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## Eye tracking techniques and medical applications: A comprehensive review

Souhad A. Lawand \*

*Pavlov St-petersburg state Medical University, Russia.*

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### Abstract

Eye tracking is a powerful tool that has been widely used to study human behavior and cognition. This article provides a comprehensive review of eye tracking techniques, their efficiencies in accurately evaluating eye movements, and their medical applications. The article discusses different eye tracking techniques, including video-based electrooculography (EOG), and scleral search coil methods, and their advantages and limitations. It also reviews the medical conditions that can be evaluated with eye tracking, including ophthalmological and neurological disorders.

**Keywords:** Eye Tracking; Medical Applications; Neurological Disorders; Ophthalmology

### 1. Introduction

Eye tracking has been used for over a century to study human behavior and cognition. Advances in technology have led to the development of various eye tracking techniques that can provide accurate and precise measurements of eye movements. Eye tracking has been applied to numerous fields, including psychology, neuroscience, marketing, and human-computer interaction. In medical applications, eye tracking has been used to evaluate ophthalmological and neurological disorders.

#### 1.1. Eye Tracking Techniques

Different eye tracking techniques have been developed to measure eye movements. These include video-based electrooculography (EOG), and scleral search coil methods.

Video-based eye trackers use cameras to record the movement of the eyes. This technique is non-invasive and can provide high spatial and temporal resolution measurements of eye movements. However, video-based eye trackers can be affected by head movements and lighting conditions.

EOG measures the electrical potential generated by the movement of the eyes. This technique is highly accurate and can provide measurements of eye movements even in complete darkness. However, EOG requires the placement of electrodes around the eyes, which can be uncomfortable and may affect natural eye movements.

Scleral search coil eye trackers involve implanting a small magnetic coil on the sclera of the eye and using a magnetic field to track the movement of the eye. This technique is highly accurate and can provide measurements of eye movements with high temporal resolution. However, scleral search coil eye trackers are invasive and can be uncomfortable for the patient.

\* Corresponding author: Lawand SA

## 1.2. Medical Applications of Eye Tracking

Eye tracking has been applied to various medical conditions, including ophthalmological and neurological disorders.

In ophthalmology, eye tracking can be used to evaluate visual function, such as visual acuity, contrast sensitivity, and eye movements. Eye tracking can also be used to evaluate eye diseases such as glaucoma and age-related macular degeneration.

In neurology, eye tracking can be used to evaluate the effects of brain injury, stroke, and neurodegenerative diseases on eye movements. Eye tracking can also be used to diagnose and monitor neurological conditions such as Parkinson's disease, multiple sclerosis, and Alzheimer's disease.

Eye tracking has also been used to evaluate developmental disorders such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD). Eye tracking can provide valuable insights into the visual attention and social cognition deficits associated with these disorders.

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## 2. Evolution of eye movement measurement techniques

The first attempts to objectively and automatically track eye motion date back to the late 19th century. Mowrer, Ruch, and Miller<sup>3</sup> found that the position of the eye could be measured by placing skin electrodes around the eye and recording potential differences. The source of the electrical energy is the cornea-retinal potential or electrostatic field which rotates with respect to the eye. The cornea remains 0.4 to 1.0 mV positive with respect to the retina; this is attributable to the higher metabolic rate at the retina. As the eye rotates, the electrostatic dipole rotates with it, and consequently, the potential difference in a plane normal to the principal axis varies, theoretically, as the sine of the angle of deviation. Of course, the nonhomogeneous nature of the conducting medium causes a wide departure from the theoretical values.

In the 1960s, the dc recording method, which was necessary to determine eye position was referred to as electro-oculography (EOG); ac recording, which is useful for the measurement of eye movement, including the fast and slow phases of nystagmus, was referred to as electronystagmography (ENG). The problem of drift in both electrodes and dc amplifiers made dc recording a difficult and frustrating practice. Gross patterns of reading movements (number of saccades per line; the number of regressions and fixation durations) were easily obtainable from ac recording with time constants of 3 to 10 sec or more. With longer time constants, even the approximate position on a line was determinable. When both vertical and horizontal recording from one or both eyes is performed, the errors introduced by coupling between the axes and by the nonlinearity of the records were considerable.

In 1964, some improvements in the cross-coupling results were from the use of "vector electro-oculography" introduced by Uenoyama and Iinuma<sup>6</sup>. In addition to simultaneously displaying the x and y coordinates of eye movements, they electrically short-circuit the two superior electrodes and the two inferior electrodes for the vertical eye movement recording.

In the 1970s, dc recording had been made much more practical with two electronic advances. New skin electrodes, especially silver-silver chloride became easily applied with adhesive tape rings, required no skin preparation other than cleaning with alcohol or acetone, are of minimal discomfort, and resist excessive polarization over many minutes of use. They also became relatively less sensitive to changes in skin resistance when led into any of the newer high-input impedance (FET) preamplifiers. Placement of a high common mode rejection preamplifier very close to the subject's head, proper grounding of the subject through an ear electrode, and use of shielded cable helped eliminate the disturbance from the electromagnetic pickup. Cornsweet and Crane separated eye rotations from translations using the multiple reflections of the eye (known as Purkinje images) and developed a very accurate eye tracker based on this technique<sup>7</sup>.

By that time, other methods of eye movement detection were also being developed. One of those techniques was based on the **corneal reflection principle**. The corneal bulge produces a virtual image of bright lights in the visual field and region. Because the radius of curvature of the cornea is less than that of the eye, the corneal reflex moves in the direction of eye movement, relative to the head. Since it only moves about half as far as the eye, it is displaced opposite to the eye movement relative to the optic axis, or the center of the pupil. Incident light from a source is reflected from the convex surface of the cornea in a pattern of diverging light and is imaged through a concave lens onto a film plate, television camera element, or photocells. The largest advance, however, was the mounting of the camera separately and carrying the visual information, including corneal reflex, and the field of view from the head to the TV or motion picture camera via coherent fiber optics cables.

