

Guidelines for Gaze-based Neural Preliminary Diagnosis

MAYAR ELFARES, Department of Computer Science, University of Stuttgart , Germany

SALMA YOUNIS*, Department of Behavioral and Cognitive Neuroscience, University of Maryland, USA

PASCAL REISERT, Department of Computer Science, University of Stuttgart , Germany

RALF KÜSTERS, Department of Computer Science, University of Stuttgart , Germany

TOBIAS RENNER, Department of Child and Adolescent Psychiatry, University Hospital Tübingen, Germany

ANDREAS BULLING, Department of Computer Science, University of Stuttgart , Germany

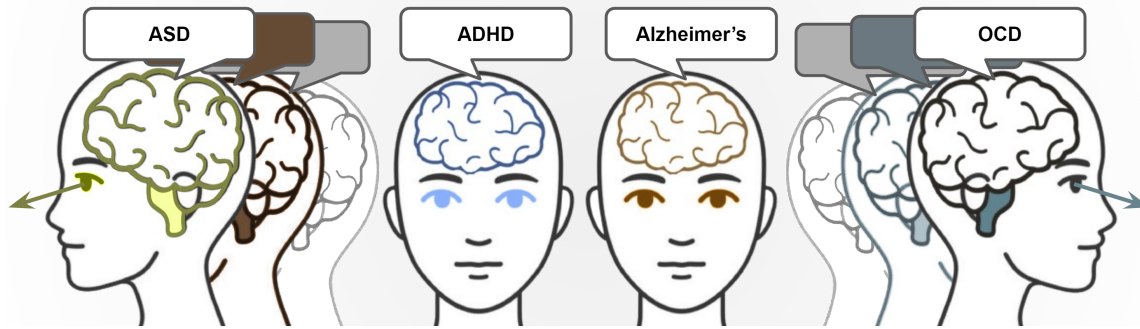


Fig. 1. "Eyes are the mirror of the mind" when it comes to diagnosing neural disorders. The subtle patterns in eye movements, e.g. fixations, saccades, and blinks, reflect underlying neural processes and cognitive functions. Studying these patterns allows us to uncover early signs of neural differences without invasive procedures.

Neural disorders refer to any condition affecting the nervous system and that influence how individuals perceive and interact with the world. Traditional neural diagnoses rely on cumbersome, time-consuming, or subjective methods, such as clinical interviews, behavioural observations, or medical imaging. Eye tracking is an attractive alternative because analysing eye movements, such as fixations and saccades, can provide more objective insights into brain function and cognitive processing by capturing non-verbal and unconscious responses. Despite its potential, existing gaze-based studies presented seemingly contradictory findings. They are dispersed across diverse fields, requiring further research to standardise protocols and expand their application, particularly as a preliminary indicator of neural processes for differential diagnosis. Therefore, this paper outlines the main agreed-upon findings and provides a systematisation of knowledge and key guidelines towards advancing gaze-based neural preliminary diagnosis.

Additional Key Words and Phrases: Gaze, Eye Tracking, Neural Disorders, Diagnosis

*Work done while interning at the University of Stuttgart.

Authors' Contact Information: [Mayar Elfares](mailto:mayar.elfares@vis.uni-stuttgart.de), mayar.elfares@vis.uni-stuttgart.de, Department of Computer Science, University of Stuttgart , Germany; Salma Younis, Department of Behavioral and Cognitive Neuroscience, University of Maryland, USA, syounis@terpmail.umd.edu; Pascal Reisert, Department of Computer Science, University of Stuttgart , Germany, pascal.reisert@sec.uni-stuttgart.de; Ralf Küsters, Department of Computer Science, University of Stuttgart , Germany, ralf.kuesters@sec.uni-stuttgart.de; Tobias Renner, Department of Child and Adolescent Psychiatry, University Hospital Tübingen, Germany, tobias.renner@med.uni-tuebingen.de; Andreas Bulling, Department of Computer Science, University of Stuttgart , Germany, andreas.bulling@vis.uni-stuttgart.de.

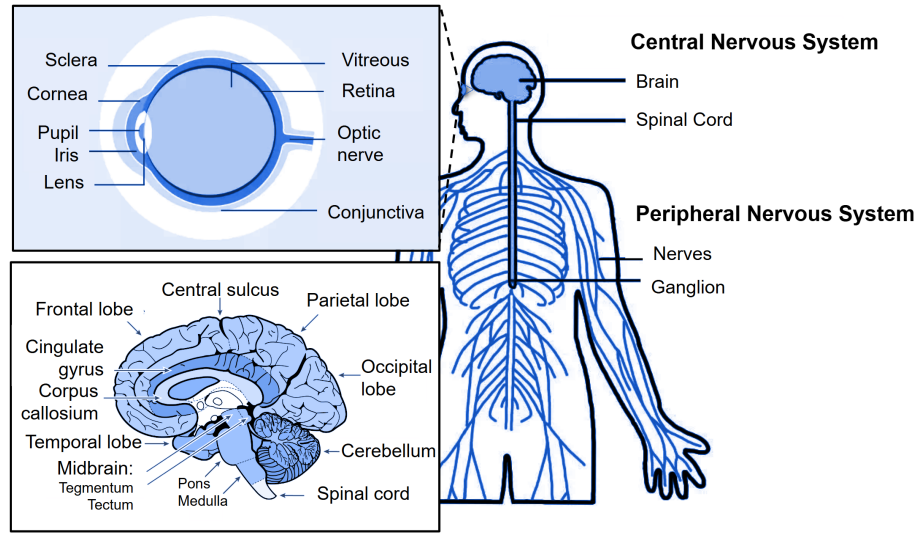


Fig. 2. The human nervous system (right) includes the central nervous system (i.e. brain and spinal cord) and the peripheral nervous system (nerves and ganglia). The eye anatomy is shown in top-left and the brain anatomy in bottom-left.

1 Introduction

Neural disorders, such as Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity Disorder (ADHD), dyslexia, Alzheimer's, and Parkinson's, help in understanding differences in the way individuals perceive and interact with the world [111, 401]. These differences result from variations in the human brain and can profoundly impact the individual's communication, learning, and behaviour. More specifically, neural disorders affect the central nervous system (i.e. brain and spinal cord) or the peripheral nervous system (i.e. nerves and ganglia), as shown in Figure 2, leading to deficits in motor, sensory, or cognitive functions [352]. These differences can bring both challenges and strengths. For example, people with ASD may have heightened attention to detail [483], while those with ADHD might excel in environments requiring quick thinking or creativity [410].

Unfortunately, conventional neural diagnosis involves a combination of tedious, time-consuming, or invasive screening processes, such as (i) subjective assessments based on clinical interviews, questionnaires, and behavioural observations influenced by factors like the patient's memory and communication ability [62, 466], (ii) invasive testing like MRI and CT scans that are expensive and can be physically uncomfortable for patients [459], (iii) lengthy processing of progressive diseases that can take months or even years [70, 481], (iv) involving multi-disciplinary specialists such as neurologists, psychiatrists, psychologists, and speech therapists [101, 220], and (v) having difficulties in early diagnosis since many neural conditions manifest with subtle or vague early symptoms [220, 265]. Without objective, real-time metrics, early diagnosis remains highly dependent on subjective reporting and clinical expertise.

Fortunately, processes in brain activation also manifest through changes in eye movement patterns, fixations (i.e. steady gaze), saccades (i.e. rapid movements between points of focus), smooth pursuit movements (tracking moving objects) and other gaze metrics [196, 459, 496]. Hence, eye-tracking research becomes particularly valuable in diagnosing and studying neural disorders because the brain and central nervous system tightly control eye movements. Around half of the brain's neural pathways are dedicated to vision and control of eye movements [43]. In addition, gaze tracking

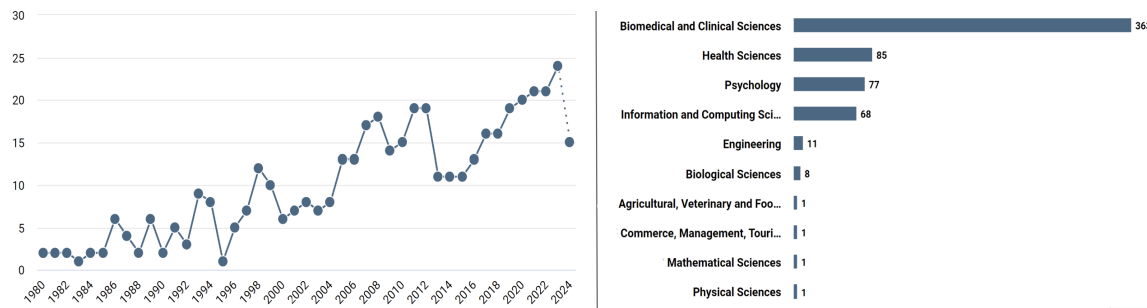


Fig. 3. The number of publications per year (left) and per the main research categories (right) for eye tracking in neural diagnosis sourced from dimensions.ai [104]

provides a non-invasive, objective indicator of neural processes to study how individuals perceive and respond to their environment due to its ability to capture non-verbal, unconscious responses that are less likely to be influenced by subjective bias or compensatory strategies [74, 260, 261, 285, 518].

Significance. Despite the potential of eye-tracking research in diagnosing neural disorders and its growing attention (c.f. figure 3), the field remains in its infancy and further research is needed to refine gaze-tracking protocols. Hence, we present this systemization of knowledge (SoK) paper to offer an overview of the neural diagnostics supported by gaze analysis based on the key agreed-upon guidelines that are supported by a broad consensus across multiple studies and convergence of findings across different fields as presented in several peer-reviewed publications (c.f. figure 3). We believe this paper contributes to the standardisation of gaze-based neural diagnosis methods and their application across diverse clinical populations, mostly to get a preliminary neural diagnosis. Therefore, readers can use this SoK to (i) get equipped with a foundational knowledge of the field, (ii) understand the potential best practices, cautionary guidelines, and expected findings for future studies, (iii) design ethical studies that consider the well-being of participants, (iv) save time and effort through our compiled structure of multidisciplinary works, (v) facilitate the collection of high-quality gaze data, addressing the current gap in research; (vi) analyse and validate the behaviour and performance of computational methods, such as AI models, by comparing their outputs against known verifiable facts as a reference; (vii) leverage guidelines as input for knowledge-based learning frameworks such as meta-learning and rule-based learning models, and ultimately, (viii) create a generic diagnostic tool that distinguishes between the different neural disorders and enables the decoupling of comorbid factors.

Contributions. Therefore, in this paper, we aim to advance research on eye tracking in neural diagnosis based on the well-established knowledge and the agreed-upon findings across the different studies we surveyed. We compiled the accepted procedures and conclusions and made the following contributions:

- We survey and present the different neural theories and the main causes and consequences of contradicting findings.
- We provide generic guidelines that can be applied to different disorders to help standardise gaze-based neural protocols and ensure ethical, valid, and scientifically sound results.
- In addition to the generic guidelines, we provide further disorder-specific guidelines by compiling different findings from the fields of neuroscience, biomedical sciences, psychology, sociology, eye-tracking, and computer science.
- Finally, we present the current status, advantages, and limitations of gaze-based neural diagnosis.

Methodology. We compiled a list of 1,692 papers on gaze and neural disorders through dimensions.ai [104]. After only including studies that are (i) peer-reviewed, (ii) written in English, (iii) utilizing gaze-based measures (e.g., fixations, saccades, pupil dilation) to evaluate neural functions or cognitive processes, and (iv) investigating gaze behaviour in relation to diagnostic procedures, excluding other papers on prognosis (e.g. [26, 428]), treatment (e.g. [69, 81, 165, 520]), the use of gaze as an assistive input tool (e.g. [49, 124, 340]), and gaze behaviour of neural experts (e.g. [88, 353, 495]), we carefully investigated 464 research papers. We classified them into the different disorders and then into six main neural classes according to [456] (some comorbidity studies have also been investigated, c.f. sections 3 and 4).

Structure. In Section 2, we start by presenting the relation between gaze and neural disorders, why gaze is an informative tool for diagnosis, and the main causes and consequences of contradicting findings in gaze-based neural disorders. In Section 3, we present the generic guidelines that can be used with studies involving *any* disorder throughout the eye-tracking pipeline, such as the participant selection and screening, experiment design, data collection and equipment, data analysis and processing, reporting and reproducibility, and ethics and privacy considerations. Then, in Section 4, we present the disorder-specific guidelines categorised by the neural class (e.g. neurodevelopmental or neurodegenerative disorders). For each disorder, we present an overview of the literature, the main eye-tracking focus, guidelines for task design, considerations, and key metrics with the expected gaze behaviour. Finally, in Section 5, we summarise the current status and limitations of gaze-based neural diagnosis.

