-1a sc (0.22, 0.19–0.22), interferon beta-1b (0.24, 0.21–0.24) and fingolimod (0.26, 0.23–0.26) and longest for dimethyl fumarate (0.54, 0.51–0.54) and glatiramer acetate (0.62, 0.60–0.62). Significant differences in pre vs post treatment ARR were present for patients on natalizumab, fingolimod and dimethyl fumarate. A sequential analysis confirmed outcome stability after approximately 1000 recorded number of events.

Conclusions We have developed a method to objectively quantify time from commencing therapy to its full effect. Time to full effect varies among therapies.

003 SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION EVOKED RESONANT NEURAL ACTIVITY PREDICTS CLINICAL RESPONSE TO DBS

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Introduction DBS can improve motor deficit in Parkinson's disease (PD) patients. Existing devices have limitations due to electrode positioning errors, fallible manual programming and delivery of continuous 'open-loop' stimulation despite fluctuating patient state. This results in partial efficacy, adverse effects and increased cost. One solution is to use an electrical feedback signal or 'biomarker' recorded from DBS electrodes. The most widely studied signal has been spontaneous local field potentials (LFPs), particularly beta band (13–30 Hz) and high frequency oscillations (HFO) (200–400 Hz). Here, we report a novel biomarker in the form of a large amplitude, evoked potential, with a characteristic oscillatory decay, termed evoked resonant neural activity (ERNA).[1]

Methods LFPs and ERNA were recorded in 14 patients with PD (28 hemispheres) undergoing STN DBS surgery. The four contacts in each electrode array were ranked according to ERNA amplitude, beta power, HFO power and proximity to the anatomically ideal stimulation location. At least 3 months after surgery, motor scores (UPDRS III, reaction time) were