In 1971, A TV camera with an image dissector was applied by Ishkawa et al. to precisely track the corneal reflex <sup>8</sup>. The main horizontal sweep is a normal full-picture left-to-right scan, which was used for the approximate location of the bright reflex, whereas every second sweep is a short (high-resolution) line centered in the part of the field containing the reflex. This combination scan of coarse slow and fine rapid sweeps was used to track vertical and horizontal eye movements over the range of  $\pm 15$  deg with a resolution of .01 deg and frequency up to 15 KHz.

However, the uncorrected linear range of all corneal reflex systems that employed a single light source for the reflex was limited to eye excursions of  $\pm 12$ -15 deg vertical or horizontal. Larger excursions placed the reflex in the nonspherical and rougher peripheral portion of the cornea and required a complex (usually computer-generated) calibration and linearization technique. The reflex range is ultimately limited by the size of the cornea and its partial disappearance behind the lids. In addition to head movements, other factors which limit the accuracy of corneal reflection methods to 0.5-1 deg are variations in cornea shape, the thickness of tear fluid, corneal astigmatism, and the production of other reflections by eyeglasses, if required for the test.

Another technique that was researched was Limbus, Pupil, and Eyelid tracking basic techniques. The sharp boundary between the iris and the sclera, called the limbus, is an easily identifiable edge that can be detected optically and tracked by a variety of means; a human observer looking at the eye can do surprisingly well in determining where the subject is looking. If the entire iris were always visible and not partially hidden by the lids, it would be a simple matter to trace its circumference and determine its center. However, because only part of the iris is normally visible, other optical methods, including pupil tracking, are necessary to find its center. When only horizontal eye movements are of concern, then the left and right extremes of the iris can be tracked, either by measuring the gross difference in reflected illumination from fixed areas of the eye on either side of the central gaze position or by tracking the limbus with a video scan system. When a vertical measurement is also required, one may track either the eyelid level, the pupil position, or the vertical motion of a visible part of the limbus. Nearly all limbus tracking systems use invisible, usually infrared, illumination. They all measure the position of the limbus relative to the photodetectors. For head-fixed photodetectors and illuminators, free head movement is possible and the measurement is of the eye relative to the head. The pupil offers a number of distinct advantages over the limbus. First, it is smaller and therefore unobscured by the eyelid for a much greater range of eye motion. For large eye motion, it presents to the observer or the observing instrument a greater portion of the round or slightly elliptical shape. The center of the pupil virtually coincides with the foveal optical axis of the eye. There is a 5-6-deg deviation between the two, but with most measurement techniques, this can generally be calibrated out. The edge of the pupil is usually a crisper, sharper boundary than that between the sclera and the iris. This makes for a higher-resolution measurement. On the other hand, the pupil, when viewed under normal illumination, appears black and therefore presents a lower contrast with its surrounding iris than the iris does with respect to the sclera. This makes it a more difficult problem to automatically discriminate the pupil. If collimated illumination is used, however, the light is reflected from the interior of the eye, and to an observer looking along the illumination axis, the pupil appears bright. This effect is often seen as "red eyes" in flash photographs where the flash lamp is close to the camera lens. Another characteristic of the pupil which provides both an advantage and a disadvantage is the fact that its diameter varies as a result of both psychological and physiological influences. This makes measuring the center of the pupil somewhat more difficult but it does provide, in many techniques, the pupil diameter as a collateral output of the measurement which may be of interest to the experimenter in correlating with the position of the eye at any point in time.

The interference of any changes in ambient illumination was overcome in most systems by illuminating the eye with chopped light and then demodulating at the same frequency. Chopper wheels in the light path are useful in immobile systems, but infrared light-emitting diodes (GaAs) are small and preferable for monitors that are built on spectacle frames to allow free head movement<sup>9</sup>. In 1974, Findlay<sup>10</sup> used a bifurcated fiber optic bundle to both illuminate the limbus and collect the reflected light.

Many implementations of these techniques yielded good results with good accuracies for a reasonable range. The output was an electrical record that can have a good frequency response. As noted, however, vertical eye movements remained a problem. The technique also required head fixing or a head-mounted device. The latter can be quite light but precludes eyeglasses. Iris coloration can also be a factor in its utilization.

Another technique was Contact Lens Method basic techniques. The most precise measurements of eye movement are made with one of the techniques employing some device tightly attached to the eye with a contact lens <sup>4,11, 12</sup>. Conventional corneal lenses are too mobile to be of use, and all measurement systems use special lenses consisting of two individually ground spherical surfaces to fit snugly over the cornea and sclera. For accurate recording, it was essential for the lens to move with the eye—both in steady displacement and during the high acceleration associated with voluntary saccades. Tight fit and lack of slip are achieved by close grinding tolerances and by the suction effect of 20

mm Hg, or more negative pressure, between the contact lens and the eye. In 1964, Fender D.H.<sup>13</sup> pointed out one way of developing the negative pressure by filling the cavity with a 2 % sodium bicarbonate solution which osmoses out through the tissue. Yabus A.L.<sup>4</sup> achieved the accurate tracking required for image stabilization work by withdrawing a small amount of fluid through a valve after applying the lens. Withdrawing air from under the contact lens was also effective for stabilization but for limited-time use because of the lack of corneal irrigation. All of the contact lens systems caused discomfort, and the very tight ones usually required the application of a topical anesthetic.

Although the contact lens systems offered the best resolution of any system down to 5-10 arc/sec, they did so in general at the sacrifice of range. They were normally applicable for the study of miniature eye movements and, with the exception of the magnetic search coil method, are inappropriate for movements of greater than 5 deg. The expense and discomfort of the contact lens made it a technique more suitable for use on a few subjects for physiological studies of fixation than for widespread investigation on the normal population. The dangers of fitting a contact lens with a negative pressure were also considered alongside the possibility of deforming the cornea, and the worse hazard of damaging the accommodation muscles as a result of the pressure stress placed upon them.

During the 80s, eye tracking had been implemented in many diagnostic devices but was mainly used to automatically maintain the optical axis of the main detecting device, such as an infrared optometer<sup>14</sup>, coincident with the visual axis of the human eye. The maximum trackable eye movement velocity in some devices was over 100 deg/s, with a time delay of about 0.13 s. Nonetheless, research on eye movements and their correlation with different disorders continued to be a popular topic and required different devices that use different techniques of eye tracking to be available. Most of these devices used high-resolution infrared (IR) oculography with digital recording and analysis techniques<sup>15</sup>.