2 Gaze as an indicator of neural processes

The concept of neural disorders offers distinct frameworks for understanding how individual variations affect perception, behaviour, and cognition [500]. The spectrum of neural disorders differ in terms of their severity, symptoms, underlying causes, and functional impact on individuals. The concept of a spectrum recognizes that these disorders are not binary (having or not having the disorder) but exist along a continuum with varying degrees of impairment or presentation [456], reflecting the complexity of understanding neural conditions. Further research continues to refine the diagnostic procedures, especially in light of new technologies like eye-tracking, which offer additional insights into brain function and behaviour [260, 261].

2.1 Eyes and the brain

The connection between neural disorders and eye tracking is grounded in the neurological control of eye movements and how visual processing reflects brain function [181, 205, 394].

Neural disorders affect various brain regions responsible for sensory processing, motor control, cognition, and emotions. For instance, Alzheimer’s disease affects the hippocampus, leading to memory deficits; Parkinson’s disease involves dopamine depletion, affecting motor control; and ADHD involves dysregulation of attention and impulsivity in the prefrontal cortex [352, 456].

The aetiology (causal origins) of neural disorders [445, 447] involves complex interactions between genetic, neurobiological, environmental, and cognitive factors. Understanding these causes can help refine gaze-based indicators for specific diagnoses (c.f. Section 4 for more details). (i) In neural disorders with genetic and neurodevelopmental basis (e.g. ASD), genes influencing synaptic plasticity, neurotransmitter function, and brain connectivity contribute to atypical gaze behaviours. (ii) For disorders caused by structural and functional brain abnormalities (e.g. Alzheimer’s and Parkinson’s), damage to specific brain regions controlling gaze and attention results in abnormal eye movement patterns. (iii) For disorders caused by neurotransmitter dysregulation (e.g. ADHD), imbalances in neurotransmitters like dopamine,

serotonin, and norepinephrine affect attention, impulsivity, and decision-making, which correlate with abnormal gaze dynamics. (iv) For disorders caused by cognitive and attentional control deficits (e.g. OCD), deficits in executive function, attention, and cognitive control also affect gaze behaviour. (v) Environmental and early-life factors (e.g. stress, trauma, or prenatal exposure to toxins) can lead to deficits in gaze processing (e.g. anxiety disorders). (vi) Other disorders (e.g. dyslexia) are caused by sensorimotor and visual processing abnormalities, affecting eye coordination and leading to gaze instability and reading difficulties.

Anatomy of the eye. The eye is a sensory organ that captures visual information and transmits it to the brain. As shown in Figure 2, the eye key structures include: (i) the cornea and lens, which focus light onto the retina, (ii) the retina, which contains photoreceptor cells (rods and cones) that convert light into electrical signals, (iii) the optic nerve, which transmits visual signals to the brain, and (iv) the fovea, which is a specialized region in the retina responsible for sharp central vision and high visual acuity.

Visual pathways. The brain's visual pathways and eye movement systems are deeply intertwined [181, 205, 394]. Eye movements such as fixations, saccades, pupil dilation, and smooth pursuits (c.f. Section 3) are controlled by different brain regions, including the visual cortex, frontal eye fields, cerebellum, and brainstem. The visual information from the retina follows the following pathway: The electrical signals from retinal ganglion cells travel through the optic nerve, which exits the back of the eye. The optic nerves from both eyes meet at the optic chiasm, located at the base of the brain. At the optic chiasm, nerve fibers partially cross over; the nasal (inner) retinal fibers cross to the opposite hemisphere, and the temporal (outer) retinal fibers remain on the same side. This crossing ensures that the left visual field is processed in the right hemisphere, and the right visual field is processed in the left hemisphere. After the optic chiasm, the reorganized visual information continues along the optic tracts to the lateral geniculate nucleus (LGN) in the thalamus. The LGN is a relay centre that processes and refines visual signals before sending them to the cortex. The LGN has six layers and organizes information based on the eye of origin (left vs. right eye) and the type of visual information (color, movement, fine detail). The LGN transmits the processed signals to the primary visual cortex (i.e. V1 or the striate cortex) in the occipital lobe at the back of the brain. V1 processes: edges, contrast, and orientation of objects, as well as the spatial organization of the visual field (retinotopic mapping). From V1, visual information is sent to higher-order visual areas for more advanced interpretation: (i) The dorsal stream (i.e. the 'Where Pathway') travels from V1 to the parietal lobe to process spatial awareness, motion detection, object location, and depth perception, which are crucial for guiding actions (e.g., reaching for an object). (ii) The ventral stream (i.e. the 'What Pathway') travels from V1 to the temporal lobe to process object recognition (faces, shapes, colors), and semantic meaning of visual stimuli, which are crucial for recognizing familiar faces, reading text, and identifying objects.

For example, saccades are coordinated by the frontal eye fields (in the frontal cortex and superior colliculus (midbrain), and fixations and smooth pursuit movements involve the cerebellum and parietal cortex [316, 341]. In addition, gaze patterns reflect some brain functions such as cognitive and perceptual processing regulated by the parietal and frontal lobes, memory and recognition through the medial temporal lobe (including the hippocampus), and decision-making through the prefrontal cortex. Furthermore, social interactions are reflected in gaze patterns, e.g. the superior temporal sulcus (STS) processes eye contact and social cues, and the amygdala interprets emotional expressions in gaze patterns. Therefore, since the neural pathways closely regulate eye movements, disruptions in eye movement patterns can serve as an indicator for neural conditions [463, 469] (c.f. Section 4 for more details).

2.2 Gaze as a diagnostic tool

Eye-tracking can be a suitable tool for neural diagnosis since it is (i) a non-invasive tool, making it particularly suitable for vulnerable populations such as children or individuals with severe neural impairments with no harmful side effects or risks. (ii) Gaze is a suitable tool for early detection since gaze patterns can reveal subtle differences in neural functioning before more noticeable symptoms arise [260, 518]. (iii) Eye-tracking provides quantitative and objective measurements (e.g., fixation duration, saccadic movements) that can be standardized and compared across individuals. This eliminates the subjectivity of many traditional behavioural assessments and allows for consistent measurements over time or between different populations [463]. (iv) Gaze tracking can assess various neural conditions by identifying impairments in areas like attention, memory, motor control, and emotional processing [260, 261]. (v) Eye-tracking data can be captured in real-time, making it a powerful tool for diagnosing and monitoring progress in neural disorders. This can provide immediate feedback to clinicians and inform adjustments to therapies or medications [171, 493]. (vi) With advances in mobile eye-tracking technology, there's potential for home-based diagnosis and monitoring, which could benefit patients who cannot frequently visit clinics or live in remote areas [2, 9, 33, 74, 97, 97, 98, 222, 251, 446].

2.3 The spectrum of challenges

Research findings in gaze behaviour in neural disorders differ due to complex factors, including differences in research methods, the multifaceted nature of neural disorders, and the interdisciplinary nature of the different fields. Below are the main causes and consequences of these conflicting viewpoints that we compiled from the literature:

Causes. Neural disorders are heterogeneous, meaning they can present with widely varying symptoms across individuals [120, 179]. For example, individuals with ASD can exhibit different degrees of social communication or sensory sensitivity, leading to differing interpretations of gaze behaviours [448]. The variability in symptoms within and across disorders causes researchers to focus on different aspects, such as social deficits, sensory sensitivities, or cognitive processes, sometimes leading to contradictory conclusions.

In addition, differences in experimental design can also contribute to such discrepancies. Studies may vary in the age group [145, 200], type of stimuli [56, 160, 172, 484], environmental conditions [198], or tasks used to measure gaze [296, 388]. For example, gaze studies in ASD may involve free-viewing tasks, structured social interactions, or specific object-based tasks, each of which may lead to different conclusions about the role of gaze in the disorder [448]. Different technological tools and data collection methods, such as head-mounted eye trackers vs. screen-based trackers, can yield varying results, further complicating consensus [129, 200].

Furthermore, gaze research intersects with multiple disciplines, including psychology, psychiatry, neurology, cognitive science, and computer science, each of which may approach the data from a different theoretical framework. For instance, psychologists may interpret gaze avoidance in social situations as a behavioural issue, while neurologists might focus on sensory processing differences [352, 500].

Moreover, eye movements are influenced by multiple neural systems, including those responsible for visual attention, motor control, and social cognition [181, 205, 394]. As a result, abnormal gaze patterns may be interpreted differently depending on which neural system researchers believe is most affected by a disorder. In ADHD, for example, some researchers emphasize deficits in motor control (leading to unstable gaze) [311, 416, 458], while others highlight attentional regulation as the primary issue [311, 330, 488, 491]. This divergence stems from the fact that gaze is modulated by multiple underlying systems, making it difficult to attribute irregularities to a single cause.

Finally, gaze behaviour can be highly dependent on contexts (e.g. particular situation's social or cognitive demands)

and individual parameters (e.g. sleep deprivation or mood) [119, 192, 201, 232, 504, 525]. This means that findings from studies using different tasks or social settings can yield contrasting results, even when studying the same disorder. For instance, gaze behaviour in individuals with anxiety may differ depending on whether they are in a low-stress or high-stress environment, leading to seemingly contradictory conclusions about the role of gaze in anxiety [197, 400].

Consequences. The above-mentioned challenges makes it difficult for researchers trying to reach a consensus on the role of eye movements in diagnosing neural disorders. This can lead to fragmentation within the research community, with different groups working under distinct assumptions, hindering the advancement of unified diagnostic and therapeutic frameworks. As a result, the progress toward developing reliable tools for neural disorders is slowed, and the broader field struggles to establish clear clinical applications for gaze-based research [31, 285].

In addition, while some researchers advocate for the use of eye-tracking as an objective indicator for diagnosing conditions [248, 448, 501], others argue that gaze behaviours are too context-dependent to serve as reliable diagnostic criteria, especially when used without other modalities [249]. This variability complicates the development of standardized clinical guidelines for using gaze data to diagnose neural disorders. This further makes clinicians hesitate to rely on eye-tracking as a predictive measure, especially with the lack of standardization across studies, further complicating efforts to implement gaze-based diagnostics in clinical settings [54, 92].

In brief, while the diversity of findings can foster innovation and deeper inquiry, it also highlights the need for more integrated research considering the multifaceted nature of gaze behaviours across neural conditions. Hence, this paper provides guidelines according to the consensus-based findings and commonly accepted procedures in the literature to standardise and advance gaze-based neural diagnosis.

3 Generic guidelines for gaze-based neural research

Conducting research on neural disorders using eye-tracking technology requires adherence to several guidelines to ensure ethical, valid, and scientifically sound results. Here, we compiled the commonly accepted key guidelines from the literature, focusing on participant well-being, accurate data collection, and methodological rigour. For all-purpose eye-tracking guidelines, we refer the reader to [198]. This paper specifically focuses on guidelines and considerations relevant to neural diagnosis. Below, we present some generic key guidelines. Then, in section 4, we present specific guidelines for each condition.

3.1 Participant Selection and Screening

Appropriate Sampling: When studying neural disorders, including a representative sample of the disorder in question is important [177, 448]. For example, in research on autism, include participants across the spectrum of severity [240, 320]. Sampling by age group is essential for ensuring that neurological and cognitive developmental changes are accurately captured [145, 200, 309]. The brain and cognitive processes vary significantly by age, and neural disorders can present differently in children, adolescents, adults, and the elderly [260, 260, 265, 527]. If possible, use age stratification, i.e., include narrow age ranges or age cohorts to analyse developmental trajectories or how symptoms manifest differently across life stages [262, 324, 371]. In addition, gender differences play a critical role in neural disorders since certain disorders may manifest differently across genders, and this should be reflected in both sampling and data analysis [260, 324, 371]. For example, boys are diagnosed with ASD at a higher rate than girls, but girls may present with less subtle symptoms [32, 387]. Finally, collect participants' current treatment status since it can influence their performance in studies, especially those involving cognitive or behavioural tasks [442, 457]. Consider comparing medicated vs

unmedicated groups when analysing data [147, 200, 458]. Similarly, family history and genetics can influence the likelihood of developing a disorder and its severity and the inheritability of certain conditions [107, 145].

Control Group Inclusion: A matched control group (e.g. age-matched or gender-matched) is a necessary baseline to compare gaze behaviour and draw meaningful conclusions about the studied disorder [194, 285, 289]. Comparing patient data with a normative dataset allows for more accurate detection of abnormalities and diagnosis [187, 259, 260].

Co-morbidities and Confounding Factors: Take into account co-occurring conditions (e.g., ADHD with ASD or OCD with anxiety) as they can influence eye-tracking data and adjust the study design to account for these variables [25, 212, 488, 523]. For certain studies, you may want to stratify participants based on single diagnoses vs. comorbid diagnoses [170, 329, 488].

3.2 Experiment Design

Task Selection: Ensure tasks are appropriate for the cognitive and sensory capabilities of the participants [285]. For example, individuals with ASD may struggle with tasks involving high social or emotional content [57, 160], and those with dyslexia may face difficulty in reading tasks [131, 502]. Design tasks that accommodate these limitations while still collecting meaningful data (c.f. section 4).

