ALTERED INTERVAL TIMING AS A NOVEL MARKER OF COGNITIVE FLUCTUATIONS IN LEBovy 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 = 0.03). 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 strongly 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.

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 pre 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 (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.
VESTIBULAR EVENT MONITORING IN THE EMERGENCY DEPARTMENT

**Methods** We undertook a structured clinical assessment combined with vestibular event-monitoring in the Emergency Department (ED).

**Results** For the structured assessment group: 54% presented with acute vestibular syndrome (AVS), 24% with episodic spontaneous vertigo (EVS), and 20% with recurrent positional-vertigo (RPV).

For AVS (n=119), most common diagnoses were vestibular neuritis (34%), stroke (34%) and vestibular migraine (13%). Nystagmus slow-phase velocity (SPV) for VN, stroke and VM were 11±5.5°/s, 5.6±2.5°/s, 5.4±5.9°/s; Mean ipsilesional video-head impulse gains were 0.51±0.29, 0.89±0.20 and 0.96±0.13. For EVS (n=53), diagnoses included vestibular migraine (63%), Meniere’s Disease (11%) and others (26%). Nystagmus SPV was 5.4±3.6°/s, 7.6±6.3°/s, 4.1±1.5°/s. In RPV (n=43), common diagnoses were posterior-canal BPPV (66%), horizontal-canal BPPV (23%), migraine (7%). Positional nystagmus SPV profile showed Peak SPV of 42.5°/s, 77.6°/s, 20.64°/s and Time-constants of 6.52s, 22.51s, 34.56s for Posterior-canal BPPV, Horizontal-canal BPPV and Atypical Positional-Vertigo. A final diagnosis was reached in 96% of patients.

In the ED control group, only 77% were separated into spontaneous or positional-vertigo. A diagnosis was provided in 57% and was concordant with the history and examination in 34%.

**Conclusion** Vestibular event-monitoring and structured clinical assessment secured a diagnosis in 96% of cases compared with 34% for the control group, reinforcing its merit.