By the beginning of the 90s, and with the emergence of laser photorefractive keratectomy units and diagnostic optical coherence tomography (OCT) devices, different technologies developed active eye-tracking systems capable of following saccadic movements and providing safety and precision during a procedure or examination. Different studies researched abnormal eye movements correlating with different disorders, both ocular and neurological, with the help of different types of eye trackers that use different techniques in eye movement evaluation. Due to the precision of search-coil eye-tracking techniques, and thanks to advancements in scleral coils (SC) and multiple Purkinje image eye trackers<sup>17</sup>, saccadic eye movements were being evaluated with a higher accuracy rate. However, some IR trackers allowed eye movement recordings at different sampling rates ranging from 250 Hz to 1000 Hz while the SC recorded at 1000 Hz, and that allowed the researchers to conclude that IR and SC trackers were in good agreement and produced similar results.

By the end of the decade, MR - eye tracker was introduced as a new method for eye movement recording in functional magnetic resonance imaging method for recording saccadic and pursuit eye movements in the magnetic resonance tomograph designed for visual functional magnetic resonance imaging (fMRI) experiments<sup>16</sup>, and at the same time, human cortical areas activated in relation to vergence eye movements were determined using positron emission tomography and an infrared limbus tracker.

At the beginning of the year 2000, wearable, lightweight, portable, wireless, and real-time streaming eye gaze trackers and interactive computer-based applications became increasingly available on the market. The use of eye trackers had extended to other areas besides healthcare and research, and they were integrated into devices for other professions, where eye tracking holds value for performance.

Different types of research and medical apparatuses came equipped with either 3-axis, or 1 kHz infrared, self-calibrating eye recorders, or other types of novel eye trackers. Some were already based on programmable CMOS image sensors<sup>18</sup>, interfaced directly to digital processing circuitry to permit real-time image acquisition and processing. That enabled researchers and healthcare providers to evaluate eye movements in a more precise manner, even at a low-frequency sampling rate of 50 Hz<sup>26</sup>.

Although visual axis alignment in laser surgeries and diagnostic tests remained to be the main area of use of eye trackers in ophthalmology, extensive research on eye movement and human behavior was conducted during this decade. A lot of research was conducted on the pediatric and even infant population in the form of investigations on developmental eye movements<sup>27</sup>, fixation and gaze disparities<sup>22</sup>, heterophoria<sup>58</sup>, and phoria quantification<sup>29</sup>, eye movements in static and dynamic activities, and saccadic eye movements in different psychological and neurological disorders<sup>25</sup>, smooth pursuit behaviors in patients with congenital malformations, such as Chiari type II<sup>21</sup>. Changes in saccades were also investigated in rare types of neurological disorders such as Rett syndrome<sup>20</sup>, Lewy body dementia<sup>29</sup>, and Niemann-Pick disease type C<sup>19</sup>.

The advanced technology and eye tracking techniques provided more detailed information on different types of saccadic eye movements previously undetectable with the naked eye, such as saccadic lens wobble artifacts and square wave jerks during fixation<sup>23</sup>. Pharmaceutical companies included eye movement tracking to evaluate the effectiveness of certain drugs in different diseases such as Parkinson's<sup>25</sup>. By the end of the decade, automated static perimetry using eye tracking was recognized as a promising method of perimetry for use with children<sup>26</sup>.

The next decade witnessed a boom in research associated with eye tracking. Advancements in technology such as holographic waveguides and artificial neural networks<sup>31</sup>, gave way to an array of novel eye trackers that used enhanced and new techniques in both eye tracking and data analysis, hence increasing eye tracker accuracy to unprecedented levels. Head-mounted video-based self-calibrating eye trackers with different tracking modes: limbal, pupil, corneal reflection, glint, and combined; 500 - 1000 Hz binocular eye-tracking, 0.5° average accuracy, and 0.01° resolution, as well as access to eye position data with 3.0 msec delay, were all features that such devices could have. Previous tracking techniques also underwent modifications and enhancements. A video-based eye-tracking methodology that can reliably detect small eye movements over 0.2 degrees (12 arc mins) with very high confidence tracked the motion of iris features to estimate velocity rather than position, yielding a better record of microsaccades, was described<sup>33</sup>. Some research results suggested that contemporary video tracking now approaches the search coil<sup>24</sup> for measuring fixational eye movements (FEMs)<sup>32</sup> but regardless of that, newer scleral contact lenses with encapsulated photodetectors for eye tracking were being proposed<sup>34</sup>.

With the development of high-end laser devices, including diagnostic scanning laser ophthalmoscopes, another eye-tracking technique was introduced<sup>35</sup>. retinal tracking systems used a co-confocal reflectometer with a closed-loop optical servo system to lock onto features in the fundus and achieve a bandwidth of greater than 1 kHz, which permits tracking at rates that greatly exceed the maximum rate of motion of the human eye.

Additionally, the progress witnessed in sensors, computer coding, algorithms, and data analysis, lead to revolutionary findings. Magnetic Angular Rate Gravity (MARG) sensors for head orientation estimation<sup>48</sup>, Hartmann-Shack (HS) sensor<sup>36</sup>, virtual reality environments, Convolutional Sparse Coding (CSC)<sup>40</sup>, two-means clustering (I2MC)<sup>44</sup>, Machine Learning-Based Analysis<sup>45</sup>, open source software<sup>49</sup>, MATLAB<sup>47</sup>, and Python-based solutions all contributed to the accuracy of eye tracking.

By this time, eye tracking was integrated into many non-ophthalmic devices such as Electroencephalograms (EEG)<sup>42</sup>, and functional MRI (fMRI)<sup>16</sup> and even reported in anesthesia<sup>70</sup>.

In ophthalmology, eye movement perimetry, including saccadic reaction time-based, could now be conducted binocularly and with the assistance of head-mounted devices, some of which used near-eye displays. Others introduced static threshold perimetry tests based on eye movement<sup>60</sup>, a threshold saccadic vector optokinetic perimetry<sup>26</sup>, an automated visual acuity test (AVAT) for infants with remote eye tracking<sup>91</sup>, a smartphone-based and tablet-based Glaucoma application<sup>97</sup>, and patients' acceptance in virtual reality (VR) headsets during perimetry<sup>74</sup>, was also appreciated.

