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Research Paper

Eyes on cognition: Exploring oculomotor correlates of cognitive function in patients with epilepsy

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ABSTRACT

Objective: This study investigates the relationship between eye tracking parameters and cognitive performance during the Trail Making Test (TMT) in individuals with epilepsy and healthy controls. By analyzing ocular behaviors such as saccade velocity, fixation duration, and pupil diameter, we aim to determine how these metrics reflect executive functioning and attentional control.

Methods: A sample of 95 participants with epilepsy and 34 healthy controls completed the TMT while their eye movements were recorded. Partial correlations, controlling for age, sex, education, medication count, seizure status and epilepsy duration, examined associations between eye tracking measures and cognitive performance derived from EpiTrack and TMT performance.

Results: In the patient group, faster TMT-A performance was associated with shorter fix- ation durations ($r = 0.31$, $p = 0.006$). Lower minimum saccade velocity correlated with slower performance on both TMT-A ($r = -0.35$, $p = 0.002$) and TMT-B ($r = -0.40$, $p < 0.001$), whereas higher peak saccade velocities were linked to worse performance (TMT-A: $r = 0.45$, $p < 0.001$; TMT-B: $r = 0.41$, $p < 0.001$). Pupil diameter findings indicated that slower TMT performance was associated with smaller minimum pupil sizes ($r = -0.23$ to $r = -0.36$), wich may indicate increased cognitive effort and attentional load. Higher EpiTrack scores also correlated with a smaller minimum pupil diameter – but only during the more demanding TMT-B – and with a more restricted saccade velocity range, reflecting greater motor control and attentional stability. No significant correlations emerged within the control group.

Conclusion: These findings highlight the potential of eye tracking as a non-invasive tool for assessing cognitive function in epilepsy. Efficient cognitive performance was characterized by stable and controlled eye movements, whereas impaired performance involved erratic saccade dynamics and prolonged fixations. Importantly, eye tracking parameters provide additional information beyond simple speed measurements, potentially enhancing the differential diagnostic capabilities of the TMT in epilepsy. The observed associations between oculomotor parameters and cognitive performance were not present in the control group, suggesting that these relationships may be specific to epilepsy. Future research should investigate whether both basic and advanced metrics of search strategies are sensitive to disease dynamics and treatment effects in epilepsy.

1. Introduction

Neuropsychological comorbidities are very common in epilepsy, ranging from single- domain impairments of varying degrees to multi-domain and global intellectual impairments [1]. Consequently, neuropsychological assessments play a pivotal role: ideally, testing should commence at the onset of epilepsy and continue periodically to track the course of the disease, assess treatment responses, and detect potential adverse effects of medical or other therapies [2]. Routine screening is frequently performed using brief, standardized tools

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designed to efficiently detect cognitive and behavioral changes. One such tool is the EpiTrack® [3], a validated screening instrument that evaluates attention and executive functions. This tool provides clinicians with a practical means of identifying subtle cognitive changes that may arise during the course of treatment, thereby facilitating timely interventions to improve patient outcomes [4]. Among its subtests, the Trail Making Test (TMT) [5] is a well-established measure of psychomotor speed and mental flexibility [6]. The TMT re- quires participants to connect numbers (TMT-A) or alternating letters and numbers (TMT-B) in ascending order, thus drawing on executive functions traditionally linked to frontal lobe activity [7]. Although overall completion time and error rates already provide a snap- shot of a patient's abilities, they cannot capture exactly how individuals visually navigate the stimuli or manage attentional resources. Recent advances in technology, information processing, and artificial intelligence suggest promising new avenues for capturing patients' cognitive abilities without relying solely on traditional paper-and-pencil approaches. Eye tracking stands out as one such approach: because eye movements naturally accompany most of our actions, measuring them under standardized conditions may reveal additional or even entirely distinct information about underlying cognitive processes [8,9]. The question arises whether, during a well-established cognitive task, these ocular data can confirm, enhance, or surpass the insights gleaned from standard neuropsychological scores.

A growing body of evidence suggests that eye tracking measures provide sensitive indicators of early or subtle cognitive impairments across a wide range of neurological and neurodevelopmental conditions [10–12]. For instance, abnormal saccadic behaviors in antisaccadic or smooth-pursuit tasks are associated with impaired inhibitory control and attentional deficits [13]. Eye tracking studies have also shown that individuals with neurodevelopmental disorders display distinctive visual search patterns, suggesting a continuum of impairment that can be quantified through gaze metrics [14]. Moreover, Tao et al. not only demonstrated that metrics such as saccade latencies, fixation durations, and scanpath lengths can effectively screen for and assess cognitive impairment in various neurological disorders, but also specifically noted the potential for eye tracking to evaluate cognitive deficits in epilepsy [12]. Building on this, research employing eye tracking has found that children with epilepsy exhibit saccadic eye movement abnormalities [15], that temporal lobe epilepsy involves impaired orienting and executive control networks identifiable through eye movements [16], and that frontal lobe epilepsy is associated with memory and attentional deficits measurable via eye tracking [17]. Eye tracking has further been used to detect early cognitive decline in mild cognitive impairment and Alzheimer's disease [11], and to monitor disorders such as amyotrophic lateral sclerosis and Parkinson's disease [18]. By quantifying gaze patterns, fixation durations, and error rates in tasks like the TMT, these objective eye tracking data may highlight subtle cognitive changes that remain undetected by conventional measures [19]. In this context, the present study uses the TMT to illustrate how eye tracking might enrich our understanding of test performance. By integrating wearable eye tracking glasses that record gaze coordinates, blinks, and pupil diameter in real time, we gain a more precise window into patients' moment-to-moment scanning strategies—information that might be particularly crucial in epilepsy, where subtle medication effects and varying seizure burdens can influence cognition in nuanced ways [20]. This approach has the potential to enhance patient monitoring and inform treatment decisions by integrating objective, technology-driven measures with existing clinical assessments. Recent research has demonstrated the feasibility of combining eye tracking with the TMT in healthy individuals, providing valuable insights into cognitive functioning [21]. However, to our knowledge, no study has explored this approach in a clinical population. Given that epilepsy is frequently associated with subtle cognitive deficits, medication effects, and seizure-related fluctuations in attention and executive function [22], eye tracking may offer an important additional layer of information beyond traditional test scores. Accordingly, the present study is the first to apply an eye tracking-based TMT in epilepsy patients. We examine whether specific eye tracking measures correlate with cognitive performance. These insights may refine our capacity to monitor cognitive status along the disease, recognize drug side effects, and tailor therapeutic strategies for patients with epilepsy. In addition, we included a small healthy control group to compare patients' oculomotor behavior with normative data and to determine whether the observed eye movement patterns are specific to epilepsy or reflect general aspects of cognitive processing. This proof-of-concept study builds upon prior work [11,12,23] by investigating whether eye tracking measures show meaningful correlations with cognitive ability during a visual search task in patients with epilepsy. By extending this research to an adult epilepsy population, we aim to establish whether eye tracking metrics can serve as a clinically valuable addition to standard neuropsychological testing.

