Eye movements abnormalities during free-viewing task in frontal lobe syndrome: a biomarker for frontotemporal lobar degeneration?

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Introduction

Frontotemporal degeneration (FTD) encompasses a complex spectrum of disorders and often poses a diagnostic challenge, particularly when distinguishing late-onset primary psychiatric disorders (PPD) from behavioural FTD (bvFTD). There is a growing need for biomarkers to aid diagnosis.
Eye movement analysis has emerged as a potential physiological surrogate marker of brain function (*1,2*).

Aim

To investigate eye movement patterns during a **free-viewing task** in patients with **FTD, PPD, and healthy controls (HC),** and to explore correlations between **eye movements and cognitive/behavioral performance.**

Material and methods

129 subjects were enrolled: **39 FTD**, **18 PPD**, and **72** age-matched **HC**. Participants viewed 20 neutral images ***(Figure 1)*** for 10 seconds each, while eye movements were recorded using **Eyelink 1000 Plus system**. Patients were classified according to established clinical criteria. The Clinical Dementia Rating (**CDR**), Montreal Cognitive Assessment (**MoCA**), and Frontal Behavioral Inventory (**FBI**) scores were used to assess disease severity, cognitive function, and behavioral symptoms, respectively.

Results

The final sample included **31 FTD** (of whom 20 bvFTD), **17 PPD**, and **72 HC (3).** The mean age was **68** years; the mean MoCA score was **19/30** for FTD and **22/30** for PPD. Patients with *frontal lobe syndrome* showed a similar visual exploration pattern, characterized by **fewer but longer fixations** and **fewer saccades** than HC ***(Figure 2)***. Compared to controls, *bvFTD* patients exhibited **more blinks** per trial, while *PPD* patients showed **more blinks** overall and a **larger mean saccadic amplitude**. The mean **saccade duration** was able to differentiate *bvFTD* from *PPD*, being higher in the latter ***(Figure 3)***. **Static (4)** ***bvFTD*** viewers displayed higher **apathy** levels, greater dementia **severity**, and poorer **cognitive** performance (language and recall) compared to **dynamic (4)** FTD viewers ($p < 0.05$). In contrast, static and dynamic PPD viewers did not differ significantly ***(Figure 4)***.

Figure 1. *An example of neutral images used in our experiment; the red circle represent a fixation (the longer is the diameter of the circle, the higher is fixation duration of the patient).*

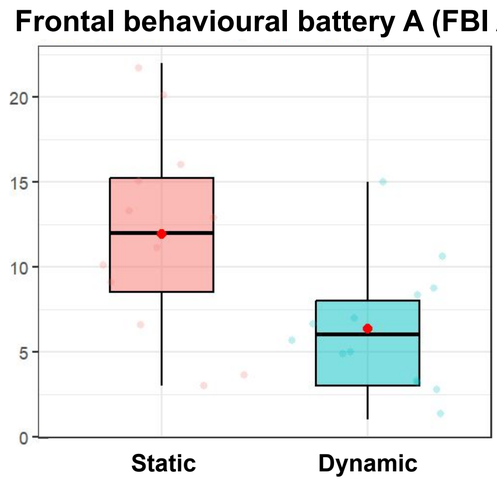

Figure 4 ***Static*** *FTD viewer (displaying fewer longer fixations on average) show a greater* ***apathy*** *(i.e. higher FBI A) than* ***dynamic*** *FTD viewer.*

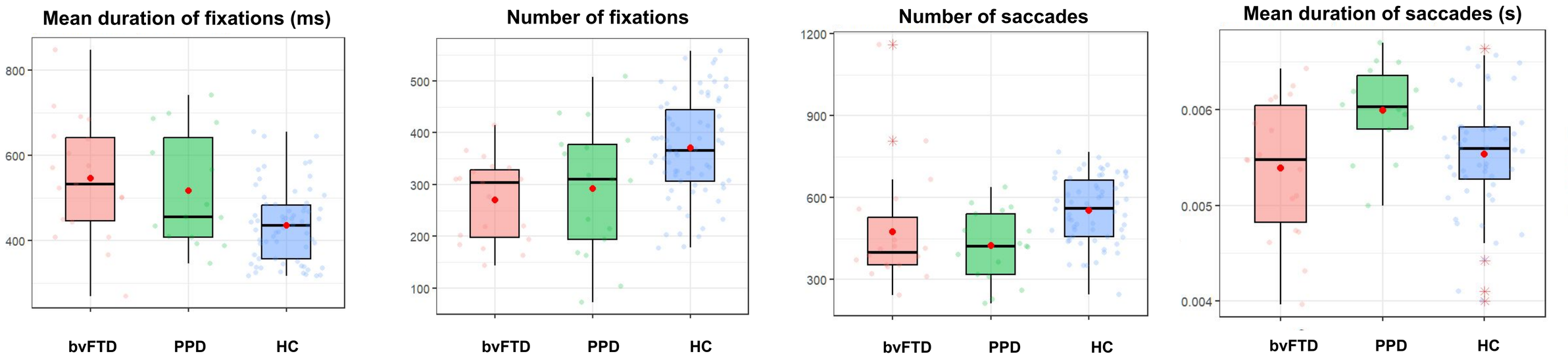

Figure 2. *Eye movement metrics in patients with frontal lobe syndrome (bvFTD and PPD) vs HC. bvFTD vs HC and PPD vs HC = $p < 0.05$.*

Figure 3. *Mean duration of saccades value differentiates bvFTD from PPD patients ($p < 0.05$)*

Discussion and conclusions

Eye movement analysis during free-viewing tasks revealed a distinct oculomotor signature in frontal-lobe syndrome compared to healthy condition. Static viewing patterns reflected greater disease severity and apathy in FTD patients. Saccadic metric could be a promising biomarker to differentiate bvFTD from PPD.
Free-viewing tasks offer a practical, non-invasive method for capturing disease-relevant information in FTD, even in patients with executive and attentional deficits.

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(1) Behler A, Knehr A, Finsel J, Kunz MS, Lang C, Müller K, Müller HP, Pinkhardt EH, Ludolph AC, Lulé D, Kassubek J. Eye movement alterations in presymptomatic C9orf72 expansion gene carriers. J Neurol. 2021 Sep;268(9):3390-3399. doi: 10.1007/s00415-021-10510-z. Epub 2021 Mar 11. PMID: 33709219; PMCID: PMC8357645.
(2) Russell LL, Greaves CV, Convery RS, Bocchetta M, Warren JD, Kaski D, Rohrer JD. Eye movements in frontotemporal dementia: Abnormalities of fixation, saccades and anti-saccades. Alzheimers Dement (N Y). 2021 Dec 31;7(1):e12218. doi: 10.1002/trc2.12218. PMID: 35005203; PMCID: PMC8719345.
(3) 9/129 patients were excluded due to poor eye tracker data quality.
(4) PCA (principal component analysis) was performed separately in FTD and PPD group: two subgroup emerged, static and dynamic viewers, the first showing longer and fewer fixations, the latter on the opposite briefer and more numerous fixations.