Stimuli: Choose visual stimuli that are relevant to the disorder, such as fearful or anxiety-inducing scenarios, facial expressions or social scenes [171], static and dynamic stimuli [172], or colours and transitions [160]. Avoid overly complex visual stimuli that lead to sensory overload [56, 484]. In addition, if your study involves tasks with verbal components, consider language barriers (e.g. native vs non-native speakers) and the need for translation or language accommodations [375, 385, 452].

Duration and Breaks: Participants with neural disorders might have limited attention spans [311, 416] or suffer from muscle fatigue/weakness [42, 150]. Design shorter tasks and provide regular breaks to maintain focus and minimize fatigue [273, 481].

3.3 Data collection and equipment

Choice of Eye-Tracking Device: For high-quality data, use high-precision eye-tracking systems that offer a good sampling rate (e.g., 60–120 Hz for general use, 250+ Hz for saccadic studies); this responsiveness ensures that no movements are missed, especially for disorders where small deviations in gaze can provide significant insights (e.g., subtle differences in social attention in ASD or reading patterns in dyslexia) [129, 200, 379, 502]. The higher resolution of these devices captures more detailed data about eye movements, including microsaccades (tiny, rapid movements) and smooth pursuits (when the eye follows a moving object), allowing a thorough fine-grained analysis [198]. Note that lower-precision eye trackers can suffer from noise (random inaccuracies in measurements) and drift (gradual inaccuracy over time). High-precision trackers minimize these issues, leading to more reliable long-term tracking and making it easier to interpret results over extended periods [122, 199].

Data Quality Control: Implement robust data cleaning techniques, as individuals with neural disorders might produce noisy data due to difficulty maintaining focus or motor control issues [189, 517]. For instance, algorithms to handle blinking [48, 257, 328], head movements [6, 266], or gaze drift [34, 105] may be necessary. Also note that external

factors, such as fatigue [119, 201, 504] or stress [192, 232, 525] can influence eye-tracking results, making it important to control these variables in experimental designs.

Setup. Use a suitable setup for the target group. For example, children or participants with mobility issues should use non-invasive, comfortable devices (e.g., screen-based eye trackers) [129, 481]. For some participants, especially those with anxiety or sensory processing difficulties, ensure that the environment is non-threatening or familiar to avoid triggering abnormal behaviour unrelated to the task [36, 82, 108, 484], cf. Section 4 for disorder-specific considerations.

3.4 Data Analysis and Processing

Custom Metrics for Disorders: Use specialized eye-tracking measures tailored to assess specific cognitive, motor, or perceptual deficits that capture the disorder-specific gaze behaviours [145, 306, 463]. For instance, in autism research, reduced fixation on eye regions of faces is a key metric, while in dyslexia, measures of saccades and fixation duration during reading tasks are critical (cf. Table 1 and Section 4 for more details).

Metric	Definition	Behaviour	Example
Fixations	A period when the gaze remains relatively still, allowing the eyes to focus on a specific point or object, commonly with a duration of 200-300ms	Sustained attention, engagement, cognitive processing (cognitive load or difficulty in processing information), interest or preference	Prolonged fixations can indicate difficulties in processing information or heightened attention to detail in Alzheimer’s disease and ASD. In contrast, shorter fixations suggest difficulties maintaining attention as in ADHD.
Saccades	Rapid eye movements between fixations, used to quickly shift attention from one point to another, commonly with a duration of 30-80 ms, an amplitude of 4-20°, and a velocity of 30-500°/s	Visual search and scanning, cognitive load, impulsivity and attention disorders	Impaired (delayed or slow) saccadic eye movements are often linked to motor control deficits in Parkinson’s disease and Huntington’s disease while erratic or rapid saccades may suggest hyperactivity or excessive scanning of the visual field as in ADHD and anxiety disorders.
Pupil dilation	Changes in the size of the pupil, often in response to light but also as a reaction to cognitive and emotional stimuli	Cognitive load (task complexity and mental effort), emotional arousal (stress, excitement, or fear), selective attention	Reduced and slower pupil dilation/constriction can be a biomarker for Parkinson’s while exaggerated dilation during cognitive tasks can be linked to Alzheimer’s. Larger baseline pupil size in response to social stimuli is linked to ASD.

Blink rate	The frequency of spontaneous blinking	Cognitive load, sustained attention, stress, anxiety, fatigue, dopaminergic activity,	Increased blinking can reflect heightened stress or obsessive-compulsive tendencies, as in OCD and anxiety disorders. In contrast, a lower blink rate is associated with impaired motor control or cognitive decline, as in Parkinson's disease and Alzheimer's disease.
Microsaccades	Small, involuntary saccades that occur during fixation to correct gaze drift, commonly for a duration of 10-30 ms, an amplitude of 10-40' (minutes where 1°=60'), and a velocity of 15-50°/s	Attention stability, cognitive fatigue or stress	More frequent microsaccades can indicate difficulty focusing or excessive scanning of the environment as in ADHD and anxiety disorders. In contrast, decreased microsaccades may signal cognitive decline or attentional deficits in Alzheimer's disease.
Smooth pursuit	Eye movements that enable the tracking of moving objects smoothly, commonly with a velocity of 10-30°/s	Motor control, attentional engagement, oculomotor coordination	Difficulties in tracking moving objects are common in Multiple Sclerosis (MS) due to deficits in coordination. Jerky smooth pursuit can signal motor system dysfunction in Dystonia and essential tremor.

Table 1. Most common metrics for gaze-base neurological behaviour as defined by Holmqvist et al. [198]. Metrics offer a structured way to interpret the findings. Each metric should be assessed alongside others, and often, multiple metrics together provide a more accurate diagnosis (cf. Section 4 for more details).

Longitudinal Studies: Neural disorders often evolve over time, so consider conducting longitudinal studies to track changes in gaze behaviour as the disorder progresses or in response to treatments [97, 383]. Note that eye gaze is likely critical for developing long-term social skills and higher-order social-cognitive abilities, such as theory of mind (ToM) and perspective taking [79, 432].

Multimodal Integration: Eye-tracking can reflect cognitive load, emotional responses, and attention shifts, but it doesn't provide direct information on underlying brain activity [181, 205, 394]. In addition, since gaze as a diagnostic tool is a relatively new research field and neural disorders often involve complex and overlapping symptoms, relying on a single diagnostic tool, with the current research state, can lead to incomplete or misleading interpretations [35, 389]. Combining multiple modalities allows for cross-validation, reducing the chances of false positives or negatives. If abnormalities are observed and cross-referenced in both eye-tracking data and another measure (e.g., EEG, MRI, subjects' and doctors' reports), the likelihood of those results being meaningful and linked to a specific neural condition is higher, especially in complex or comorbid cases where symptoms of different disorders overlap [50, 324]. Therefore, consider

combining eye-tracking data with other physiological or cognitive measures (e.g., EEG, MRI, behavioural observations) to gain a holistic understanding of how gaze behaviour relates to the neural condition [35, 202, 249, 256].

Statistical Analysis and Hypothesis Testing. Once gaze data has been collected, statistical analysis is crucial to extract meaningful patterns and test hypotheses about the neural disorder. The goal is to determine whether there are significant differences in gaze behaviour between groups (e.g., patients vs healthy controls or medicated vs unmedicated patients) or over time (e.g., disease progression) [187, 194, 259, 285]. For this, develop clear, testable hypotheses based on the research question [159, 198, 392, 406], such as "Patients with Parkinson's disease will have longer saccade latencies compared to healthy controls.". Then, select the appropriate statistical test based on the data type and research design; here, we refer the reader to and highlight key guidelines following [15, 303]:

- Parametric Tests: For normally distributed data, including:
 - T-Tests: e.g. compare the average fixation duration between patients with Alzheimer's disease and healthy controls during a memory recall task to check for significant differences between the two groups (i.e. two-sample t-test) [480].
 - ANOVA (Analysis of Variance): e.g. compare gaze patterns across multiple groups (e.g., Parkinson's patients, Alzheimer's patients, and healthy controls), a one-way ANOVA could be used to determine if there are significant differences in saccade velocity between the groups, with Parkinson's patients showing the slowest velocities due to motor deficits [17].
 - Repeated-Measures ANOVA: e.g. assess how fixation duration changes over time during a cognitive task in the same group of participants, a repeated-measures ANOVA could account for within-subject variations. For instance, fixation duration could increase over time as participants become more fatigued during a long, attention-heavy task [206].
- Non-Parametric Tests: For data that does not meet normality assumptions, including:
 - Mann-Whitney U-Test: E.g. if fixation durations between two groups (e.g., healthy controls and stroke patients) are highly skewed or don't follow a normal distribution, the Mann-Whitney U-test can be used to compare the distributions between groups [73].
 - Kruskal-Wallis Test: e.g. for more than two groups (e.g., different subtypes of autism), when fixation duration is not normally distributed, a Kruskal-Wallis test can determine whether the groups differ significantly. For example, different subtypes of autism could display varying gaze patterns, with some subtypes showing a preference for non-social stimuli (e.g., objects instead of faces) [13].
- Mixed-Effects Models: For repeated measures data (e.g., where gaze data is collected at multiple time points or across multiple conditions). For example, in a longitudinal study where gaze data is collected from the same patients with multiple sclerosis (MS) at different stages of the disease, a linear mixed-effects model can be used to account for both fixed effects (e.g., disease stage) and random effects (e.g., individual variability) [300]. Another example is if gaze data is nested within tasks (e.g., multiple visual tasks completed by the same subject), mixed-effects models can also handle these nested structures. For instance, gaze data from various attention tasks for each participant with ADHD can be modelled to see if task difficulty affects gaze measures differently across subjects [446].
- Correlation Analysis: To investigate relationships between gaze metrics and other variables, such as cognitive test scores or brain activity, including:
 - Pearson's Correlation: E.g. when examining the relationship between average fixation duration and cognitive test scores (e.g., memory recall performance) in Alzheimer's patients, Pearson's correlation can be used for

normally distributed data to test if there will be a negative correlation between fixation duration and memory test performance, with longer fixations indicating poorer cognitive function [480].

- Spearman’s Rank Correlation: If the data is non-normally distributed (e.g., fixation duration data is skewed), Spearman’s rank correlation can be used to assess the relationship between fixation duration and disease severity scores [186]. E.g. in Parkinson’s patients, Spearman’s Rank is used to check if there will be a positive correlation between fixation duration and disease severity, with more severe motor symptoms being associated with longer fixation durations [449].
- Correct for Multiple Comparisons: Eye-tracking experiments often involve a large number of gaze metrics (e.g., fixation duration, saccade velocity, etc.). Applying a correction method (e.g., Bonferroni correction) is necessary to reduce the risk of false positives. For example, after running several independent t-tests for each gaze metric, the p-value threshold can be adjusted using the Bonferroni correction, which divides the significance level by the number of comparisons (e.g., three tests) [268].

In addition to p-values, reporting effect sizes (Cohen’s delta, eta squared) and confidence intervals provide information on the practical significance of the findings, which is especially important in clinical settings [314, 455, 509].

It is also essential to analyze gaze data in segments depending on the type of stimulus (e.g., visual scene, text, social stimuli) to assess which cognitive or visual processes are impaired [73, 324, 371].

With complex (high-dimensional) non-linear patterns that may be difficult to identify through traditional statistical methods, machine learning models can be applied [3, 386, 453].

Data visualization. Data visualization is a supplementary step in understanding and interpreting neurological gaze data. It transforms raw values into visual formats that highlight patterns, anomalies, or trends in gaze behaviour, making it easier to communicate results to both clinicians and researchers [392, 524]. Common visualizations in eye-tracking analysis include:

- Heatmaps: These visualize where participants are looking most frequently. Areas with more fixations are represented with "hotter" colours (e.g., red), and areas with fewer fixations are shown with "cooler" colours (e.g., blue) [434]. For example, in a study on autism spectrum disorder (ASD), a heat map could show whether participants with ASD focus less on the eyes in images of human faces, indicating social attention deficits [240, 412].
- Scanpaths: These trace the sequence and direction of eye movements, showing how a person visually explores a scene or object [378]. For example, scanpaths could be used in Alzheimer’s research to show how patients’ gaze patterns become more erratic when navigating visual scenes, reflecting a cognitive decline in spatial awareness [58].
- Time-Series Plots: These visualize how gaze metrics (e.g., pupil dilation, fixation duration) change over time during a task [236]. For example, in a cognitive load experiment, a time-series plot might show that Alzheimer’s patients exhibit greater fluctuations in pupil dilation over time, indicating increased difficulty in maintaining attention [451].
- Gaze-Overlaid Videos: By overlaying gaze data on videos of stimuli (e.g., a movie scene or interactive interface), the participant’s attention shifts can be tracked over time [475]. For example, for assessing visual attention deficits in ADHD, a gaze-overlaid video can illustrate the participant’s difficulty in maintaining focus on relevant stimuli [37].

3.5 Reporting

Transparency: Provide clear documentation of study protocols, participant characteristics, data preprocessing steps, and analytical techniques to ensure applicability [109, 129].