2. Methods

2.1. Participants

A total of 105 adult patients with epilepsy were initially recruited from the Department of Epileptology at the University Hospital Bonn between September 2024 and January 2025. Of these, 10 had to be excluded due to missing data or technical issues during eye tracking acquisition or upload, resulting in a final sample of 95 patients (age range: 18–76 years, mean age = 38.0 years, SD = 16.9) included in the analyses. Table 1 summarizes the demographic and clinical characteristics of the sample. The sample consisted of both in- patients and outpatients, with 48.4 % being female. Participants provided written informed consent, and the study was approved by the University Hospital Bonn local Ethics Committee (approval number: 2024–307-BO). Participants were included in the study if they were aged 18 years or older, had a confirmed diagnosis of epilepsy, and were able to complete the neuropsychological testing. Exclusion criteria comprised severe visual impairment that could not be corrected by glasses, the use of

Table 1
Demographic and clinical characteristics of the patient sample.

Variable	M (SD) / n (%)
Age (years)	38.0 (16.9)
Gender	
Male	49 (51.6 %)
Female	46 (48.4 %)
Age at onset (years)	27.4 (19.8)
Duration of epilepsy (years)	10.6 (6.5)
Epilepsy type	
Generalized epilepsy	14 (14.7 %)
Focal epilepsy	81 (85.3 %)
Frontal	4 (4.9 %)
Temporal	53 (65.4 %)
Parietal	2 (2.5 %)
Multifocal	5 (6.2 %)
Unknown	17 (21.0 %)
Number of ASM	
0	21 (22.1 %)
1	26 (27.4 %)
2	29 (30.5 %)
3	10 (10.5 %)
4 or more	9 (9.5 %)
Seizure freedom	
Seizure free	24 (25.3 %)
Not seizure free	71 (74.7 %)
Handedness	
Right-handed	83 (87.4 %)
Left-handed	5 (5.3 %)
Ambidextrous	7 (7.4 %)
Education level	
≤ 10 years	31 (31.6 %)
> 10 years	64 (67.4 %)

Values are mean (M) and standard deviation (SD) for continuous variables, and n (%) for categorical variables. $N = 95$.

ophthalmic drugs that may affect pupil diameter or ocular behavior (e.g. antiglaucoma medication, antihistamines, corticosteroids) and significant cognitive impairment that would prevent valid testing. The participants were 27.4 years (SD = 19.8; range 0–75) old at epilepsy onset. The majority (85.3 %) had a focal epilepsy. Among those, 65.4 % were classified as temporal, 6.2 % as multifocal, 4.9 % as frontal, 2.5 % as parietal, and 21.0 % had an unknown localization. Educational backgrounds varied among participants; in total, 31.6 % of participants had 10 or less years of formal education. Participants with known intellectual disability (ID) were excluded. The proportion of individuals with fewer than 11 years of formal education is in line with the general population in Germany [24], and all participants were cognitively capable of completing the tasks.

To allow interpretation of oculomotor behavior relative to normative patterns, a healthy control group (n = 34) was additionally recruited from the local community. Control participants were free of neurological or psychiatric disorders and reported normal or corrected- to-normal vision.

The control group consisted of 11 males (32.4 %) and 23 females (67.6 %), with an average age of 32.65 years (SD = 15.88, range = 18–82). Regarding educational attainment, 17.6 % of the control group had 10 or fewer years of formal education. 94.1 % were right-handed.

The two groups did not differ significantly in age ($t(61.44) = -1.67$, $p = 0.100$) or sex distribution ($t(61.28) = 2.00$, $p = 0.060$). However, a highly significant group difference emerged for educational attainment, $t(94.50) = 5.00$, $p < 0.001$, with the control group reporting substantially higher levels of formal education. Consequently, education was included as a covariate in all group comparisons involving cognitive and eye tracking measures.

2.2. Neuropsychological assessment

Before initiating the cognitive assessments, patients completed a brief anamnesis to gather relevant clinical history. This included subjective complaints such as memory difficulties, concentration issues, and general cognitive or emotional concerns. Additionally, information on medical background, current medication, and epilepsy-related details was collected.

Cognitive performance was evaluated using the EpiTrack 3rd edition [3], a 12–15 min screening procedure for executive functions in patients with epilepsy. EpiTrack comprises six subtests measuring response inhibition, psychomotor speed, mental flexibility, verbal/lexical fluency, visuomotor planning, and verbal working memory. The combined performance across these subtests yields an age-adjusted total score (range 9–49), with higher scores indicating better cognitive function. This instrument has proven useful in monitoring cognitive function and potential medication-related side effects in epilepsy [25–28]. Standardized instructions from the EpiTrack protocol were followed.