Phorias<sup>58</sup>, tropias, fusional vergence<sup>86</sup>, strabismus<sup>83</sup>, amblyopia<sup>94</sup>, and refraction-related eye movement disorders were all researched with more accurate methods based on novel eye-tracking techniques<sup>125</sup>, e.g. chromatic pupillometry was suggested to investigate how melanopsin-mediated intrinsically photosensitive retinal ganglion cell (ipRGC) signals are integrated binocularly<sup>66</sup>, similarly, rod, cone, and melanopsin contributions to human pupil flicker were also researched<sup>73</sup>.

More research was being done on patients with retinal disorders such as age-related macular degeneration<sup>50</sup>, diabetic retinopathy<sup>56</sup>, and geographic atrophy<sup>75</sup>, Stargardt disease<sup>105</sup>. Additionally, pupillary light responses and their correlation with glaucoma were intensively investigated, and were found to be valuable in Leber's hereditary optic neuropathy<sup>78</sup>, and even for the functional evaluation of retinal implants, such as Argus II<sup>79</sup> and a 44-Channel Suprachoroidal Retinal Prosthesis<sup>101</sup>. Moreover, eye movement tracking was used for the noninvasive evaluation of artificial eye motility<sup>92</sup>. Finally, an optical eye tracking system for noninvasive and automatic monitoring of eye position and movements in radiotherapy treatments of ocular tumors was proposed<sup>57</sup>.

The appreciation of different types of saccades in different life tasks amongst different age categories, whether static or in motion, became widely researched for different objectives. Thanks to the enhanced visualization and pupillometric capabilities of eye trackers, attention was also given to pupil reactions in day-to-day life tasks or different health disorders, an example of which was pupil oscillations assessment in the detection of patients with unilateral optic neuritis<sup>68</sup>. Studies related pupillary changes in response to cognitive processing to activity in the locus coeruleus (LC)

<sup>80</sup>, which is the main hub of the brain's noradrenergic system and is thought to modulate the operations of the brain's attentional systems.

Research in both therapeutics and diagnostics tackled psychological conditions such as schizophrenia <sup>110</sup>, attention deficit disorders (ADHD) <sup>113</sup>, bipolar disorder <sup>86</sup>, and anxiety <sup>53</sup>, alongside developmental disabilities such as autism and Asperger's syndrome <sup>85</sup>, developmental dyslexia (DD) <sup>90</sup>, Down syndrome <sup>65</sup>, Fetal alcohol spectrum disorder (FASD) <sup>114</sup>, hemiplegic cerebral palsy <sup>104</sup>, and finally neurological, like amyotrophic lateral sclerosis (ALS) <sup>115</sup>, multiple sclerosis (MS) <sup>71</sup>, essential tremor (ET) <sup>96</sup>, progressive supranuclear palsy (PSP) <sup>98</sup>, and concussions <sup>87,121</sup> were conducted with the help of different eye trackers. At the same time, research on Parkinson's disease <sup>124</sup>, multiple system atrophy (MSA) <sup>99</sup>, Alzheimer's <sup>84,118,123</sup>, Gaucher disease <sup>88,131</sup>, Huntington disease <sup>100</sup>, Machado-Joseph disease (MJD) <sup>102</sup>, and other neurodegenerative diseases with the help of eye trackers continued to evolve. Neuropsychiatric disorders such as Gilles de la Tourette syndrome (GTS) <sup>69</sup> were also being researched with the help of fMRIs and eye tracking <sup>32</sup>.

By the end of 2019, more than 1000 research articles were published on topics related to eye tracking, and mobile eye tracking was now applied in vision science, educational science, developmental psychology, marketing research (using virtual and real supermarkets), clinical psychology, usability, architecture, medicine, and more. Mobile gaze-tracking systems with near-eye displays based on gaze-tracking algorithms were presented as prototypes <sup>54</sup> and pupillary responses were researched as a potential biomarker for cardiovascular risk <sup>106</sup>.

With the beginning of 2020, and regardless of the extreme conditions humanity has been put in with the beginning of that year, due to rapid methodological and technological advances as well as the development of cost-efficient and portable eye trackers, e.g. a laser emitting contact lens for eye tracking <sup>132</sup>, different researches compared the available techniques and methods in order to establish some kind of standards in both data capture and analysis.

Researchers in ophthalmology and neurology addressed topics such as the comparison of image-based quantification methods in evaluating fixation stability using a remote eye tracker in abnormal Phoria <sup>107</sup>, Amblyopia <sup>108</sup>, and Myopia <sup>128</sup>. Other investigations described the extraction of Nystagmus patterns from eye-tracker data with CSC <sup>40</sup>, and the use of pupillometric recordings and Saccadic eye movements in Glaucoma diagnostics <sup>76,125, 127</sup>.

Different diagnostic tests based on eye tracking were being proposed, amongst them: functional colour vision <sup>112</sup>, phoria measurement <sup>117</sup>, magnetic resonance (MR)-based Eye Tracking <sup>126</sup>, automated computer-based memory assessment <sup>133</sup>, and automated visual acuity test (AVAT) for infants <sup>91</sup>.

Taking into consideration that eye-movement behavior has been accepted as a reliable tool to identify cognitive and behavioral patterns in individuals with different neuropsychiatric disorders, researchers continue to implement eye tracking in investigating saccades and antisaccades of patients suffering from Alzheimer's disease <sup>123</sup>, Ataxia <sup>122</sup>, behavioral variant frontotemporal Dementia (bvFTD) <sup>123</sup>.

Eye movement alterations were proposed as potential clinical biomarkers for concussion in children <sup>119</sup>, for the definition of phenotypes in Gaucher Disease <sup>131</sup>, reflexive and volitional saccadic eye movements for the distinction of progressive supranuclear palsy (PSP) from Parkinson's Disease (PD) <sup>98</sup>, whereas altered saccadic inhibition was suggested as a marker of corticostriatal function in Cervical Dystonia <sup>130</sup>, smooth pursuit dysfunction in multiple sclerosis and traumatic brain injuries <sup>134,136</sup>, and saccadic eye movement in Genetic Generalized Epilepsy (GGE) <sup>137</sup>. Even COVID-19 patients' eye movements were tracked for alterations <sup>111</sup>.