Pre-registration: Pre-registration refers to the practice of registering a research study’s methodology, hypotheses, and analysis plans in a public registry before data collection begins to promote transparency, reduce the risks of bias, and improve the credibility of scientific findings [185, 343]. Pre-registration is becoming increasingly recognized as a "golden standard" in research reporting, especially in fields prone to exploratory analyses [498] or p-hacking [506], e.g. gaze-based neural studies [139, 381, 477]. Studies are commonly pre-registered on platforms like ClinicalTrials.gov [337] or the Open Science Framework (OSF) [138].

Reproducibility. Wherever possible, share the code or software used for data analysis (e.g., Python, MATLAB, R scripts) on public repositories like GitHub [163] or OSF [138]. This allows others to reproduce the exact analysis pipeline [109, 326]. In addition, whenever possible, make the gaze data available on public repositories, following ethical guidelines (e.g., via Dryad [106], Zenodo [137]), allowing other researchers to replicate the findings [129, 198].

For further reporting guidelines for general eye-tracking studies, we refer the reader to [129].

3.6 Ethics and Privacy Considerations

In addition to the general ethics and privacy considerations for general eye tracking studies [348], further considerations arise for neural applications.

Informed Consent: Participants, especially those with neural disorders, must be fully informed about the research goals, procedures, and potential risks before agreeing to participate [129, 198]. Ensure that proper consent is obtained, possibly through guardians or caregivers, when working with vulnerable populations, such as children or individuals with cognitive impairments (e.g., ASD or Alzheimer’s) [224, 375, 531]. Participants should also have the right to withdraw their consent and request the deletion of their personal data at any time [360], e.g. commonly achieved through an end-user license agreement (EULA) [4]. Consents could be generated for eye tracking experiments using [113]. For specific use-cases, Open Brain Consent [180] provides several consent forms for different jurisdictions, languages, and/or guidelines that could be adapted to the specific experiment ¹.

¹For stronger privacy guarantees, privacy-preserving mechanisms could be adopted, e.g. differential privacy [91, 283, 290, 443], federated learning [115, 123], and secure computation protocols [116, 355].

Consent example of a free-viewing task [113].

Replace the [text between brackets] with your experiment details:

Dear participant,

You have volunteered to participate in this study. Here you will now receive some information about your rights and the procedure of the following experiment. Please read the following sections carefully.

1) Purpose of the study

In this study, we will investigate [how humans perceive images by recording eye movements using an eye tracker].

2) Study procedure

The study will proceed as follows: We perform [an eye test (visual acuity and dominant eye)].

The eye tracker needs to be calibrated, for this, a moving dot will appear on the monitor which you will follow with your gaze.

We will present [different pictures on the screen. Your task is to freely explore these pictures].

Including the questionnaires and preparations, the experiment takes about [one] hour.

3) Risks and side effects

According to current knowledge, this study is harmless and painless for the participants. By participating in this study, you are not exposing yourself to any particular risks and there are no known side effects. However, because this study is new in its entirety, the occurrence of as-yet-unknown side effects cannot be completely ruled out.

Important: Please inform the experimenter immediately if you [have a neural disease, if strong (light) stimulation can trigger migraine, or if you have had an epileptic seizure]. If you have any questions about this, please contact the experimental investigator.

4) Termination of the experiment

Participation in the study is voluntary. You may withdraw your consent to participate in this study at any time without giving any reason and without any disadvantages. Even if you terminate the study prematurely you will be remunerated accordingly for the time spent up to that point.

If you experience [headaches or any other kind of discomfort] during the experiment, please inform the experimental investigator immediately.

5) Confidentiality

Your data will only be stored in pseudonymized form (e.g. "sub-003"). [The mapping file will be deleted after the completion of the data collection. The data will be made available for scientific publications, but also as open scientific data for third parties.]

6) Remuneration

The study will be remunerated with [15 euros] per hour. Partial half hours will be rounded up.

7) Declaration of consent

I hereby confirm that I have understood the participant information described above and that I agree to the stated conditions of participation, in particular:

[an unlimited storage of my pseudonymized data, the usage of my pseudonymized data for the current research project and for other exclusively scientific purposes, a publication of my pseudonymized data as open data.]

.....

Place, date, signature

Ethical Approval and Institutional Review Boards (IRBs). Before conducting studies, research involving human subjects needs to be approved by an IRB or ethics committee [346, 347], which ensures the study complies with ethical and legal standards, e.g. the General Data Protection Regulation (GDPR) [360], or the Medical Device Regulation (MDR) [361] in the EU and/or the Health Insurance Portability and Accountability Act (HIPAA) [345], the California Consumer Privacy Act (CCPA) [344], or the Food and Drug Administration (FDA) [136] in the US. Ethical boards evaluate whether data collection processes respect patient privacy, minimize harm, and maintain the confidentiality of sensitive gaze and neural data.

4 Specific guidelines for gaze-based neural research

Neural disorders can be categorised into a diverse group of conditions that affect the nervous system, which includes the brain, spinal cord, and nerves. They can result from structural, biochemical, or electrical variations and can impact movement, communication, cognition, and behaviour.

We emphasize that it is crucial to determine whether gaze patterns are merely an epiphenomenon or a direct reflection of neural function [118, 302, 403, 503]. An epiphenomenon is a phenomenon that occurs alongside another condition but does not necessarily cause or result from it. For example, in dyslexia, eye movement abnormalities (e.g., longer fixations, more regressions) are often observed, however, these do not directly cause reading difficulties; rather, they emerge as a byproduct of phonological and language processing deficits. In this case, gaze abnormalities are not necessarily indicative of a core neural deficit, but rather reflect higher-level cognitive processing difficulties. In contrast, eye movements can directly reflect the functional state of neural networks, particularly in disorders affecting attention control, executive function, or motor planning. For example, in attention disorders (e.g., ASD and ADHD), gaze behaviour is tightly linked to neural mechanisms governing attention allocation, inhibition, and sensory integration. These processes involve specific brain networks, such as the fronto-parietal network (for voluntary attention and saccade control), the dorsal attention network (for top-down attentional guidance), and ventral attention network (for reorienting attention to unexpected stimuli). Hence, in these cases, gaze abnormalities are not just symptoms but are rooted in underlying neural dysfunctions.

We also recommend adopting a transdiagnostic framework, recognizing that many neural disorders involve overlapping but distinct disruptions in neural circuits (c.f. Section 3). A transdiagnostic framework focuses on functional (or dysfunctional) neural networks that cut across traditional diagnostic boundaries. In other words, since many neural disorders share overlapping dysfunctions in brain circuits that control attention, perception, and cognitive control, rather than studying each disorder in isolation (e.g., ASD vs. ADHD), a network-based approach considers which neural systems are affected and how they vary across individuals. Therefore, instead of treating disorders categorically, gaze analysis should be contextualized within broader neural dysfunctions to improve diagnostic accuracy and treatment outcomes.

In the following, as shown in Figure 4, we introduce a taxonomy for the main categories along with specific guidelines for conducting gaze-based diagnosis research. For each disorder, we compiled the agreed-upon key eye-tracking focus, task design, considerations, and metrics that were widely employed or recommended in the literature.

4.1 Neurodevelopmental Disorders

Autism Spectrum Disorder (ASD): ASD affects social communication and behaviour, with a wide range of symptoms and severity levels. Most commonly, ASD is qualitatively characterized by deficits in social interaction, restrictive and repetitive patterns of behaviour or interests, attentional disengagement, and impairments in communication

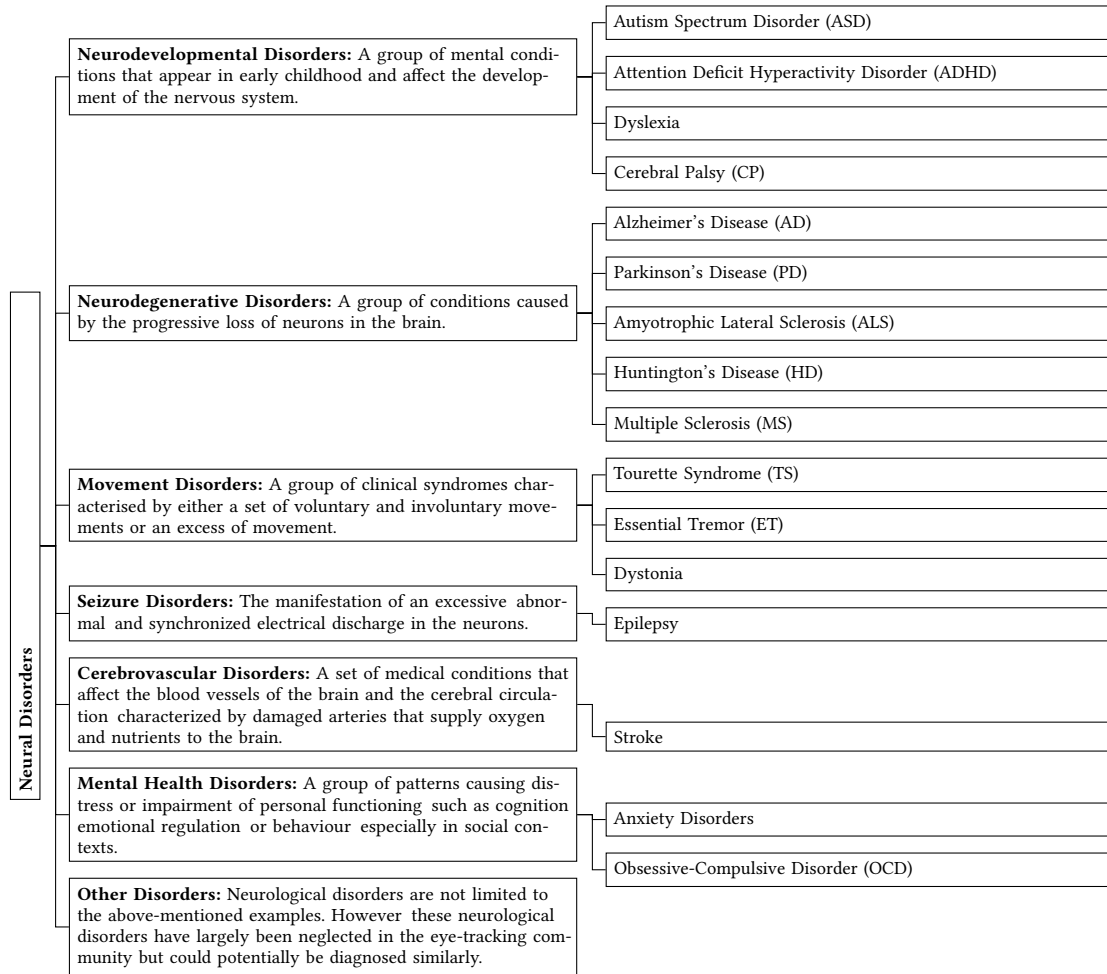


Fig. 4. Categories and definitions of neural disorders adapted from the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (DSM-5) [456]. Note that the same disorder can have different categories in different fields; in this paper, we classify disorders according to their primary class.

[78, 86, 226, 505]. Impairments across sensory modalities (touch, smell, vision, hearing, taste) could be correlated with an inability to respond to social cues, poor social problem-solving, and increased isolation in ASD [228, 248, 356, 407, 501]. However, the most reliably replicated sign of ASD is differences in social attention, found in attenuated eye gaze [37, 248, 448, 501]. Such atypical gaze patterns are consistent across age groups, suggesting that gaze-tracking could be used as an early indicator for ASD diagnosis, potentially identifying ASD-related behaviours in infancy before other symptoms are noticeable [93, 407]. Furthermore, the assumption that individuals with ASD exhibit 'impaired' attentional orientation and engagement behaviours has been both corroborated and disputed in various contexts due to experimental differences mentioned above (c.f. section 2). Some studies [177, 227, 435] have shown an association between reduced visual fixation on the eye region and greater social difficulties. Other studies [29, 46, 229, 358, 415, 513] have indicated that ASD individuals were indeed slower to initially fixate and maintain fixation on faces. They spend

significantly less time looking at faces relative to non-social stimuli in comparison to typically developing (TD) individuals; nonetheless, they showed optimal facial identification, gender discrimination, and emotional recognition abilities, which corroborate those of other studies [28, 161, 471, 497], which propose that deficits related to facial processing in ASD do not begin with the initial eye movement, but may begin more downstream and that individuals with ASD might use facial information differently (e.g. increased gaze towards the mouth more than both eyes).