Trail Making Test. The TMT, as part of the EpiTrack battery, consists of the following: **TMT-A:** Participants connect circled numbers (1–25) in ascending order with a pen as quickly as possible. The primary outcome measure is the time (in seconds) required to complete the sequence, reflecting psychomotor speed. **TMT-B:** Participants connect alternating numbers and letters (1–A–2–B–3–C, etc.) in ascending order, measuring cognitive flexibility. Completion time (in seconds) is recorded as the primary outcome.

Other EpiTrack Subtests. **Interference:** The Interference subtest evaluates response inhibition. Participants are required to rapidly process visual stimuli (numbers "1″ and "2″) while inhibiting automatic responses by applying opposing rules. The total time (in seconds) to complete the task is recorded.

Maze: A visuomotor planning subtest in which participants navigate a simple maze un- der time pressure. Performance is measured in seconds, capturing both motor coordination and anticipatory visual planning skills.

Fluency: A verbal fluency task in which participants generate as many words as possible that begin with a specific starting letter within one minute per letter. This test captures phonemic retrieval speed.

Digits: A verbal working memory subtest where participants repeat sequences of numbers in backward order. The length of correctly recalled digit spans reflects working memory capacity.

2.3. Eye Tracking procedure

During a part of the neuropsychological testing (TMT-A and TMT-B), participants wore a mobile eye tracking headset (Pupil Labs Neon). Eye movement (gaze coordinates, blinks) and pupil diameter were recorded at a sampling rate of 200 Hz. The forward-facing scene camera captured the participant's field of view at 30 Hz. The device uses infrared-based pupil tracking, ensuring high precision and robustness even under varying lighting conditions. Calibration was performed individually for each participant before testing, following the manufacturer's standard procedure. This involved participants focusing on predefined fixation points to ensure accurate mapping of gaze coordinates within the visual field. Additionally, the interpupillary distance (IPD) was measured for each participant and entered into the system to enhance the accuracy of gaze tracking. Special frames with interchange- able eyeglasses were used to accommodate participants with myopia or hyperopia, allowing them to take part in the study. To enhance the spatial accuracy of gaze mapping during task execution, AprilTags—a type of visual fiducial marker—were strategically placed at the corners of the testing environment for the TMT tasks. These tags facilitated precise alignment between the participant's gaze data and specific task components (e.g., TMT-A/B sheets). The integration of AprilTags ensured consistent spatial referencing across participants and minimized potential errors in gaze localization.

2.4. Data processing and analysis

Raw eye tracking data were exported and processed using the Pupil Labs Cloud software (Pupil Cloud) and Python scripts. Key variables extracted for each task included: Saccade parameters (e.g., minimal/maximal/average velocity, total saccades, saccades normalized to task duration), Blink count (total and normalized), Fixation parameters (total number, average fixation duration) and Pupil diameter (minimum, maximum, average per eye). An overview of the extracted eye tracking metrics, their operational definitions, behavioral cor- relates, and neurobiological underpinnings is provided in Table 2.

Cognitive outcome measures included TMT completion time (seconds) and the EpiTrack total score, along with subtest-specific performance indices (Interference, Maze, Fluency, Digits). Preliminary analyses indicated that age and gender were significantly associated with several oculomotor and pupillometry variables. For instance, pupil diameter decreased with age, and females exhibited larger pupil diameters than males. These findings are consistent with previous research on age- and sex-related differences in autonomic reactivity and visual function [43,49]. Therefore, age and sex were included as covariates in all subsequent correlation analyses. In addition, epilepsy-specific clinical variables—including ASM count, epilepsy duration, and seizure freedom status—were entered as covariates in all patient group analyses, given their potential impact on oculomotor function [15,50]. To evaluate group-level differences in both cognitive performance (EpiTrack total score, TMT-A, TMT- B) and oculomotor parameters, analyses of covariance (ANCOVAs) were conducted with group (epilepsy vs. control) as the between-subjects factor and highest school qualification included as a covariate to control for differences in educational attainment.

To examine associations between oculomotor behavior and cognitive performance within each group, partial pearson correlation analyses were performed separately for patients and healthy controls. In the epilepsy group, we controlled for age, sex, education (type of school qualification), ASM count, epilepsy duration, and seizure freedom status

Table 2
Eye tracking metrics, their definitions, behavioral correlates, and neurobiological underpinnings.

Metric	Operational Definition	Behavioral Correlates	Neurobiological Underpinnings
Saccade Count (normalized)	Saccades per second = Total number of saccades (rapid, ballistic eye movements shifting gaze from one point to another), normalized by trial duration	Decreases under cognitive load (top-down inhibitory control) [29]	Saccade frequency regulated by frontal eye fields and superior colliculus, and decreases under cognitive load due to top-down inhibition from dorsolateral prefrontal cortex [29,30].
Saccade Velocity (mean, min, max)	Velocity of a saccadic movement measured in pixel per second (px/s)	Decreases under cognitive load, increases with arousal, decreases with age [29,31,32]	Saccade velocity is modulated by the frontal eye fields, parietal cortex, and supplementary eye field [33,34].
Fixation Duration (mean)	Mean duration of all fixations (ms), defined as periods of gaze stability (minimum duration > 80 ms)	Increases with cognitive load, memory load, and task complexity [35–37]	Fixation duration is modulated by dorsolateral and medial frontal cortex via executive and inhibitory control [30,38].
Pupil Diameter (min, max)	Average, maximum, and minimum pupil size measured per eye (mm)	Increases with working memory load, cognitive effort, attentional demand, arousal, and task difficulty [39–44]	Linked to the noradrenergic system (locus coeruleus) [41] and to attentional and arousal mechanisms [42]; modulated by age, sex, and task demands [43,44].
Blink Count (normalized)	Number of spontaneous blinks per second	May increase under cognitive load, fatigue, or stable task conditions with reduced visual processing demands (task-dependent) [37,45–47]	Spontaneous, reflexive, and voluntary blinks are regulated by brainstem reflex circuits and higher cognitive-emotional processes [47,48].