The concept of psycho-ophthalmology has become more and more constant, especially after establishing that smooth pursuit eye movements are one of the most evaluated eye-tracking tasks in schizophrenia (SZ) and bipolar disorder (BD) <sup>110</sup>.

When it came to ADHD <sup>113</sup>, clinical decision-making was being enhanced when combining psychophysiological sensors with computerized neuropsychological tests, or integrating an eye tracker with conventional CPT indices, but so was the clinical evaluation of prolonged disorders of consciousness more effective when supported with eye tracking <sup>138</sup>. Additionally, eye tracking was also being integrated into cognitive rehabilitation for different disorders including Rett Syndrome (RTT) <sup>20,114</sup>.

Eye tracking was also being used in medicine as an educational training tool for the assessment and verification of students and professionals. Certain research analyzed the possibility of using eye-tracking tools to verify the skills and

training of people engaged in laboratory medicine <sup>119</sup>, and others examined performance differences between expert and novice neurosurgeons under a surgical microscope with the goal of evaluating surgical expertise <sup>120</sup>.

In conclusion, there is no dispute that eye-tracking has reached a certain level of clinical significance and will continue to develop, and it would only be fair in our age to present what chatGPT had to say about eye tracking in general:

- Eye tracking provides objective data: Unlike subjective tests, such as self-reported symptoms or surveys, eye tracking provides objective data about a patient's eye movements, gaze patterns, and other visual behavior. This data can help clinicians make more informed decisions about a patient's diagnosis and treatment.
- Eye tracking can aid in the diagnosis of neurological and cognitive disorders: Eye tracking can help detect early signs of neurological and cognitive disorders, such as Alzheimer's disease and Parkinson's disease. By analyzing eye movements and gaze patterns, clinicians can identify changes in visual attention and cognitive processing that may be indicative of these conditions.
- Eye tracking can improve surgical outcomes: Eye tracking technology can be used during surgery to ensure that the surgeon is operating in the correct location and avoiding critical structures. This can lead to improved surgical outcomes and reduced complications.
- Eye tracking can be used in sports medicine: Eye tracking can help athletes and coaches identify weaknesses in visual attention and focus, which can impact performance. By analyzing eye movements during sports activities, clinicians can develop targeted training programs to improve visual skills.
- Eye tracking can aid in the diagnosis and treatment of eye disorders: Eye tracking can help diagnose and monitor a wide range of eye disorders, including amblyopia, strabismus, and nystagmus. By analyzing eye movements and gaze patterns, clinicians can develop targeted treatments to improve vision and prevent further deterioration.

Overall, eye tracking has become an important tool in all aspects of human medicine, and it can provide valuable information to support clinical decision-making.

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### 3. Conclusion

Eye tracking is a powerful tool that can provide accurate and precise measurements of eye movements. Different eye tracking techniques have been developed to suit different applications, and each technique has its advantages and limitations. Eye tracking has numerous medical applications, particularly in ophthalmology and neurology. Eye tracking can provide valuable insights into the mechanisms underlying various medical conditions and can be used to diagnose and monitor these conditions. Further research is needed to fully explore the potential of eye tracking in medical applications.

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### Compliance with ethical standards

#### *Disclosure of conflict of interest*

I have no conflict of interest to report.

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### References

- [1] Mackworth JF and Mackworth NH. Eye fixations recorded on changing visual scenes by the television eye-marker. *J Opt Soc Am* 1958; 48: 439–445.
- [2] Mackworth NH and Thomas EL. Head-mounted eye marker camera. *J Opt Soc Am* 1962; 52: 713–716.
- [3] Mowrer OH, Ruch TC, Miller NE : The corneoretinal potential differences as the basis of the galvanometric method of recording eye movements. *Am J Physiol* 114 : 423-428, 1936
- [4] Yarbus A.L. Eye movements and vision. *Neuropsychologia* 1967; 6: 222.
- [5] Robinson DA. A method of measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans Biomed Eng* 1963; 10: 137–145.
- [6] Uenoyama K. et al. Vector-Electro-Oculography and its clinical application. *Brit. J. Ophthal.* (1964) 48, 318.
- [7] Cornsweet TN, Crane HD. Accurate two-dimensional eye tracker using first and fourth Purkinje images. *J Opt Soc Am.* 1973 Aug;63(8):921-8. doi: 10.1364/josa.63.000921. PMID: 4722578.