- **Key Eye-Tracking Focus:** Social attention, gaze fixation on faces, and responses to social stimuli.
- **Task Design:** (i) Use dynamic social scenes (e.g., videos of people interacting) to measure how individuals with ASD focus on social cues like facial expressions, eye regions, and gestures [171, 172, 296]. (ii) In addition to social stimuli, non-social stimuli are used as a control to contrast gaze patterns. For instance, show participants neutral objects to see if their attention differs from social stimuli [323, 441]. (iii) Avoid overly complex visual stimuli, as sensory overload can easily overstimulate ASD participants [56, 484].
- **Considerations:** (i) ASD participants may have difficulty sitting still, so shorter tasks or frequent breaks are important to maintain engagement [273, 481]. (ii) Some individuals with ASD have heightened sensitivity to bright lights or sudden movements, so use gentle transitions in stimuli [57, 160].
- **Metrics:** (i) Reduced fixation on the eye region of faces is often a key indicator in ASD studies [90, 448]. (ii) Saccadic patterns when looking at social stimuli can help measure social engagement. i.e. quick eye shifts can indicate disengagement [448, 528]. (iii) Pupil dilation can indicate cognitive load or emotional response, but it is not a conclusive biomarker for ASD [67, 149]. (iv) Additionally, heatmaps and scan path visualization can indicate how attention is distributed during specific tasks, often showing less focus on socially relevant areas (i.e. ROI) in ASD participants [248, 501]. (v) Delayed or reduced blinking might correlate with difficulties in social engagement, interpreting social cues, or sensory processing, while heightened blink frequency could be linked to increased stress or discomfort [14, 271].

Attention Deficit Hyperactivity Disorder (ADHD): ADHD is characterized by inattention, hyperactivity, and impulsivity [456]. One of the most notable gaze-related differences in individuals with ADHD is reduced sustained attention to task-relevant stimuli [311, 330, 488, 491]. ADHD participants may exhibit shorter fixation durations and more frequent saccadic movements, indicating difficulty in maintaining attention. Eye-tracking studies [5, 45, 311, 425, 446, 488] have demonstrated that individuals with ADHD tend to shift their gaze more frequently and are less able to remain focused on a single point of interest, especially during tasks that require prolonged attention such as reading or visual search tasks, where sustained gaze on relevant areas is critical for performance. Additionally, eye-tracking research in ADHD often focuses on impulsivity (less goal-oriented eye movements as opposed to attention, indicated by shorter fixation durations, higher saccade frequency and amplitudes, increased blink rate and microsaccades, and fluctuating pupil size)[311, 416, 458], as measured by premature gaze shifts or difficulties in controlling eye movements. For instance, in tasks like the antisaccade task, where participants are instructed to suppress automatic eye movements toward a distractor and instead look in the opposite direction, individuals with ADHD tend to show higher error rates, reflecting impaired inhibitory control. This aligns with the impulsivity and difficulty with self-regulation seen in ADHD. Other gaze-related metrics used in ADHD research include pupil dilation where some studies [247, 399, 494] suggest that children and adults with ADHD may show abnormal patterns of pupil dilation when faced with cognitive demands, reflecting differences in the way their brains allocate attention and resources. Gaze variability is another important metric, where individuals with ADHD display greater variability in where they direct their attention, indicating challenges in maintaining a stable focus on task-relevant areas [71, 320].

- Key Eye-Tracking Focus: Sustained attention, impulsive saccades, and visual exploration.
- Task Design: (i) Use tasks that require visual attention over time, such as continuous performance tasks (CPT), to observe lapses in attention [278]. (ii) Implement tasks that challenge impulse control, such as "go/no-go" tasks where participants must inhibit responses to certain stimuli [388, 523].
- Considerations: (i) ADHD participants may struggle with longer tasks, so break up the sessions and avoid tasks that require sustained effort without rewards [311, 416]. (ii) Incentives like gamified tasks can help keep participants engaged throughout the study [87, 210, 270].
- Metrics: (i) Track fixation durations and saccade frequencies. Short fixations and frequent saccades may indicate attentional difficulties [5, 276, 311, 425, 488]. (ii) Blink rate can be an additional measure, as higher rates may correlate with inattention [18, 144, 311]. (iii) Individuals with ADHD, with a tendency to have smaller baseline pupil sizes, may exhibit a delayed or exaggerated pupil dilation response to cognitive tasks or emotional stimuli [247, 399, 494]. (iv) Individuals with ADHD often exhibit poorer smooth pursuit than TD individuals and might demonstrate increased saccadic intrusions (i.e., jerky eye movements) during pursuit [275, 402, 460]. (v) Microsaccades are increased and can have altered frequency, potentially linked to difficulties in visual fixation and attentional control (i.e. reduced microsaccadic inhibition) [144, 357].

Dyslexia: Dyslexia is a learning disorder that affects reading and language processing [456]. Dyslexia is primarily characterized by difficulties with phonological processing and word decoding, but studies [44, 131, 339, 411, 502, 512] indicate that eye movement patterns during reading can offer valuable insights into the cognitive challenges faced by individuals with dyslexia. Compared to TD, individuals with dyslexia tend to have longer fixation durations, reflecting the increased cognitive load required to decode words [379, 492, 530]. Additionally, dyslexic readers exhibit more frequent regressive saccades, indicating difficulties in word recognition and comprehension, as they often need to re-scan previously read words to make sense of the text [63, 131]. Studies also highlight that dyslexic readers may show more variable saccadic amplitudes, meaning their eye movements between words are less consistent, further slowing down reading speed and reducing comprehension [63, 379]. Dyslexic readers typically show increased pupil dilation during reading tasks, suggesting that their brains are working harder to process the same visual and phonological information as non-dyslexic readers (i.e. cognitive effort) [359, 502].

- Key Eye-Tracking Focus: Reading difficulties, word recognition, and saccadic movements during reading tasks.
- Task Design: (i) Use text-based tasks where participants read sentences or paragraphs, allowing researchers to track eye movements during reading [44, 131, 339, 411, 502]. (ii) Include different reading difficulty levels, such as phonemically complex words or sentences, to evaluate how gaze changes with increasing reading challenge [44, 315]. (iii) Include non-text control tasks (e.g., images or symbols) to assess if dyslexia-related gaze behaviours are specific to reading or extend to other visual tasks [114, 243, 467].
- Considerations: (i) Tasks should be adapted to the participant's reading level (e.g. age), as dyslexia may result in significant variation in reading ability [131].
- Metrics: (i) Fixation duration and regressions (returning to previously viewed text) are important indicators of reading difficulty [379, 411]. (ii) Measure saccade length — shorter saccades and more frequent regressions typically indicate reading difficulty [379, 502].

Cerebral Palsy (CP): A motor disability caused by damage to the developing brain, affecting movement and posture and impacting the oculomotor system, leading to eye movement difficulties, reduced visual tracking ability, and gaze

stability issues [456]. Gaze-based research in CP focuses on assessing visual, cognitive, and motor control impairments that are often associated with this condition. Research [238, 299] shows that individuals with CP may have slower saccades, reduced accuracy in their eye movements, and difficulties with smooth pursuit, particularly in tasks that require precise gaze coordination with physical movements. These challenges are linked to motor control issues affecting the muscles responsible for eye movement, which can also hinder overall visual perception [409]. In addition, individuals with CP may struggle to maintain consistent attention on visual stimuli, often exhibiting longer fixation durations and delayed response times to visual cues [263, 299, 413]. These abnormalities are thought to stem from a combination of motor impairments and cognitive difficulties, such as challenges with executive function and attention regulation [413, 439].

- Key eye-tracking focus: Oculomotor impairments include gaze stability, smooth pursuit, controlling saccades, visual attention, and cognitive response.
- Task design: (i) Use smooth pursuit to measure motor coordination between eyes and head [10, 30, 155]. (ii) Design tasks that require maintaining gaze on a fixed target for a sustained period to assess fixation stability and motor control over eye movements [238, 299]. (iii) Display different objects or faces and ask participants to focus on specific ones to assess visual recognition and attention, a valuable way to evaluate memory and comprehension in individuals with severe CP [30, 79].
- Considerations: (i) Individuals with CP often have involuntary movements that can interfere with head-mounted or screen-based eye trackers [409]. Recalibrate the system frequently and use systems that allow for greater movement tolerance and use head stabilization techniques. (ii) Some individuals with CP may also have cognitive delays or sensory impairments (e.g., cortical visual impairment) [409, 413, 439]. Adjust stimuli to ensure they are visually simple and easy to comprehend, minimising cognitive overloads, such as large, contrasting shapes or images. (iii) Calibration can be difficult for individuals with motor impairments who struggle to focus on specific points for extended periods [30, 409]. Use simplified calibration processes or allow more time for calibration to ensure accurate tracking. (iv) Where possible, incorporate adaptive technology like gaze-controlled communication devices for participants with severe motor impairments, enabling them to express cognitive responses without physical input [148].
- Metrics: (i) Measure the latency (time delay) in initiating saccades and the accuracy in reaching visual targets. Individuals with CP may have delays or inaccuracies due to motor control issues [409]. (ii) Saccade velocity (speed of eye movement) and saccade amplitude (distance of eye movement) can also be indicative of motor impairments [238]. (iii) Assess how long participants can maintain a steady fixation on a target without drifting [30, 409]. Fixation instability may reflect motor control challenges that are common in CP. (iv) Measure total fixation time on relevant stimuli, especially in tasks where attention to a specific target is required [299, 413]. (v) Smooth pursuit gain measures how closely the eyes track a moving object. In individuals with CP, reduced smooth pursuit gain (i.e., inability to follow a moving target smoothly) can reflect both motor and coordination difficulties [10, 30, 155]. (vi) Use scanpath analysis to evaluate how participants explore visual stimuli. Irregular scanpaths may indicate difficulties in planning or controlling eye movements [263, 468].

4.2 Neurodegenerative Disorders

Alzheimer's Disease (AD): A progressive disorder causing memory loss, confusion, and cognitive decline due to brain cell death. It further impacts visual processing and oculomotor control [456]. In individuals with AD, gaze-based studies typically reveal longer fixation durations and increased difficulty in shifting gaze from one visual target to

another [16, 211, 490]. These oculomotor impairments are linked to the degeneration of brain regions responsible for executive function, spatial orientation, and visual attention [70, 456]. For instance, tasks that require visual search or attention to multiple objects are often challenging for Alzheimer's patients, who tend to have slower and less accurate saccades, reflecting difficulties in efficiently scanning their environment [281, 292, 304, 366, 522]. Additionally, people with AD often show reduced attention to important visual cues, such as faces or emotionally relevant stimuli, which correlates with their broader cognitive and memory deficits [84, 211, 374, 390, 451]. A particular area of interest is eye movement behaviour in reading tasks [125, 173, 175, 188]. Alzheimer's patients exhibit increased fixation times on words and more frequent regressive saccades (backward eye movements), indicating difficulties in decoding text and retaining information across sentences. These reading difficulties are tied to the memory and comprehension deficits (i.e. language processing and cognitive decline) that define the disease [126, 291].

- **Key Eye-Tracking Focus:** Visual attention, memory recall, and fixation patterns during memory tasks.
- **Task Design:** (i) Use tasks involving object or face recognition to assess memory and attention, such as presenting familiar versus unfamiliar faces and tracking gaze [374, 451]. (ii) Implement visual search tasks to measure how participants scan and process visual information, such as finding a target among distractors [304, 366].
- **Considerations:** (i) Dementia can affect attention span and comprehension. Tasks should be simple and visually clear to prevent confusion [393]. (ii) Avoid complex stimuli or rapid changes, as they may overwhelm or confuse participants with cognitive impairment [522].
- **Metrics:** (i) Measure fixation duration and time to first fixation on familiar objects or faces versus novel ones [211, 451]. (ii) Track scanpaths to analyze how participants explore visual stimuli, as irregular patterns can indicate cognitive impairment [134, 390, 393]. (iii) Pupil dilation is another measure that is studied, as the reduced response to stimuli can indicate changes in cognitive effort or arousal during tasks. Individuals with Alzheimer's tend to have abnormal pupil responses, reflecting the increased cognitive load as they attempt to process information [140, 168, 390]. (iv) Alzheimer's patients typically exhibit a reduced blink rate, which may reflect cognitive slowing and decreased sensory engagement [112, 325, 438]. (v) Alzheimer's patients often show altered oblique microsaccadic behaviour. This may reflect impaired visual attention and gaze stability, potentially indicating that the brain is attempting to compensate for visual or cognitive decline by making more frequent small eye movements [7, 234]. (vi) Alzheimer's patients may also demonstrate reduced accuracy in smooth pursuit. Patients may find it difficult to maintain fixation on moving objects, leading to more frequent corrective saccades to reposition the gaze [135, 143, 526].

Parkinson's Disease (PD): A disorder affecting movement, characterized by tremors, stiffness, and slow movement. It further impacts areas of the brain responsible for eye movement and visual processing [125, 258]. A key feature of PD is bradykinesia (slowness of movement), which is often reflected in slower saccadic movements and longer fixation durations [99, 193, 231, 282, 426, 442, 485]. Individuals with Parkinson's may struggle to initiate saccades or exhibit hypometric saccades, meaning their eyes undershoot visual targets, requiring multiple corrective movements [245, 382, 419, 442]. These abnormalities can be particularly noticeable in tasks that require shifting attention, such as visual search or reading, suggesting a disruption in the coordination between cognitive planning and motor execution in PD [121, 166, 195, 469]. In addition, Parkinson's patients frequently show deficits in smooth pursuit, particularly in tracking objects with predictable motion, often leading to jerky or interrupted eye movements [190, 305, 369, 510, 519]. Furthermore, patients with PD may struggle with visual attention tasks, particularly those that involve divided attention or responding to multiple stimuli [60, 193, 442, 450].