(yes/no). In the healthy control group, partial correlations were adjusted for age, sex, and education.

Given the exploratory nature of the study, multiple correlations were computed. To control for false positives due to multiple testing, p-values were adjusted using the False Discovery Rate (FDR) correction according to Benjamini and Hochberg (1995) [51]. Statistical analyses were performed using IBM SPSS (version 29) and Python. Statistical significance was set at $p < 0.05$ for all analyses.

3. Results

3.1. Descriptive statistics and group-level differences in cognitive and oculomotor parameters

Participants with epilepsy had an average EpiTrack total score of 31.1 (SD = 5.5, range = 13–44). According to categorical classification, 31.6 % of patients showed significant impairment, 16.8 % mild impairment, 44.2 % performed within the average range, and 7.4 % demonstrated above-average performance. Overall, 48.4 % of epilepsy patients exhibited performance below the normative range, indicating substantial cognitive deficits. TMT-A completion times ranged from 12 to 117 s (mean = 35.0 s, SD = 18.3), while TMT-B completion times ranged from 25 to 300 s (mean = 96.7 s, SD = 55.3).

In comparison, healthy controls performed significantly better on all cognitive metrics. Their average EpiTrack score was mean = 36.85 (SD = 2.55, range = 29–40), with 67.6 % performing within the average range and 29.4 % reaching the highest performance category. Only one participants performance (2.9 %) was mildly impaired. Average TMT-A completion time in the control group was 24.70 s (SD = 9.38), and 58.18 s (SD = 25.31) for TMT-B. The descriptives for the cognitive measures are summarized in Table 3.

Cognitive performance differed significantly between patients and healthy controls across all measures, even after controlling for differences in educational attainment. Patients showed lower EpiTrack total scores ($F = 21.86$, $p < 0.001$; mean difference = 5.75 points), longer TMT-A completion times ($F = 6.25$, $p = 0.014$; mean difference = 10.30 s), and longer TMT-B times ($F = 6.66$, $p = 0.011$; mean difference = 38.52 s).

Next, Eye tracking measures were evaluated separately for TMT-A (see Table 4) and TMT-B (see Table 5).

To investigate whether eye movement patterns differed systematically between groups, we subsequently compared oculomotor parameters between patients and controls. Analyses focused on 11 predefined eye tracking variables per task. Group differences were assessed using ANCOVAs with education included as a covariate and FDR-corrected p-values.

During TMT-A, significant group effects were observed for several oculomotor parameters. Compared to controls, epilepsy patients showed longer average fixation durations ($F = 7.15$, $p = 0.015$) and slower

Table 4
Descriptive statistics of eye tracking data during TMT-A (patients vs. controls).

Eye Tracking Parameters	Patients M (SD)	Controls M (SD)	Comparison *F*
Normalized Saccade Count (sacc./s)	3.3 (0.7)	3.6 (0.5)	3.78
Average Fixation Duration (ms)	**259.5 (49.6)**	**228.9 (40.4)**	**7.15***
Normalized Blink Count (bli./s)	0.0 (0.1)	0.06 (0.08)	0.83
Minimum Saccade Velocity (px/s)	**775 (110)**	**874 (111)**	**20.25****
Maximum Saccade Velocity (px/s)	10362 (2759)	10497 (2930)	0.03
Average Saccade Velocity (px/s)	**2736 (448)**	**3291 (1370)**	**13.37****
Minimum Pupil Diameter Right (mm)	2.8 (1.0)	2.8 (1.1)	0.00
Maximum Pupil Diameter Right (mm)	**4.2 (0.8)**	**4.8 (0.9)**	**13.63****
Average Pupil Diameter Right (mm)	**3.7 (0.8)**	**4.3 (0.9)**	**14.76****
Minimum Pupil Diameter Left (mm)	2.8 (1.0)	2.9 (1.1)	0.00
Maximum Pupil Diameter Left (mm)	**4.3 (0.9)**	**4.9 (0.9)**	**9.51****
Average Pupil Diameter Left (mm)	**3.7 (0.8)**	**4.3 (0.9)**	**12.98****

Values are means (M) and standard deviations (SD). F-statistics refer to ANCOVAs comparing patients ($N = 95$) and controls ($N = 34$), with education as covariate and FDR correction. *$p < 0.05$, **$p < 0.01$.

Table 3
Descriptive statistics of the cognitive measures in the epilepsy and control group, with group comparisons.

	Patients (N = 95)				Controls (N = 34)				*F*
	M	SD	Min	Max	M	SD	Min	Max	
EpiTrack Score	31.1	5.5	13	44	36.9	2.5	29	40	**21.86****
TMT-A (s)	35.0	18.3	12	117	24.7	9.4	11.4	64.0	**6.25***
TMT-B (s)	96.7	55.3	25	300	58.2	25.3	23.8	150.7	**6.66***

Values are mean (M), standard deviation (SD), minimum (Min), and maximum (Max). Group comparisons are based on ANCOVAs. *$p < 0.05$, **$p < 0.01$.

Table 5
Descriptive statistics of eye tracking data during TMT-B (patients vs. controls).