- [8] Ishikawa, S., Yamakazi, A., Inabi, K., & Naito, M, A new instrument for registering eye movement (X-Y Tracker). *Acta Soc. OphthalmologyJap.*. 1971, 75,1110-1117
- [9] Young, L.R., Sheena, D. Survey of eye movement recording methods. *Behavior Research Methods & Instrumentation* 7, 397–429 (1975). <https://doi.org/10.3758/BF03201553>
- [10] Findlay, J. M. A simple apparatus for recording microsaccades during visual fixation. *Quarterly Journal of Experimental Psychology*, 1974,26.167-170.
- [11] Ditchburn, R. W., & Ginsborg, B. L. Involuntary eye movements during fixation. *Journal of Physiology*, 1953, 119, 1.
- [12] Riggs L A., Ratliff. R., Cornsweet J. C., Cornsweet T. N. The disappearance of steadily fixated test objects. *Journal of the Optical Society or America*. 1953. 43, 495.
- [13] Fender D. H. Contact lens stability. *Biomedical Science and Instrumentation*, 1964, 2. 43-52.
- [14] Okuyama F, Tokoro T, Fujieda M. Eye-tracking infra-red optometer. *Ophthalmic Physiol Opt*. 1990 Jul;10(3):291-9. PMID: 2216479.
- [15] Ross DE, Ochs AL, Hill MR, Goldberg SC, Pandurangi AK, Winfrey CJ. Erratic eye tracking in schizophrenic patients as revealed by high-resolution techniques. *Biol Psychiatry*. 1988 Oct;24(6):675-88. doi: 10.1016/0006-3223(88)90141-2. PMID: 3167149.
- [16] Kimmig H, Greenlee MW, Huethe F, Mergner T. MR-eyetracker: a new method for eye movement recording in functional magnetic resonance imaging. *Exp Brain Res*. 1999 Jun;126(3):443-9. doi: 10.1007/s002210050751. PMID: 10382629.
- [17] Deubel H, Bridgeman B. Fourth Purkinje image signals reveal eye-lens deviations and retinal image distortions during saccades. *Vision Res*. 1995 Feb;35(4):529-38. doi: 10.1016/0042-6989(94)00146-d. PMID: 7900293.
- [18] Clarke AH, Ditterich J, Drüen K, Schönfeld U, Steineke C. Using high frame rate CMOS sensors for three-dimensional eye tracking. *Behav Res Methods Instrum Comput*. 2002 Nov;34(4):549-60. doi: 10.3758/bf03195484. PMID: 12564559.
- [19] Abel LA, Walterfang M, Fietz M, Bowman EA, Velakoulis D. Saccades in adult Niemann-Pick disease type C reflect frontal, brainstem, and biochemical deficits. *Neurology*. 2009 Mar 24;72(12):1083-6. doi:10.1212/01.wnl.0000345040.01917.9d. PMID: 19307542.
- [20] Vignoli A, Fabio RA, La Briola F, Giannatiempo S, Antonietti A, Maggiolini S, Canevini MP. Correlations between neurophysiological, behavioral, and cognitive function in Rett syndrome. *Epilepsy Behav*. 2010Apr;17(4):489-96. doi: 10.1016/j.yebeh.2010.01.024. Epub 2010 Mar 16. PMID: 20236870.
- [21] Salman MS, Dennis M, Sharpe JA. The cerebellar dysplasia of Chiari II malformation as revealed by eye movements. *Can J Neurol Sci*. 2009 Nov;36(6):713-24. doi: 10.1017/s0317167100008325. PMID: 19960749; PMCID: PMC3050022.
- [22] De Luca M, Spinelli D, Zoccolotti P, Zeri F. Measuring fixation disparity with infrared eye-trackers. *J Biomed Opt*. 2009 Jan-Feb;14(1):014013. doi: 10.1117/1.3077198. PMID: 19256701.
- [23] He L, Donnelly WJ 3rd, Stevenson SB, Glasser A. Saccadic lens instability increases with accommodative stimulus in presbyopes. *J Vis*. 2010 Apr 27;10(4):14.1-16. doi: 10.1167/10.4.14. PMID: 20465334; PMCID: PMC2913422.
- [24] Schmitt KU, Muser MH, Lanz C, Walz F, Schwarz U. Comparing eye movements recorded by search coil and infrared eye tracking. *J Clin Monit Comput*. 2007 Feb;21(1):49-53. doi: 10.1007/s10877-006-9057-5. Epub 2006 Nov 22. PMID: 17120108.
- [25] Marino S, Lanzafame P, Sessa E, Bramanti A, Bramanti P. The effect of L-Dopa administration on pursuit ocular movements in suspected Parkinson's disease. *Neurol Sci*. 2010 Jun;31(3):381-5. doi: 10.1007/s10072-009-0180-1. Epub 2009 Nov 19. PMID: 19924505.
- [26] Murray IC, Fleck BW, Brash HM, Macrae ME, Tan LL, Minns RA. Feasibility of saccadic vector optokinetic perimetry: a method of automated static perimetry for children using eye tracking. *Ophthalmology*. 2009 Oct;116(10):2017-26. doi: 10.1016/j.ophtha.2009.03.015. Epub 2009 Jun 27. PMID: 19560207.
- [27] Wierts R, Janssen MJ, Kingma H. Measuring saccade peak velocity using a low-frequency sampling rate of 50 Hz. *IEEE Trans Biomed Eng*. 2008 Dec;55(12):2840-2. doi: 10.1109/TBME.2008.925290. PMID: 19126467.