- **Key Eye-Tracking Focus:** Eye movement control, including saccadic movements, smooth pursuit, and fixation stability.

- Task Design: (i) Use tasks that require smooth pursuit to assess motor control related to eye movements [190, 510, 519]. (ii) Include gaze-following tasks to assess whether eye-tracking can identify difficulties in attention and motor integration [193, 485]. (iii) Use antisaccadic tasks to understand the inhibitory mechanisms [61, 182, 282, 499].
- Considerations: (i) Parkinson's participants may struggle with motor control, so ensure that the eye-tracking system can account for potential head movements or tremors [429].
- Metrics: (i) Measure saccade latency, saccade amplitude, and fixation duration, as motor delays can manifest in these aspects [245, 287, 382, 419, 429]. (ii) Assess smooth pursuit gain (the ratio of eye velocity to target velocity), as reduced gain is common in Parkinson's [190, 519]. (iii) Measure pupil dilation to measure cognitive effort during tasks since Parkinson's patients often show abnormal pupil responses [391, 485]. (iv) People with PD often exhibit less stable fixations, with increased fixation duration and more difficulty in maintaining a steady gaze (increased drifts) [370, 396, 485]. (v) PD patients often show a reduction in the frequency of microsaccades due to the corrective behaviour [317, 354].

Amyotrophic Lateral Sclerosis (ALS): Also known as Lou Gehrig's disease, ALS leads to the gradual degeneration of motor neurons, affecting voluntary muscle control [456]. While ALS typically spares the muscles responsible for eye movement until the later stages, gaze-based studies provide valuable insights into the cognitive deficits and communication challenges faced by ALS patients [24]. Eye-tracking studies have revealed slower saccades and difficulty in maintaining steady fixation on visual targets, which may reflect the spread of motor neuron degeneration to the muscles controlling eye movement [16, 39, 65, 383, 527]. These oculomotor impairments, although usually mild, can be used to monitor disease progression and help distinguish ALS from other neurodegenerative disorders, such as Parkinson's or Alzheimer's disease, where eye movement abnormalities are more pronounced earlier in the disease course [421]. In addition, while ALS is primarily a motor disorder, up to 50% of patients experience some form of cognitive impairment, often in the form of executive dysfunction or frontotemporal dementia (FTD) [336, 414]. Eye-tracking tasks that measure visual attention, working memory, and decision-making can help detect these cognitive deficits [233, 342, 417]. For example, ALS patients with cognitive impairment may show longer fixation times or difficulty in shifting gaze during tasks that require decision-making or response inhibition, indicating problems with cognitive control and flexibility [65, 241, 280, 383].

- Key Eye-Tracking Focus: Oculomotor Control
- Task Design: (i) Use antisaccade tasks to assess higher-order executive functions and control over involuntary motor movements [39, 383, 421]. (ii) Include smooth pursuit tasks to measure the progression of ALS over time [178, 216, 280]. (iii) Fixation stability tasks can further detect motor impairments in ALS [39, 383]. (iv) ALS patients may experience frontotemporal dementia, leading to cognitive decline [414]. Designing tasks that measure both motor and cognitive performance separately.
- Considerations: (i) Ensure that patients with severe motor impairment can participate in the tasks (c.f. 3).
- Metrics: (i) Measure fixation duration; irregular fixation durations may indicate difficulties in motor control, which can reflect ALS progression [65, 383, 527]. (ii) Measure saccadic latency and amplitude; increased saccadic latency (slower reaction times) or irregular saccade amplitudes (deviations in the distance of eye movements) are key metrics in identifying motor control issues in ALS patients [39, 280, 335]. (iii) Assess smooth pursuit gain; lower pursuit gain could suggest impaired motor coordination, which becomes prominent as ALS progresses [178, 280]. (iv) Measure the error rate in antisaccade tasks; high error rates (looking towards a stimulus instead of away) can reveal deficits in cognitive control and executive function, often associated with ALS-related cognitive impairments [39, 383, 421].

(v) ALS patients can show abnormalities in pupil responses, leading to altered responses to light or cognitive tasks. Some ALS patients exhibit reduced pupil reactivity, potentially because of dysautonomia, which may impact the speed and extent of dilation and constriction [223, 351]. (vi) ALS may lead to reduced microsaccade frequency and amplitude, especially as the disease progresses. These changes likely arise from the degeneration of motor neurons that impact the precision of small eye movements [39, 178, 335].

Huntington's Disease (HD): A genetic disorder causing the progressive breakdown of nerve cells in the brain, affecting movement, cognition, and causing psychiatry conditions [456]. A prominent oculomotor symptom in HD is the impairment of voluntary saccadic eye movements [40, 51, 167, 376, 427]. Individuals with Huntington's often show slowed saccades and increased latency in initiating them [237, 277, 365, 397]. Studies using eye-tracking have found that HD patients take longer to initiate saccades and frequently require multiple attempts to reach visual targets accurately [267, 350, 474]. In addition to saccadic abnormalities, Huntington's disease also affects smooth pursuit; studies have revealed that HD patients have impaired smooth pursuit, often exhibiting jerky and fragmented eye movements [16, 242, 362, 440]. These deficits are early indicators of the motor control dysfunctions seen in HD. Cognitive dysfunction is another key feature of HD. For instance, individuals with HD often show prolonged fixation durations and difficulty in shifting attention between different visual stimuli, reflecting impairments in cognitive flexibility and decision-making [40, 51, 253, 350, 432]. These cognitive symptoms often appear before significant motor decline. They can be tracked using eye movements, which may provide early diagnostic clues and help monitor the cognitive aspects of HD over time [405, 408, 432].

- Key Eye-Tracking Focus: Oculomotor dysfunction and cognitive decline.
- Task Design: (i) The most commonly used tasks for HD patients involve testing the accuracy and speed of saccadic eye movements. Both reflexive (in response to a suddenly-appearing stimulus) and voluntary saccades (self-initiated look at a stimulus on command) can be impaired in HD [40, 51, 363, 376, 487]. (ii) Employ antisaccade tasks; HD patients often have trouble suppressing the reflex to look at the stimulus, revealing both motor and cognitive control issues [40, 51, 182, 365]. (iii) Smooth pursuit tasks are also recommended since HD patients tend to show lower smooth pursuit gain [23, 242, 362, 440]. (iv) Use fixation tasks as patients with HD often require corrective eye movements to hold their gaze [23, 40, 376].
- Considerations: (i) Check early vs. advanced stages through longitudinal studies: In the early stages, HD patients may have relatively subtle oculomotor impairments before HD becomes clinically evident [405]. (ii) Since HD affects both motor and cognitive functions, task designs should account for both types of deficits. For example, tasks that require simultaneous movement and decision-making can be valuable for identifying early impairments [254, 350, 376].
- Metrics: (i) Increased latency and reduced accuracy of saccadic eye movements are hallmark features of HD [55, 237, 277, 397]. (ii) Measure smooth pursuit gain as it typically decreases in HD patients [242, 362, 440]. (iii) High error rates in antisaccade tasks are also common in HD [40, 51, 182, 365]. (iv) Measure the fixation stability: HD patients may have difficulty maintaining fixation on a single point, with increased instability and corrective saccades [40, 41]. (v) Patients with HD often show an increased frequency of microsaccades during fixation, suggesting difficulty in maintaining a stable gaze [397, 515].

Multiple Sclerosis (MS): MS is a chronic condition where the immune system attacks the myelin sheath of nerve fibres, leading to a range of symptoms like numbness, fatigue, and difficulty walking [456]. Eye-tracking technology has proven valuable in studying these effects, as it can assess visual dysfunction, which is one of the earliest and most

common symptoms of MS, such as delayed saccades, prolonged fixation durations, and increased saccadic latency [97, 153, 293, 301]. Eye-tracking can detect internuclear ophthalmoplegia (INO - an oculomotor disorder common in MS) saccadic abnormalities by measuring the misalignment of gaze or impaired coordination between the eyes [174, 225, 333]. Furthermore, research shows that MS patients may exhibit increased microsaccades during attempts to maintain a steady gaze [153, 293, 301]. Eye-tracking technology is also able to precisely quantify the amplitude and frequency of nystagmus (a disruption in visual stability that makes it difficult for individuals to focus on stationary objects) [128, 174, 338, 380]. Moreover, eye-tracking has been used to assess smooth pursuit deficits, which often manifest as jerky or fragmented tracking [95, 230, 422]. By analyzing smooth pursuit metrics, eye-tracking can offer insights into how MS affects sensorimotor integration and visual processing, helping to differentiate MS from other neurological conditions. Finally, MS frequently leads to cognitive dysfunction, particularly in areas such as working memory, executive function, and visual attention [158, 373]. Eye-tracking studies have shown that individuals with MS may have difficulty maintaining attention during visual tasks, leading to longer fixation times or difficulties shifting their gaze between targets [301, 516].

- **Key Eye-Tracking Focus:** Oculomotor dysfunction (as deficits in smooth pursuit, saccadic movements, and fixation) and cognitive and motor decline.
- **Task Design:** (i) Use saccadic tasks; MS patients often show abnormal (reflexive and voluntary) saccadic behaviour, such as increased latency (reaction time) and hypermetric saccades (reduced saccade amplitude). Common tasks involve looking at a series of stimuli that appear in different locations to assess the speed and accuracy of saccadic movements [153, 301, 422]. (ii) Add smooth pursuit tasks; MS patients may show reduced smooth pursuit gain, which means they rely more on corrective saccades to follow the moving target [95, 230, 422]. (iii) Fixation tasks: MS patients may exhibit difficulty maintaining stable fixation, and frequent involuntary corrective saccades (nystagmus) are common [128, 301, 338, 380]. (iv) Since MS can affect cognitive functions like attention and processing speed, employ tasks that combine motor (eye movement) and cognitive challenges. For example, antisaccade tasks that require patients to inhibit reflexive saccades and look in the opposite direction of a stimulus help assess executive function [301, 516].
- **Considerations:** (i) MS symptoms vary widely between patients; patients may show early signs of oculomotor issues even if other symptoms are mild [301, 380]. (ii) MS progresses unpredictably, with periods of remission and relapse. Eye-tracking tests should be conducted over time to monitor fluctuations in symptom severity [152, 293, 380]. (iii) Due to reduced blink rate or incomplete blinks, many MS patients experience dry eye symptoms, which may lead to compensatory blinking in response to eye irritation [433].
- **Metrics:** (i) Increased latency and hypometric saccades (shortened eye movements) are common in MS patients [153, 293, 301]. (ii) Smooth pursuit gain is commonly reduced in MS patients [95, 230, 422]. (iii) Check for nystagmus (involuntary eye movements), particularly during fixation tasks for eye stability [338, 380]. (iv) MS can lead to delays in pupil dilation and constriction. This can result in slower or reduced pupil responses to light and other stimuli [94, 96, 217, 327, 454]. (v) Microsaccades in MS are often less frequent and more variable in both amplitude and direction, which may reflect broader impairments in motor coordination. This variability can interfere with stable gaze maintenance, particularly during tasks requiring precise focus [422–424].

4.3 Movement Disorders

Tourette Syndrome (TS): TS is mainly characterized by repetitive, involuntary movements and vocalizations (tics) but also affects attention, cognitive control, and impulsivity [456]. Eye-tracking technology has been used to study how individuals with TS process visual stimuli and how their tics and associated cognitive challenges influence eye movement patterns and visual attention [142, 156, 157, 231, 329]. Individuals with TS may exhibit difficulties in sustaining attention or filtering out distractions, which can affect their ability to maintain stable fixation or perform tasks that require continuous eye movements [157, 307]. Eye-tracking can objectively measure these deficits, for instance, by tracking how long individuals with TS can fixate on a visual target or how efficiently they perform in visual search tasks [1, 418]. Furthermore, while most tics in TS are motor or vocal, some individuals may experience ocular tics or tics that interfere with their normal eye movements [27, 255, 465, 486]. Eye tracking can help researchers better understand how these tics interact with normal visual processing. For example, studies have shown that tics can disrupt gaze stability and interfere with smooth pursuit movements, particularly when patients are trying to suppress their tics, leading to a compensatory increase in saccadic eye movements or other gaze abnormalities [110, 182, 460]. Additionally, individuals with TS may exhibit a higher frequency of premature saccades or errors in task performance when asked to withhold or redirect their gaze, reflecting difficulties in cognitive control [279, 461].