Eye Tracking Parameters	Patients M (SD)	Controls M (SD)	Comparison *F*
Normalized Saccade Count (sacc./s)	**3.1 (0.5)**	**3.5 (0.4)**	**11.81****
Average Fixation Duration (ms)	259.2 (67.9)	232.8 (31.1)	3.01
Normalized Blink Count (bli./s)	0.1 (0.1)	0.1 (0.1)	2.16
Minimum Saccade Velocity (px/s)	**725 (98)**	**795.9 (86)**	**11.30****
Maximum Saccade Velocity (px/s)	13111 (3454)	12494 (2659)	0.32
Average Saccade Velocity (px/s)	**2982 (397)**	**3559 (1403)**	**13.72****
Minimum Pupil Diameter Right (mm)	1.9 (0.7)	2.0 (1.0)	1.29
Maximum Pupil Diameter Right (mm)	**4.2 (0.8)**	**4.8 (0.9)**	**8.83****
Average Pupil Diameter Right (mm)	**3.6 (0.8)**	**4.2 (0.9)**	**12.34****
Minimum Pupil Diameter Left (mm)	1.9 (0.7)	2.1 (1.0)	1.74
Maximum Pupil Diameter Left (mm)	**4.3 (0.8)**	**4.8 (0.9)**	**6.15***
Average Pupil Diameter Left (mm)	**3.6 (0.7)**	**4.2 (0.9)**	**10.25****

Values are means (M) and standard deviations (SD). F-statistics refer to ANCOVAs comparing patients ($N = 95$) and controls ($N = 34$), with education as covariate and FDR correction. *$p < 0.05$, **$p < 0.01$.

minimum ($F = 20.25$, $p < 0.001$) and average saccadic velocities ($F = 13.37$, $p = 0.002$). In addition, pupil diameter measures differed significantly: patients exhibited reduced maximum ($F = 13.63$, $p = 0.002$) and average pupil diameters ($F = 14.76$, $p = 0.002$) in the right eye, as well as in the left eye ($F = 9.51$ and 12.98, $p = 0.007$ and $p = 0.002$, respectively).

During TMT-B, significant group differences were found for the total number of sac- cades ($F = 11.81$, $p = 0.002$), minimum saccade velocity ($F = 11.30$, $p = 0.003$), and average saccade velocity ($F = 13.72$, $p = 0.002$). Epilepsy patients also showed significantly reduced maximum and average pupil diameters in the right eye ($F = 8.83$ and 12.34, $p = 0.007$ and $p = 0.002$), and in the left eye ($F = 6.15$ and 10.25, $p = 0.025$ and $p = 0.004$).

3.2. Analysis of patient group

3.2.1. TMT-A eye tracking parameters and cognitive measures

All results on the associations between eye tracking parameters recorded during TMT-A and cognitive measures in the patient group are presented in Table 6 and elaborated in the following section.

Eye Tracking Parameters TMT-A and EpiTrack Score: When examining ocular movements during TMT-A, partial correlations controlling for age, ASM, education, seizure freedom, epilepsy duration and sex indicated that participants with higher EpiTrack scores had shorter fixations ($r = -0.30$, $p = 0.006$), higher minimal ($r = 0.29$, $p = 0.006$), and lower peak saccade velocities ($r = -0.35$, $p = 0.001$). No significant effects for pupil diameter and saccade frequency emerged once the covariates were taken into account. Overall, these findings suggest that better cognitive performance was associated with briefer fixations and less variable saccadic activity during TMT-A.

Table 6
Partial correlation matrix of eye tracking parameters and cognitive measures during TMT-A.

	EpiTrack Score	TMT-A	TMT-B
Normalized Saccade Count (sacc./s)	0.19	−0.21	−0.08
Average Fixation Duration (ms)	**−0.30****	**0.31****	0.15
Normalized Blink Count (bli./s)	−0.07	0.21	0.12
Saccade Min Velocity (px/s)	**0.29****	**−0.35****	**−0.30****
Saccade Max Velocity (px/s)	**−0.35****	**0.45****	**0.42****
Saccade Avg Velocity (px/s)	0.00	−0.03	−0.01
Min Pupil Diameter Right (mm)	0.14	**−0.28****	**−0.23***
Max Pupil Diameter Right (mm)	−0.11	0.10	0.18
Avg Pupil Diameter Right (mm)	−0.05	−0.03	0.03
Min Pupil Diameter Left (mm)	0.15	**−0.29****	**−0.23***
Max Pupil Diameter Left (mm)	−0.14	0.11	**0.26***
Avg Pupil Diameter Left (mm)	−0.01	−0.05	0.02

Partial correlation coefficients are reported, controlling for education, number of ASM, epilepsy duration, sex, age, and seizure freedom (yes/no). $p < 0.05$, ** $p < 0.01$, $N = 95$. All p-values are FDR-corrected using the Benjamini-Hochberg procedure.

Eye Tracking Parameters TMT-A and performance on the TMT: Longer TMT- A times were tied to longer average fixation durations ($r = 0.31$, $p = 0.006$). In terms of velocity, slower task performance corresponded to lower minimum ($r = -0.35$, $p = 0.002$) yet higher maximum saccade speeds ($r = 0.45$, $p < 0.001$). Furthermore, participants who took longer to complete TMT-A showed larger minimum pupil diameters in both the right ($r = -0.28$, $p = 0.023$) and left eyes ($r = -0.29$, $p = 0.017$). After FDR correction, the negative correlation between saccade frequency and TMT-A completion time no longer reached statistical significance ($r = -0.21$, FDR-adjusted $p = 0.107$), although the pattern of results remained consistent with the overall trend.

These relationships indicate that slower TMT-A performance is marked by more extreme velocity endpoints, longer fixations, and bigger minimum pupil sizes.

In TMT-B, partial correlations showed that slower performance correlated significantly with lower minimum saccade velocity ($r = -0.30$, $p = 0.006$) and higher maximum saccade velocity ($r = 0.42$, $p < 0.001$) measured during TMT-A. Smaller minimum pupil diameters in the left and right eye ($r = -0.23$, $p = 0.045$; $r = -0.21$, $p = 0.046$) and larger maximum pupil diameters in the right ($r = 0.29$, $p = 0.007$) and left eye ($r = 0.20$, $p = 0.050$; did not reach significance after FDR correction) were also associated with slower TMT-B performance. These findings suggest that slower performance in TMT-B is associated with both lower minimum and higher peak saccade velocities recorded during TMT-A, as well as greater pupil dilation.

Eye Tracking Parameters TMT-A and performance on other EpiTrack Sub-tests: As an exploratory analysis, we examined associations between TMT-A eye tracking parameters and performance on EpiTrack subtests (Interference, Maze, Fluency, Digit Span).