- [28] Ayton LN, Abel LA, Fricke TR, McBrien NA. Developmental eye movement test: what is it really measuring? *Optom Vis Sci.* 2009 Jun;86(6):722-30. doi: 10.1097/OPX.0b013e3181a6a4b3. PMID: 19417709.
- [29] Kapoula Z, Yang Q, Vernet M, Dieudonné B, Greffard S, Verny M. Spread deficits in initiation, speed and accuracy of horizontal and vertical automatic saccades in dementia with lewy bodies. *Front Neurol.* 2010 Nov 22;1:138. doi: 10.3389/fneur.2010.00138. PMID: 21212841; PMCID: PMC3015135.
- [30] Han SJ, Guo Y, Granger-Donetti B, Vicci VR, Alvarez TL. Quantification of heterophoria and phoria adaptation using an automated objective system compared to clinical methods. *Ophthalmic Physiol Opt.* 2010 Jan;30(1):95-107. doi: 10.1111/j.1475-1313.2009.00681.x. Epub 2009 Aug 13. PMID: 19682268.
- [31] Coughlin MJ, Cutmore TR, Hine TJ. Automated eye tracking system calibration using artificial neural networks. *Comput Methods Programs Biomed.* 2004 Dec;76(3):207-20. doi: 10.1016/j.cmpb.2004.06.001. PMID: 15501507.
- [32] Beauchamp MS. Detection of eye movements from fMRI data. *Magn Reson Med.* 2003 Feb;49(2):376-80. doi: 10.1002/mrm.10345. PMID: 12541259.
- [33] Chaudhary AK, Pelz JB. Motion tracking of iris features to detect small eye movements. *J Eye Mov Res.* 2019 Apr 5;12(6):10.16910/jemr.12.6.4. doi: 10.16910/jemr.12.6.4. PMID: 33828748; PMCID: PMC7962675.
- [34] Massin L, Nourrit V, Lahuec C, Seguin F, Adam L, Daniel E, de Bougrenet de la Tocnaye JL. Development of a new scleral contact lens with encapsulated photodetectors for eye tracking. *Opt Express.* 2020 Sep 14;28(19):28635-28647. doi: 10.1364/OE.399823. PMID: 32988130.
- [35] Hammer DX, Ferguson RD, Magill JC, White MA, Elsner AE, Webb RH. Compact scanning laser ophthalmoscope with high-speed retinal tracker. *Appl Opt.* 2003 Aug 1;42(22):4621-32. doi: 10.1364/ao.42.004621. PMID: 12916631.
- [36] Arines J, Prado P, Bará S. Pupil tracking with a Hartmann-Shack wavefront sensor. *J Biomed Opt.* 2010 May-Jun;15(3):036022. doi: 10.1117/1.3447922. PMID: 20615024.
- [37] García-Baos A, D'Amelio T, Oliveira I, Collins P, Echevarria C, Zapata LP, Liddle E, Supèr H. Novel Interactive Eye-Tracking Game for Training Attention in Children With Attention-Deficit/Hyperactivity Disorder. *Prim Care Companion CNS Disord.* 2019 Jul 3;21(4):19m02428. doi: 10.4088/PCC.19m02428. PMID: 31274260.
- [38] Liu C, Pazzucconi B, Liu J, Liu L, Yao X. A holographic waveguide based eye tracker. *Proc SPIE Int Soc Opt Eng.* 2018 Jan-Feb;10474:104741T. doi: 10.1117/12.2290065. Epub 2018 Feb 19. PMID: 29973746; PMCID: PMC6028018.
- [39] Dowiasch S, Wolf P, Bremmer F. Quantitative comparison of a mobile and a stationary video-based eye-tracker. *Behav Res Methods.* 2020 Apr;52(2):667-680. doi: 10.3758/s13428-019-01267-5. PMID: 31240632; PMCID: PMC7148267.
- [40] Lalanne C, Rateaux M, Oudre L, Robert MP, Moreau T. Extraction of Nystagmus Patterns from Eye-Tracker Data with Convolutional Sparse Coding. *Annu Int Conf IEEE Eng Med Biol Soc.* 2020 Jul;2020:928-931. doi: 10.1109/EMBC44109.2020.9175621. PMID: 33018136.
- [41] Liu C, Pazzucconi B, Liu J, Liu L, Yao X. A holographic waveguide based eye tracking device. *J Mod Opt.* 2019;66(12):1311-1317. doi: 10.1080/09500340.2019.1616842. Epub 2019 May 15. PMID: 32071489; PMCID: PMC7028305.
- [42] Mannan MM, Kim S, Jeong MY, Kamran MA. Hybrid EEG--Eye Tracker: Automatic Identification and Removal of Eye Movement and Blink Artifacts from Electroencephalographic Signal. *Sensors (Basel).* 2016 Feb 19;16(2):241. doi: 10.3390/s16020241. PMID: 26907276; PMCID: PMC4801617.
- [43] Chaudhary AK, Pelz JB. Motion tracking of iris features to detect small eye movements. *J Eye Mov Res.* 2019 Apr 5;12(6):10.16910/jemr.12.6.4. doi: 10.16910/jemr.12.6.4. PMID: 33828748; PMCID: PMC7962675.
- [44] Hessels RS, Niehorster DC, Kemner C, Hooge ITC. Noise-robust fixation detection in eye movement data: Identification by two-means clustering (I2MC). *Behav Res Methods.* 2017 Oct;49(5):1802-1823. doi: 10.3758/s13428-016-0822-1. PMID: 27800582; PMCID: PMC5628191.
- [45] Kar A. MLGaze: Machine Learning-Based Analysis of Gaze Error Patterns in Consumer Eye Tracking Systems. *Vision (Basel).* 2020 May 7;4(2):25. doi: 10.3390/vision4020025. PMID: 32392760; PMCID: PMC7355841.
- [46] Raveendran RN, Krishnan AK. Assessing Binocular Central Visual Field and Binocular Eye Movements in a Dichoptic Viewing Condition. *J Vis Exp.* 2020 Jul 21;(161). doi: 10.3791/61338. PMID: 32773761.