- Key Eye-Tracking Focus: Gaze control, including the relationship between tics and eye movements.
- Task Design: (i) Use tasks that challenge gaze stability, such as tasks where participants need to maintain focus on a fixed point [157, 307]. (ii) Include response inhibition tasks (e.g., antisaccadic tasks where participants must look away from a stimulus) to evaluate impulse control [110, 182, 461].
- Considerations: Tourette syndrome may involve tics that interrupt the study, so the tasks should be designed to accommodate potential interruptions [85, 156, 157, 329]. (ii) Provide rest periods to manage fatigue and tic exacerbations [461].
- Metrics: (i) Measure saccadic control (ability to suppress unwanted eye movements) and gaze stability [110, 182, 279, 461]. (ii) Track whether tics coincide with interruptions in eye movements, such as loss of fixation during a task [157, 307].

Essential Tremor (ET): ET is the most common tremor disorder and primarily manifests as involuntary, rhythmic shaking of the hands, head, or voice [456]. Research has shown that individuals with ET may also experience cognitive symptoms and oculomotor abnormalities, making eye-tracking a useful tool for assessing the broader neurological impact of the disease [189, 231, 517]. Studies have found that individuals with ET may show mild impairments in saccadic control, such as slowed saccadic velocity and increased latency in initiating saccades [53, 162]. In addition, eye-tracking studies suggest that individuals with ET may experience increased tremor-related instability during fixation, resulting in small, involuntary eye movements that disrupt gaze stability [189, 517]. Fixation instability in ET patients may also contribute to difficulties in tasks requiring sustained attention, such as reading or tracking moving objects. Furthermore, research has shown that ET patients may exhibit impaired smooth pursuit, characterized by jerky or fragmented tracking of moving stimuli [162, 189, 517]. Although ET is primarily known as a motor disorder, some individuals experience mild cognitive impairment, particularly in areas of executive function and visual processing. Eye-tracking tasks that measure response inhibition or attention-shifting can provide insights into these cognitive symptoms. For example, individuals with ET may show longer fixation durations or have difficulty shifting their gaze when required, indicating deficits in cognitive flexibility [209, 395, 437].

- **Key Eye-Tracking Focus:** Oculomotor control, subtle cognitive impairments.
- **Task Design:** (i) Use fixation tasks since tremor-related involuntary eye movements (micro-saccades or nystagmus) may become evident as patients struggle to maintain a steady gaze [189, 517]. (ii) Use smooth pursuit tasks since ET patients might experience difficulty in smoothly following a moving target due to tremor involvement in the oculomotor system, leading to an increase in corrective saccades [162, 189, 517]. (iii) Conduct reflexive and voluntary saccadic tasks since ET patients may exhibit normal saccadic function but might also display increased latency due to cognitive processing difficulties, which are sometimes associated with long-term ET [53, 162]. (iv) Implement dynamic visual acuity tasks to assess the patient's ability to focus on moving objects and help reveal oculomotor dysfunctions such as tremor-related issues with eye muscle control [162, 162, 250].
- **Considerations:** (i) ET is often confused with Parkinson's disease because of overlapping tremor symptoms. Eye-tracking may help differentiate the two by identifying distinct oculomotor patterns such as smooth pursuit impairments (more common in Parkinson's patients than in ET patients) [237, 295, 517, 529]. (ii) The severity of tremors can fluctuate, and eye-tracking metrics should be interpreted in light of the tremor's current state. Repeated measurements over time may be necessary to assess tremor variability [295, 395].
- **Metrics:** (i) Analysing the fixation stability regarding frequency and amplitude of corrective saccades can quantify tremor severity in the oculomotor system [189, 517]. (ii) Measure the smooth pursuit gain (reduced in ET patients, indicated by more corrective saccades) [162, 189, 517]. (iii) Measure the saccadic latency and accuracy to detect any subtle cognitive involvement or differentiate ET from similar disorders like Parkinson's disease [53, 162]. (iv) Check for the presence of small, involuntary microsaccades or nystagmus during fixation tasks to indicate tremor-related dysfunction in the eye muscles [72, 237, 332].

Dystonia: Dystonia involves sustained or repetitive muscle contractions that cause twisting and abnormal postures [456]. Dystonia primarily affects motor functions, but recent studies have explored how eye movements and gaze behaviours are impacted, particularly in focal dystonias, such as blepharospasm (affecting the eyes) [83, 100, 127, 218] and cervical dystonia (affecting the neck) [208, 420]. For example, individuals with blepharospasm often exhibit increased blink rates and longer blink durations, leading to interruptions in gaze fixation and disrupted visual input [83, 100, 127, 218]. Furthermore, individuals with cervical dystonia may experience difficulty in maintaining a steady gaze or performing smooth pursuit movements, as their abnormal head postures affect the alignment of the eyes and visual field [208, 420]. Eye-tracking can measure these deficits, including delayed saccades or increased saccadic latency, as patients struggle to maintain or shift their gaze in the intended direction due to muscle contractions in the neck [208, 298]. Gaze-based research is also valuable for studying sensorimotor integration deficits in dystonia. For example, studies [102, 208, 482] have found that dystonia patients may exhibit impaired anticipatory gaze movements, suggesting that the brain has difficulty integrating visual information with motor planning. This impairment in sensorimotor integration is particularly evident in tasks that require precise coordination of eye and hand movements, such as tracking a moving target or reaching for an object while maintaining visual fixation. Similarly, for task-specific dystonias, such as writer's cramp or musician's dystonia, where involuntary muscle contractions occur only during specific tasks, eye-tracking has been used to measure how visual attention and gaze stability are affected during the performance of these tasks [221, 297]. For instance, individuals with musician's dystonia may experience difficulties maintaining steady fixation on musical notes or sheet music, as their motor symptoms interfere with gaze control and visual processing during performance [288]. Finally, note that since dystonia primarily affects voluntary muscles, eye movements are not always as prominently impacted as in other movement disorders like Parkinson's disease or Huntington's disease [103].

- **Key Eye-Tracking Focus:** Oculomotor dysfunction (e.g. eye movement coordination, abnormal saccadic movements, and smooth pursuit), fixation stability, and blink rate.
- **Task Design:** (i) Design simple visual fixation tasks to detect issues with maintaining a steady gaze due to muscle spasms or involuntary contractions [208, 420]. (ii) Add smooth pursuit tasks to identify problems with tracking and oculomotor control [191, 237]. (iii) Measure reflexive and voluntary saccades to assess how well dystonia patients can initiate and control rapid eye movements [208, 298].
- **Considerations:** (i) In cases of cervical dystonia, head movements might interfere with gaze tracking. Special equipment like chin rests or head restraints can help isolate eye movements for more accurate measurement [38, 420]. (ii) Dystonia often leads to muscle fatigue, so task design should account for this by providing breaks to prevent discomfort and poor data quality [367].
- **Metrics:** (i) Measure saccadic latency, which may be delayed in dystonia patients [208, 298]. (ii) Measure the smooth pursuit gain, often diminished in dystonia [191, 208, 420]. (iii) Measure fixation duration since unstable or prolonged fixation durations are common in dystonia [208, 420]. (iv) Measure the blink frequency as either reduced or excessive blinking can signal dystonic eye dysfunction [103, 103, 364]. (v) Finally, tiny and involuntary eye movements (microsaccades) and tremors may be particularly relevant to detecting subtle forms of dystonia that affect the ocular muscles [191, 298].

4.4 Seizure Disorders

Epilepsy: Epilepsy is a disorder characterized by recurrent seizures, which are abnormal electrical activity in the brain [456]. The relationship between eye tracking and epilepsy can provide insights into the visual processing deficits, cognitive impairments, and oculomotor abnormalities that often accompany this disorder, especially in individuals with focal seizures originating in brain regions related to vision and attention, such as show delays in saccadic eye movements, difficulties with gaze fixation, and abnormal smooth pursuit [22, 204]. For instance, studies have found that people with epilepsy exhibit increased saccadic latency due to disruptions in neural networks responsible for coordinating eye movements as a biomarker for attention [176, 294, 473]. In addition to saccades, eye-tracking can also measure fixation stability and gaze shifts during epileptic events or interictal periods (the time between seizures) [164, 204, 207, 319]. Some individuals with epilepsy experience oculomotor seizures, where eye movements are directly affected by abnormal brain activity. This can include sustained upward gaze or sideward eye deviation [22, 472]. Additionally, during postictal states (after a seizure), individuals may show impaired gaze control or prolonged fixations, reflecting temporary deficits in cognitive processing and attention recovery [133, 215, 521]. Furthermore, people with epilepsy often show deficits in tasks requiring sustained visual attention or complex decision-making, and eye-tracking metrics like fixation duration and visual search patterns can provide insights into these cognitive challenges [207, 294, 349]. For example, individuals with epilepsy may exhibit longer fixation times or difficulty disengaging attention from irrelevant stimuli, indicating impairments in cognitive flexibility and attentional control. Furthermore, by tracking eye movements during visual field tests, researchers can assess how epilepsy impacts visual perception and the ability to scan the visual environment, especially for patients who report visual disturbances or difficulty navigating their surroundings [108, 132, 204, 269].

- **Key Eye-Tracking Focus:** Seizure-related eye movements, postictal gaze behaviour, photosensitivity, and gaze deviation.
- **Task Design:** (i) Design gaze-following tasks for detecting irregular saccades and smooth pursuit dysfunctions caused by seizures [176, 473]. (ii) Add stimulus-induced tasks to trigger epileptic episodes through visual stimuli (e.g.,

flickering lights) for patients with photosensitive epilepsy [108, 132]. (ii) Use visual attention tasks to measure visual distraction, fixations, and response times to stimuli caused by seizure-related brain changes [132, 204, 269]. (iii) Track pre- and post-seizure movements to map how the brain's control over eye movement fluctuates with seizure activity [133, 215].

- Considerations: (i) Experimental design should account for how frequent and long seizures last. Shorter tasks may be needed to avoid triggering discomfort or seizures during testing [472, 514]. (ii) In photosensitive epilepsy patients, careful consideration must be given to the intensity and type of visual stimuli to avoid inducing seizures [131, 184].
- Metrics: (i) Measure the saccadic accuracy since misfiring neurons during seizures can disrupt accurate eye movements [176, 294, 331]. (ii) Expect unsteady or prolonged fixations, particularly after seizures, indicating reduced control over gaze stability [204, 319]. (iii) Seizures, particularly photosensitive ones, may cause abnormal pupil dilation responses [8, 146]. (iv) Smooth pursuit gain helps identify coordination problems during seizure events [176, 473].

4.5 Cerebrovascular Disorders

Stroke: A sudden interruption in the blood supply to the brain, caused by a clot (ischemic stroke) or rupture of a blood vessel (hemorrhagic stroke), leading to brain damage. Strokes can lead to a wide range of neurological impairments depending on the location and severity of the brain damage, and visual dysfunction is one of the common consequences, as strokes frequently disrupt the neural pathways responsible for eye movements and visual processing [456]. Individuals who experience strokes often suffer from abnormal saccadic behaviour, including prolonged saccadic latency, decreased saccadic accuracy, and hypometric saccades [11, 186, 398, 404]. In addition, eye-tracking studies have shown that patients with stroke-related damage exhibit increased fixation instability and involuntary gaze shifts, which can impact their ability to process visual information effectively, especially for tasks that require sustained attention, such as reading or tracking moving objects [11, 12, 214, 404]. Another key focus of gaze-based stroke research is on visual neglect, a common post-stroke condition, especially after right-hemisphere strokes. Patients with hemispatial neglect may fail to perceive or respond to stimuli on one side of their visual field despite having normal vision [312, 462, 476]. In other words, stroke patients with neglect may exhibit asymmetrical scanning behaviour, where their gaze is heavily biased toward the non-neglected side. Furthermore, stroke survivors may exhibit difficulties with visual attention and executive function, such as a longer time to shift their gaze between visual targets, which is indicative of slowed cognitive processing and reduced flexibility in attentional control [11, 462]. Furthermore, patients may show fragmented pursuit or delays in initiation of smooth pursuit, particularly when the stroke affects areas of the brain involved in motion detection or motor control of the eyes [11, 12, 404].

- Key Eye-Tracking Focus: Visual field deficits, attention recovery, and oculomotor control post-injury.
- Task Design: (i) Use visual search tasks to evaluate spatial neglect or deficits in visual attention (e.g., finding targets on a screen) [11, 462, 476]. (ii) Include object tracking tasks to measure how well participants follow moving stimuli [11, 12, 404].
- Considerations: (i) Depending on the severity of the stroke or brain injury, participants may experience visual field loss or difficulty controlling eye movements, so tasks should be adjusted accordingly [274, 404]. (ii) Design tasks assessing visual and cognitive recovery over time [368].
- Metrics: (i) Track fixation stability, reaction times, and scan path efficiency (the ability to search and find relevant information in a visual field) [73, 213]. (ii) Measure visual field exploration to detect any neglect or inattention to one side of the visual field [312, 462, 476]. (iii) Measure saccadic patterns: short saccades often indicate limited

visual exploration or spatial neglect, while long saccades may suggest compensatory strategies or difficulty in motor control [11, 186, 398, 404]. (iv) Strokes can cause asymmetrical or abnormal pupil dilation responses. This can manifest as sluggish or incomplete dilation in response to light or other stimuli [244, 313]. (v) Microsaccade frequency and amplitude may be diminished. They may be irregular in direction and amplitude, reflecting disrupted motor coordination and impaired control over small, corrective eye movements [7, 151].