These results are presented in Supplementary Table A.8.

For the Interference task, only maximum saccade velocity showed a significant association with performance ($r = 0.29$, $p = 0.006$), with higher peak saccade speeds linked to slower task completion. In the Maze subtest, better performance was associated with a higher normalized saccade count ($r = -0.23$, $p = 0.028$), longer average fixation durations ($r = 0.32$, $p = 0.002$), and lower minimum saccade velocity ($r = -0.23$, $p = 0.032$), suggesting more efficient and stable visual processing. No TMT-A eye tracking parameters showed significant correlations with performance on the Fluency or Digit Span subtests.

3.2.2. TMT-B EyeTracking parameters and cognitive measures

The partial correlations between eye tracking parameters and cognitive measures during TMT-B in the patient group are detailed in Table 7.

Eye Tracking Parameters TMT-B and EpiTrack Score: When analyzing ocu- lar behavior during TMT-B, minimum saccade velocity correlated positively with the Epi- Track Score ($r = 0.32$, $p = 0.003$), whereas maximum saccade velocity correlated negatively ($r = -0.28$, $p = 0.009$). These findings suggest that participants with higher cognitive perfor- mance displayed a reduced saccade velocity range, characterized by faster minimal speeds yet lower peak speeds. Additionally, minimum pupil diameter in the right ($r = 0.34$, $p = 0.002$) and left eye ($r = 0.28$, $p = 0.013$) both showed positive relationships with EpiTrack, indicating that better performers had larger minimal pupil sizes during TMT-B.

Eye Tracking Parameters TMT-B and TMT performance: Several parameters also associated significantly with TMT-B performance. Minimum saccade velocity showed a negative correlation ($r = -0.40$, $p < 0.001$), implying that participants with higher minimal speeds

Table 7
Partial correlation matrix of eye tracking parameters and cognitive measures during TMT-B.

	EpiTrack Score	TMT-B	TMT-A
Normalized Saccade Count (sacc./s)	0.15	−0.02	−0.06
Average Fixation Duration (ms)	−0.18	0.04	0.22
Normalized Blink Count (bli./s)	−0.13	0.24	0.15
Saccade Min Velocity (px/s)	**0.32****	**−0.40****	**−0.25***
Saccade Max Velocity (px/s)	**−0.28***	**0.41****	**0.31****
Saccade Avg Velocity (px/s)	0.16	−0.11	−0.22
Min Pupil Diameter Right (mm)	**0.34****	**−0.36****	**−0.30****
Max Pupil Diameter Right (mm)	−0.11	0.14	0.07
Avg Pupil Diameter Right (mm)	−0.03	0.01	−0.01
Min Pupil Diameter Left (mm)	**0.28***	**−0.31****	**−0.26***
Max Pupil Diameter Left (mm)	−0.10	0.15	0.07
Avg Pupil Diameter Left (mm)	0.01	−0.01	−0.03

Partial correlation coefficients are reported, controlling for education, number of ASM, epilepsy duration, sex, age, and seizure freedom (yes/no). $p < 0.05$, ** $p < 0.01$, $N = 95$. All p-values are FDR-corrected using the Benjamini-Hochberg procedure.

finished TMT-B more rapidly. In contrast, maximum saccade velocity demonstrated a positive association ($r = 0.41$, $p < 0.001$), indicating that larger velocity peaks aligned with slower performance. Pupil diameter likewise played a role: smaller minimum pupil diameters in both the right ($r = -0.36, p = 0.001$) and left ($r = -0.31, p = 0.008$) eye were linked to faster TMT-B times. Thus, slower TMT-B performance was characterized by lower minimum but higher maximum saccade velocities and larger minimal pupil sizes. For TMT-A, slower performance were associated with lower minimum saccade velocities ($r = -0.25$, $p = 0.018$), higher maximum saccade velocities ($r = 0.31$, $p = 0.005$) and larger minimum pupil diameters in both eyes ($r = -0.30$, $p = 0.004$ and $r = -0.26$, $p = 0.014$). These patterns closely mirror those found for TMT-B. The association between longer fixation durations and poorer TMT-B performance ($r = 0.22$, $p = 0.110$) was not statistically significant after correction.

Eye Tracking Parameters TMT-B and performance on other EpiTrack Sub-tests: In addition to the main analyses, we carried out exploratory correlations between eye tracking measures recorded during TMT-B and performance on other EpiTrack subtests (Interference, Maze, Fluency, Digit Span). Results are reported in Supplementary Table A.8. For the Interference task, lower minimum saccade velocity ($r = -0.25$, $p = 0.018$) and higher maximum saccade velocity ($r = 0.25$, $p = 0.021$), as well as smaller minimum pupil diameter in the right eye ($r = -0.23$, $p = 0.034$), were linked to slower completion times, suggesting that a broader saccadic velocity range and increased pupillary effort may be associated with reduced inhibitory control. In the Maze subtest, longer fixation durations ($r = 0.24$, $p = 0.024$) and lower minimum saccade velocity ($r = -0.25$, $p = 0.021$) were associated with better performance. For Digit Span, higher minimum saccade velocity was related to better performance ($r = 0.29$, $p = 0.005$). No significant correlations were found with Fluency.

3.3. Analysis of control group

In a next step, we examined whether the associations between eye tracking parameters and cognitive performance observed in the epilepsy group were also present in the healthy control group. To this end, partial correlations were computed between oculomotor metrics and Trail Making Test (TMT) performance, controlling for age, sex, and years of education. During the TMT-A condition, no significant associations were observed between any of the eye tracking variables and task performance. For TMT-B, two correlations reached nominal significance: faster completion times were associated with higher maximum saccadic velocity ($r = 0.374$, $p = 0.038$) and higher average saccadic velocity ($r = 0.360$, $p = 0.047$). However, these associations did not survive correction for multiple comparisons (FDR).