4.6 Mental Health Disorders with Neurological Components

Anxiety: Anxiety disorders, which include generalized anxiety disorder (GAD), social anxiety disorder, panic disorder, and specific phobias, often result in abnormal patterns of eye movements as individuals with anxiety tend to exhibit hypervigilance toward perceived threats [456]. People with anxiety disorders frequently display a tendency to fixate on negative or threatening cues in their environment, such as angry or fearful faces, dangerous objects, or even ambiguous stimuli [64, 77, 197, 264, 321, 478, 507]. Eye-tracking studies have shown that anxious individuals exhibit faster initial fixations and longer gaze durations on threatening stimuli than neutral or positive stimuli (i.e. threat hypervigilance), leading to an overestimation of threats in their environment. After an initial fixation on a threatening stimulus, many anxiety sufferers exhibit gaze avoidance, meaning they quickly divert their gaze away from the source of anxiety [76, 154, 507, 508]. This pattern reflects both a heightened awareness of potential threats and a strategy to reduce the discomfort associated with prolonged exposure to these stimuli. Moreover, eye-tracking studies indicate that individuals with anxiety tend to scan their environments differently, displaying more disorganized or scattered visual search patterns [117, 169, 284, 334]. This may be due to an inability to disengage from threatening stimuli or a heightened state of alertness that makes it difficult to focus on non-threatening aspects of their surroundings. Furthermore, high levels of anxiety are associated with impaired cognitive flexibility and difficulties in focusing attention. Eye-tracking technology has demonstrated that anxious individuals often have trouble shifting their attention away from negative stimuli, which can lead to rumination and repetitive negative thinking [66, 68, 169, 197, 310].

- **Key Eye-Tracking Focus:** Attentional bias toward threat, gaze avoidance, and hypervigilance.
- **Task Design:** (i) Use tasks with both threatening and neutral stimuli (e.g., images of faces showing fear versus neutral expressions) to assess gaze patterns in response to potential threats [169, 197]. (ii) Include emotional Stroop tasks where participants respond to emotional and neutral words or images to measure attentional biases [197, 478].
- **Considerations:** (i) Participants with anxiety may find certain stimuli (e.g., images of fearful or angry faces) distressing. Ensure tasks are well-balanced to avoid overwhelming participants [197, 400]. (ii) Desensitization or anxiety management strategies might be needed before or after tasks involving emotional stimuli [400].
- **Metrics:** (i) Measure first fixation latency (how quickly a participant looks at a threat-related stimulus) and total gaze time on threatening versus neutral stimuli, fixations usually have longer durations [76, 154, 246, 507, 508]. (ii) Gaze avoidance of threatening stimuli (such as quickly looking away from negative stimuli) is a key feature in social anxiety studies [76, 154, 507, 508]. (iii) Other visual search patterns can be assessed through metrics such as saccadic latency, fixation density, and gaze entropy [117, 169, 284, 334]. (iv) Anxiety often leads to a larger baseline pupil size, reflecting increased arousal or alertness [52, 430, 511]. (v) Anxiety is commonly associated with an elevated blink rate, potentially due to heightened arousal and stress, as well as dry eyes [252, 322]. (vi) Anxiety often leads to an increased frequency of microsaccades, as people with anxiety may have difficulty maintaining a steady gaze due to hypervigilance and scanning behaviours [235, 318]. (v) Finally, anxiety can interfere with smooth pursuit

accuracy, leading to a less steady or slightly fragmented tracking of moving objects, especially if the object or task is anxiety-provoking [239, 431].

Obsessive-Compulsive Disorder (OCD): A mental health condition characterized by intrusive thoughts (obsessions) and repetitive behaviours (compulsions), often driven by an overwhelming need to reduce anxiety [456]. Individuals with OCD tend to exhibit hypervigilance and increased attention toward stimuli that are relevant to their obsessions (e.g., contamination fears, symmetry concerns) [36, 219, 444]. Eye-tracking studies have demonstrated that individuals with OCD often show longer fixation durations and difficulty disengaging from stimuli that trigger obsessive thoughts [36, 82, 470]. For example, in tasks where participants are shown neutral versus contamination-related images, those with contamination fears may fixate longer on contaminated objects, indicating an attentional bias toward perceived threats [21, 464]. In addition, after an initial fixation on obsession-related stimuli, some OCD patients may quickly avert their gaze as part of an avoidance strategy, attempting to reduce anxiety associated with the visual stimuli [82, 130]. For example, individuals with OCD may exhibit gaze avoidance when viewing asymmetrical or disordered visual patterns. Eye-tracking can quantify these patterns by measuring the speed and frequency of gaze shifts away from anxiety-provoking stimuli, providing objective insights into the compulsive avoidance behaviours seen in OCD [141, 272]. Eye-tracking research has also been useful in examining the cognitive control deficits often seen in OCD, such as inhibitory control and cognitive flexibility [80]. Individuals with OCD may have difficulty shifting attention between tasks or stimuli, leading to perseverative gaze behaviours, where they continue to focus on a particular stimulus even when it is no longer relevant [36, 82, 89]. This can be particularly evident in visual search tasks, where individuals with OCD may exhibit slower response times and longer fixations on irrelevant or distracting stimuli, reflecting an inability to flexibly redirect attention [19, 286]. Furthermore, individuals with OCD often display rigid, repetitive search patterns, which may be linked to the compulsions to check or verify certain visual information repeatedly (e.g., ensuring objects are properly aligned or that an environment is clean) [36, 203, 489].

- Key Eye-Tracking Focus: Fixation patterns on obsessive stimuli, avoidance behaviours, and gaze dwelling and scanning patterns.
- Task Design: (i) Present obsessive stimuli tasks with stimuli related to common OCD obsessions (e.g., cleanliness, contamination, threatening faces) to show how attention is biased toward certain stimuli. Similarly, OCD patients may be sensitive to symmetry and order, and tasks that involve visual arrays of objects can measure whether their gaze patterns reveal heightened attention to imbalance or disarray [36, 82, 470]. (ii) Add decision-making tasks since OCD is linked with indecision and the need for reassurance. Require participants to make choices or verify the information to assess how these cognitive patterns influence gaze behaviour, such as excessive revisiting of options [36, 203, 489].
- Considerations: (i) The frequency and nature of compulsive checking behaviours, both in real life and within experimental tasks, need to be carefully monitored, as these can lead to repetitive gaze patterns or scanning behaviour that needs to be distinguished from normal cognitive processing [36, 82, 470].
- Metrics: (i) Measure fixation duration as OCD patients may have longer fixations on objects of obsession, signalling excessive focus or rumination [36, 59, 82]. (ii) Measure gaze dwell time: Total time spent focusing on distressing or obsession-related stimuli can provide a measure of the intensity of obsessive attention [20, 36]. (iii) OCD can delay saccadic movements between fixations as patients deliberate or hesitate in their gaze shifts due to obsessive thoughts [183, 308, 436]. (iv) Repeated scanning of the same object or scene, as seen in compulsive checking behaviours, can be quantified through metrics like revisit count and scanning patterns [47, 75, 479]. (v) OCD patients may show changes

in pupil dilation in response to obsession-related stimuli due to heightened arousal or stress, which can be measured with eye-tracking technology [372, 377, 384].

Summary: Based on the most common and agreed-upon methods and findings in the literature, these disorder-specific guidelines ensure that eye-tracking studies are tailored to the unique characteristics of each neurological condition, providing better data quality and more meaningful insights into the relationship between gaze behaviours and neurological dysfunction.

In Table 2, we summarized the key disorder-specific eye-tracking metrics discussed in Table 1. Note that (i) certain metrics vary significantly between individuals, especially in disorders like anxiety and OCD, where fixation and blink rates may be affected by personal triggers or stress levels, (ii) some disorders may have overlapping biomarker characteristics, so multiple metrics are often used together to improve diagnostic precision, and (iii) in disorders like autism and ADHD, social context or task requirements may alter certain eye-tracking metrics (e.g., fixation duration in social vs. non-social contexts). Therefore, here, we present the primary eye-tracking biomarkers and highlight how each metric may differ by neurological condition for preliminary diagnosis. However, these metrics need to be further tailored depending on specific diagnostic needs or research goals.

Disorder	Fixations	Saccades	Pupil Dilation	Blink Rate	Microsaccades	Smooth pursuit
ASD	Abnormal durations, fewer on social cues	Erratic amplitude, atypical patterns	Altered dilation to social cues	Abnormal in social situations	-	Difficulty tracking faces/social stimuli
ADHD	Shorter duration, impulsive shifting	Increased frequency, reduced inhibition	Hypo- or hyper-reactivity	High, associated with impulsivity	Reduced inhibition	Reduced tracking accuracy
Dyslexia	Extended duration on text	Slower initiation	-	-	-	-
CP	Reduced stability, tremor in fixations	Limited range, slow initiation	-	-	-	Difficulty following smooth targets
AD	Increased duration, fewer fixations	Prolonged latency, reduced amplitude	Reduced response to stimuli	Decreased blink rate	Oblique behaviour	Reduced tracking ability
PD	Shorter duration, tremor presence	Increased latency, reduced peak velocity	Decreased reactivity	Reduced blink rate	Reduced frequency, increased latency	Saccadic intrusions, jerky tracking
ALS	Irregular duration, difficulty maintaining	Slowed initiation, irregular amplitude	Normal but can vary	-	Reduced frequency and amplitude	Reduced tracking, effortful movements
HD	Increased fixation duration	Prolonged latency, jerky movements	-	-	Erratic, often exaggerated	Poor tracking, saccadic intrusions
MS	Unstable fixations	Delayed initiation, limited range	Slower reactivity	-	Altered frequency, instability	Reduced accuracy and steadiness
TS	Brief fixations, affected by tics	Normal but may be influenced by tics	-	Increased, associated with tics	Increased during tics	-
ET	Stable but can show slight tremor	Normal latency, occasional tremors	-	-	Normal, some tremor effects	Mild issues with smoothness

Dystonia	Longer duration	Increased latency, restricted range	Reduced or excessive blinking	-		Irregular frequency and amplitude	Low smooth pursuit gain
Epilepsy	Unsteady and prolonged	Inaccurate	Abnormal during seizures	-		Normal but can show suppression	Fluctuations during seizures
Stroke	Longer duration, less stable	Irregular	Reduced response	-		Reduced frequency and amplitude	Reduced smooth pursuit accuracy
Anxiety	Longer duration, fixation on threats	Slower, smaller amplitude	Overreactivity to stimuli	Increased, especially in social anxiety		Increased during anxiety-provoking stimuli	Altered, may show instability
OCD	Increased duration on specific areas	Delayed	-	Reduced blink rate		Repeated, erratic around specific areas	-

Table 2. Summary of Section 4 of the primary eye-tracking metrics for specific disorders, A '-' indicates that the corresponding metric is not a biomarker for the disorder (i.e. unaffected).

5 Conclusion

Taking the guidelines outlined in the paper into account, conducting research on neural disorders using eye tracking requires a careful balance of ethical considerations and appropriate experimental design, ensuring that the tasks, environment, and data collection methods are adapted to the capabilities and needs of individuals with neural conditions is key to obtaining reliable and useful insights.

Limitations: However, several limitations exist: Gaze-based neural diagnosis is still in its infancy, and further research is needed to refine these methods and explore how they can be integrated into clinical practice. While eye-tracking provides a wealth of data, interpreting gaze patterns in the context of specific neural disorders can be complex. For example, a specific gaze pattern (e.g., reduced fixation on faces) might be seen in several disorders like ASD, anxiety, or even depression, making it challenging to isolate a single diagnosis based on gaze alone. In addition, gaze behaviour varies significantly among individuals, even within the same diagnostic group. Some individuals with ASD, for example, might show typical eye movements, while others may show marked differences. This variability can make it difficult to develop standardized benchmarks that apply universally across all individuals within a disorder group. Furthermore, technical issues such as calibration errors, sensitivity to head movements, and lighting conditions can also affect data quality, especially when working with individuals with motor impairments (e.g., Parkinson's or ALS). Moreover, eye-tracking results are often context-dependent, meaning that results can vary based on the task, environment, or stimuli presented.

Current State: While gaze tracking can provide valuable insights into cognitive and attentional processes, it is currently insufficient for a standalone diagnosis. In its current status, it often needs to be used alongside other diagnostic tools (e.g., neuroimaging and neuropsychological assessments) to get a complete understanding of the disorder. Finally, eye-tracking primarily highlights symptoms rather than root causes, making it a valuable tool for preliminary assessment but not a definitive diagnostic method.

Therefore, in this paper, we provide the first guidelines for gaze-based neural diagnosis based on careful evaluation, comparison, and structuring of consensus-based methods and findings in the literature. We aim that our paper enables more structured eye tracking studies that can be used in clinical setups and can ultimately advance the preliminary diagnosis of neural disorders.

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