These results suggest that, within the control group, eye movement characteristics were not systematically related to cognitive task performance. A full overview of the correlations for the control group is provided in the supplementary materials (see Tables B.9 and B.10).

4. Discussion

4.1. Overview of findings

The present study investigated how eye tracking parameters recorded during the TMT relate to cognitive measures in individuals with epilepsy. In addition, a healthy control group was included to determine whether observed oculomotor-cognitive associations are specific to epilepsy-related pathology. In people with epilepsy, we found that higher EpiTrack scores and faster TMT completion were associated with more efficient visual search strategies, characterized by shorter fixations and a restricted saccade velocity range between minimum and maximum speeds. In contrast, poorer performance featured longer fixations and wider velocity extremes. Although eye tracking was only collected during TMT-A and TMT-B, the resulting parameters still showed associations with performance in other EpiTrack sub- tests, particularly those with strong visuomotor or speed components (Interference, Maze), as expected. In contrast, tests emphasizing verbal fluency or working memory (Fluency, Digits) showed virtually no significant relationships, highlighting the specificity of eye track- ing measures to tasks with a visual and speed-related component. In general, these raw eye tracking metrics predominantly seem to index basal psychomotor speed, even though the EpiTrack encompasses higher-order cognitive processing as well [3]. Importantly, in the healthy control group, no significant associations between eye tracking parameters and cognitive performance were found, and variability in both eye movements and cognitive scores was considerably lower than in patients. This suggests that the oculomotor-cognitive relationships observed in patients may depend on disease-related disruptions, which create the cognitive and oculomotor variability necessary for such associations to emerge. Moreover, direct comparisons revealed significant differences between patients and controls in several oculomotor metrics, including minimum and average saccade velocity, maximum and aver- age pupil diameter, fixation duration (TMT-A), and normalized saccade count (TMT-B) — findings that align with previous studies reporting altered saccadic dynamics in epilepsy populations compared to healthy individuals [15,16,52]. These group differences further suggest that epilepsy may disrupt basic oculomotor control mechanisms, even independent of cognitive task performance.

While TMT-A (primarily reflecting psychomotor speed) and TMT-B (emphasizing cognitive flexibility) displayed broadly similar patterns in the patient group, TMT-B yielded stronger correlations between pupil diameter and overall executive performance. In particular, minimum pupil diameter in both eyes during TMT-B correlated positively with the EpiTrack total score, a relationship absent in TMT-A. This contrast likely reflects TMT-B's heightened task demands or difficulty, wherein rapid alternation between letters and numbers under time pressure may better capture the broader cognitive functions assessed by EpiTrack beyond psychomotor speed. Our findings highlight specific eye tracking parameters, particularly fixation duration, extreme saccade velocities, and minimum pupil diameter, as being linked to cognitive performance. Although the correlations were small to moderate, they indicate a meaningful connection between eye movement dynamics and executive function. Importantly, these modest correlation strengths suggest that eye tracking metrics are not merely redundant proxies for total completion time or test scores—thereby potentially offering differential diagnostic value. In other words, they might help further distinguish between good and poor performance where simple completion times fall short. By contrast, measures like average pupil diameter, average saccade velocity, and blink rate showed no significant association with EpiTrack or TMT performance.

4.2. Saccade velocity and executive control

A key insight is that a "constrained" or reduced range of saccade velocity—encompassing higher minimum speeds but avoiding excessively high peaks—appears to indicate stable and controlled scanning. Such optimal velocity regulation may reduce cognitive load and reflect stronger engagement of the frontoparietal network, crucial for goal-directed attention and executive control [33,53]. In line with the core cortical saccadic network described by Jarvstad and Gilchrist [34], effective interplay among the frontal eye fields, parietal cortex, and supplementary eye field likely underpins this balance of saccade initiation and inhibition. By maintaining a higher minimum speed, individuals can sustain efficient visual exploration while avoiding the erratic "jumps" that hamper performance. Conversely, erratic or excessively high saccade peaks suggest less controlled attentional allocation and may signal suboptimal inhibitory control. Heitz and Schall [54] demonstrated that adjustments in saccadic speed-accuracy tradeoffs contribute to optimized search efficiency in cognitively demanding tasks, while Ghahghaei and Verghese [55] showed that efficient saccade planning, requiring clear target discrimination and sufficient preparation time, enhances visual search performance. In epilepsy, disruptions to frontoparietal circuits could undermine the ability to sustain this optimal velocity range, leading to slower or more variable saccade speeds. Since the TMT requires rapid alternation and sustained attention, saccade velocity may function as a practical proxy for how effectively epilepsy patients deploy attentional and motor resources. Thus, our findings that faster minimum saccade speeds are associated with better TMT performance likely indicate a well-regulated frontoparietal network, whereas erratic velocity ranges might reflect the functional impact of seizures, subclinical discharges, or medication-driven changes to saccadic control pathways.

4.3. Fixation duration and task efficiency

We also observed that longer fixations were linked to slower TMT-A completion, suggesting difficulties in attentional disengagement or a heightened cognitive load. Prior eye- movement research shows that extended fixations often signal deeper or more effortful processing [56,57]. In the TMT-A, where rapid scanning and frequent transitions are essential, such additional processing time accumulates, ultimately delaying task completion. From a neurobiological standpoint, the frontoparietal network—particularly the frontal eye fields and posterior parietal cortex—helps govern when and how fixations begin and end [30,58]. If these circuits are strained or disrupted in epilepsy (e.g., through seizure activity or subclinical discharges), reorienting the gaze may become more challenging, resulting in extended dwell times. These observations align with evidence that executive control deficits, such as diminished inhibitory control or slowed processing speed, manifest in ocular behaviors, highlighting how prolonged fixations may reveal deeper neural inefficiencies—whether due to structural changes, network dysfunctions, or medication side effects. Supporting this, Lüthi et al. [38] demonstrated that inhibition of the dorsolateral prefrontal cortex (DLPFC) via transcranial magnetic stimulation (TMS) alters visual exploration strategies, affecting response selection and attentional control, both of which are critical for efficient eye movement behavior.

4.4. Pupil diameter findings

Our pupil diameter results align with prior studies indicating age- and sex-related differences [43,44]. Similar to earlier reports, we observed a negative relationship between age and pupil diameter, emphasizing the need for age correction in ocular research. Moreover, female participants tended to have larger pupils than males during cognitively demanding tasks, consistent with findings by Campbell et al. [59] and Tsitsi et al. [23]. After controlling for these demographic and other clinical factors, participants performing more slowly on the TMT showed larger minimal pupil diameters, aligning with research linking greater dilation to heightened mental effort or arousal [41]. Numerous studies further connect pupillary responses to a wide range of cognitive processes, including memory encoding [60], attentional load [42], executive or working memory [61–63] and perceptual decision making [64]. Notably, in the more cognitively demanding TMT-B, these pupillary effects were associated with cognitive performance on the EpiTrack, underscoring the role of executive load in driving pupil dynamics.

4.5. Clinical relevance

From a clinical standpoint, these findings open promising avenues for monitoring cognitive function in epilepsy. Capturing parameters such as saccade velocity and fixation duration in real time could enable the early detection of medication side effects or emerging cognitive decline, In our sample, significant differences in multiple eye tracking parameters were observed triggering more thorough neuropsychological evaluations when needed. between patients and healthy controls, further supporting the potential diagnostic value of oculomotor measures in distinguishing pathological from normal cognitive functioning. How- ever, eye tracking data can only complement standard paper-and-pencil tests if they provide additional insights beyond traditional test results. In particular, they may help identify individuals with subtle deficits who might otherwise pass conventional screening. Additionally, because eye movements and pupillary responses can be measured non-invasively and without conscious effort, this approach could benefit nonverbal individuals and patients with generalized epilepsy who experience developmental impairments [41].

4.6. Limitations and future directions

Despite the robust associations observed after controlling for age, sex, education, medication count, seizure status and epilepsy duration, several limitations warrant caution. First, this was a cross-sectional study, so the direction of causality remains unclear. Erratic eye movements might impede efficient search, or broader attentional and affective factors could drive both ocular behavior and task performance. Longitudinal designs would help clarify whether shifts in eye tracking parameters predict cognitive fluctuations over time. Second, our sample came from a specialized epilepsy clinic serving newly diagnosed or more complex cases, which may limit the generalizability of our findings to less severe populations. Third, we did not systematically analyze the distinct effects of different drug classes or dosages on eye movements. Fourth, we pooled patients with focal epilepsy regardless of lesion localization. While this allowed for adequate statistical power, it may have masked region-specific effects. Frontal, temporal, and parietal areas contribute differently to oculomotor control and attention, and lesion location might systematically influence eye movement patterns or their relation to task performance. Future studies should examine whether the observed associations differ depending on lesion topography. Since the majority of our sample consisted of patients with temporal epileptogenic focus, the reported findings most likely reflect functional characteristics of this subgroup. In addition, while the inclusion of a healthy control group provided important initial insights, the relatively small sample size and high educational attainment within this group likely reduced cognitive variability, limiting the potential to detect oculomotor-cognitive associations in healthy participants. This limited variability is, however, not unexpected, as cognitive performance in healthy individuals— particularly on basic attention and executive tasks such as the EpiTrack—is typically more homogeneous, with less pronounced interindividual differences than in clinical samples.

Finally, practical barriers such as technology cost, accessibility, and complexity of data analysis could influence the feasibility of implementing wearable eye tracking in everyday clinical settings. Nonetheless, this study adds to a growing body of literature indicating that real-

time ocular metrics can reveal subtle yet clinically relevant patterns often overlooked by conventional tests [10–12,23]. By capturing moment-to-moment changes in saccade velocity, pupil size, and fixation duration, eye tracking could be particularly valuable in populations with fluctuating cognitive status, such as epilepsy. Incorporating these techniques into the TMT may provide a richer profile of executive functioning and attentional allocation, ultimately informing more personalized treatments and precise monitoring of disease or medication effects.

Building on this proof-of-principle study, several future directions merit exploration. Future studies should integrate advanced analytical approaches—such as scanpath analysis, fixation sequencing, or machine-learning models—to differentiate between efficient and inefficient visual strategies, thereby better capturing not only speed-related components of the EpiTrack but also aspects of higher-order cognitive processing [65]. Second, medication- specific analyses are needed to clarify how individual anti-seizure drugs shape ocular behavior, and whether these effects relate to broader cognitive changes. Finally, while our inclusion of a healthy control group provided initial evidence suggesting that the observed eye-movement–cognition associations may indeed reflect disease-specific mechanisms, larger comparative studies with matched and cognitively more heterogeneous control samples are needed to further clarify whether these associations are unique to epilepsy or reflect more general cognitive alterations. By pursuing these lines of research, we can further harness eye tracking as a non-invasive, time-efficient tool for monitoring cognitive status, optimizing treatment strategies, and enhancing its differential diagnostic value in epilepsy.

CRediT authorship contribution statement

Sarah Al-Haj Mustafa: Formal analysis, Data curation, Investigation, Writing – original draft, Writing – review & editing. **Anna Jansen:** Formal analysis, Software, Visualization, Writing – review & editing. **Melissa Steininger:** Formal analysis, Software, Visualization, Writing – review & editing. **Johannes Müllers:** Conceptualization, Project administration, Resources, Software, Supervision, Writing – review & editing. **Rainer Surges:** Resources, Writing – review & editing. **Randi von Wrede:** Conceptualization, Supervision, Writing – review & editing. **Björn Krüger:** Conceptualization, Resources, Software, Supervision, Writing – review & editing. **Christoph Helmstaedter:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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During the preparation of this work, the authors used generative AI tools in order to refine and proofread the manuscript. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Appendix A. Supplementary data

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