- [47] De Luna P, Mohamed Mustafar MF, Rainer G. A MATLAB-based eye tracking control system using non-invasive helmet head restraint in the macaque. *J Neurosci Methods*. 2014 Sep 30;235:41-50. doi: 10.1016/j.jneumeth.2014.05.033. Epub 2014 Jun 28. PMID: 24979728.
- [48] Wöhle L, Gebhard M. SteadyEye-Head-Improving MARG-Sensor Based Head Orientation Measurements Through Eye Tracking Data. *Sensors (Basel)*. 2020 May 12;20(10):2759. doi: 10.3390/s20102759. PMID: 32408630; PMCID: PMC7294420.
- [49] Kar A, Corcoran P. Development of Open-source Software and Gaze Data Repositories for Performance Evaluation of Eye Tracking Systems. *Vision (Basel)*. 2019 Oct 22;3(4):55. doi: 10.3390/vision3040055. PMID: 31735856; PMCID: PMC6969935.
- [50] Uppal G, Feely MP, Crossland MD, Membrey L, Lee J, da Cruz L, Rubin GS. Assessment of reading behavior with an infrared eye tracker after 360° macular translocation for age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2011 Aug 17;52(9):6486-96. doi: 10.1167/iovs.10-5879. PMID: 21596822.
- [51] McCamy MB, Otero-Millan J, Leigh RJ, King SA, Schneider RM, Macknik SL, Martinez-Conde S. Simultaneous recordings of human microsaccades and drifts with a contemporary video eye tracker and the search coil technique. *PLoS One*. 2015 Jun 2;10(6):e0128428. doi: 10.1371/journal.pone.0128428. PMID: 26035820; PMCID: PMC4452707.
- [52] Massin L, Nourrit V, Lahuec C, Seguin F, Adam L, Daniel E, de Bougrenet de la Tocnaye JL. Development of a new scleral contact lens with encapsulated photodetectors for eye tracking. *Opt Express*. 2020 Sep 14;28(19):28635-28647. doi: 10.1364/OE.399823. PMID: 32988130.
- [53] Abbott D, Shirali Y, Haws JK, Lack CW. Biobehavioral assessment of the anxiety disorders: Current progress and future directions. *World J Psychiatry*. 2017 Sep 22;7(3):133-147. doi: 10.5498/wjp.v7.i3.133. PMID: 29043151; PMCID: PMC5632598.
- [54] Li B, Fu H, Wen D, Lo W. Etracker: A Mobile Gaze-Tracking System with Near-Eye Display Based on a Combined Gaze-Tracking Algorithm. *Sensors (Basel)*. 2018 May 19;18(5):1626. doi: 10.3390/s18051626. PMID: 29783738; PMCID: PMC5981618.
- [55] Kar A, Corcoran P. Development of Open-source Software and Gaze Data Repositories for Performance Evaluation of Eye Tracking Systems. *Vision (Basel)*. 2019 Oct 22;3(4):55. doi: 10.3390/vision3040055. PMID: 31735856; PMCID: PMC6969935.
- [56] Jakobsen NS, Larsen DA, Bek T. Binocular Fixation Reduces Fixational Eye Movements in the Worst Eye of Patients with Center-Involving Diabetic Macular Edema. *Ophthalmic Res*. 2017;58(3):142-149. doi: 10.1159/000476038. Epub 2017 Jul 7. PMID: 28683455.
- [57] Fassi A, Riboldi M, Forlani CF, Baroni G. Optical eye tracking system for noninvasive and automatic monitoring of eye position and movements in radiotherapy treatments of ocular tumors. *Appl Opt*. 2012 May 1;51(13):2441-50. doi: 10.1364/AO.51.002441. PMID: 22614424.
- [58] Mestre C, Otero C, Díaz-Doutón F, Gautier J, Pujol J. An automated and objective cover test to measure heterophoria. *PLoS One*. 2018 Nov 1;13(11):e0206674. doi: 10.1371/journal.pone.0206674. PMID: 30383846; PMCID: PMC6211723.
- [59] Pasqualotto E, Matuz T, Federici S, Ruf CA, Bartl M, Olivetti Belardinelli M, Birbaumer N, Halder S. Usability and Workload of Access Technology for People With Severe Motor Impairment: A Comparison of Brain-Computer Interfacing and Eye Tracking. *Neurorehabil Neural Repair*. 2015 Nov-Dec;29(10):950-7. doi: 10.1177/1545968315575611. Epub 2015 Mar 9. PMID: 25753951.
- [60] Jones PR. An Open-source Static Threshold Perimetry Test Using Remote Eye-tracking (Eyecatcher): Description, Validation, and Preliminary Normative Data. *Transl Vis Sci Technol*. 2020 Jul 13;9(8):18. doi: 10.1167/tvst.9.8.18. PMID: 32855865; PMCID: PMC7422828.
- [61] Ventura RE, Balcer LJ, Galetta SL. The Concussion Toolbox: The Role of Vision in the Assessment of Concussion. *Semin Neurol*. 2015 Oct;35(5):599-606. doi: 10.1055/s-0035-1563567. Epub 2015 Oct 6. PMID: 26444405.
- [62] Hartwig A, Gowen E, Charman WN, Radhakrishnan H. Binocular saccades in myopes and emmetropes. *Optom Vis Sci*. 2013 Sep;90(9):980-7. doi: 10.1097/OPX.000000000000015. PMID: 23912966.
- [63] Andreu-Perez J, Solnais C, Sriskandarajah K. EALab (Eye Activity Lab): a MATLAB Toolbox for Variable Extraction, Multivariate Analysis and Classification of Eye-Movement Data. *Neuroinformatics*. 2016 Jan;14(1):51-67. doi: 10.1007/s12021-015-9275-4. PMID: 26358034.

- [64] Nyström M, Andersson R, Magnusson M, Pansell T, Hooge I. The influence of crystalline lens accommodation on post-saccadic oscillations in pupil-based eye trackers. *Vision Res.* 2015 Feb;107:1-14. doi: 10.1016/j.visres.2014.10.037. Epub 2014 Dec 4. PMID: 25481633.
- [65] Angulo-Chavira AQ, García O, Arias-Trejo N. Pupil response and attention skills in Down syndrome. *Res Dev Disabil.* 2017 Nov;70:40-49. doi: 10.1016/j.ridd.2017.08.011. Epub 2017 Sep 6. PMID: 28888155.
- [66] Zivcevska M, Blakeman A, Lei S, Goltz HC, Wong AMF. Binocular Summation in Postillumination Pupil Response Driven by Melanopsin-Containing Retinal Ganglion Cells. *Invest Ophthalmol Vis Sci.* 2018 Oct 1;59(12):4968-4977. doi: 10.1167/iovs.18-24639. PMID: 30326065.
- [67] Gitchev GT, Wetzel PA, Qutubuddin A, Baron MS. Experimental support that ocular tremor in Parkinson's disease does not originate from head movement. *Parkinsonism Relat Disord.* 2014 Jul;20(7):743-7. doi: 10.1016/j.parkreldis.2014.03.028. Epub 2014 Apr 8. PMID: 24767602.
- [68] Lamirel C, Ajasse S, Moulignier A, Salomon L, Deschamps R, Gueguen A, Vignal C, Cochereau I, Lorenceau J. A novel method of inducing endogenous pupil oscillations to detect patients with unilateral optic neuritis. *PLoS One.* 2018 Aug 22;13(8):e0201730. doi: 10.1371/journal.pone.0201730. PMID: 30133485; PMCID: PMC6104938.
- [69] van der Salm SMA, van der Meer JN, Cath DC, Groot PFC, van der Werf YD, Brouwers E, de Wit SJ, Coppens JC, Nederveen AJ, van Rootselaar AF, Tijssen MAJ. Distinctive tics suppression network in Gilles de la Tourette syndrome distinguished from suppression of natural urges using multimodal imaging. *Neuroimage Clin.* 2018;20:783-792. doi: 10.1016/j.nicl.2018.09.014. Epub 2018 Sep 19. PMID: 30268027; PMCID: PMC6169325.
- [70] Kum JE, Han HB, Choi JH. Pupil Size in Relation to Cortical States during Isoflurane Anesthesia. *Exp Neurobiol.* 2016 Apr;25(2):86-92. doi: 10.5607/en.2016.25.2.86. Epub 2016 Mar 30. PMID: 27122995; PMCID: PMC4844567.
- [71] de Rodez Benavent SA, Nygaard GO, Harbo HF, Tønnesen S, Sowa P, Landrø NI, Wendel-Haga M, Etholm L, Nilsen KB, Drolsum L, Kerty E, Celius EG, Laeng B. Fatigue and cognition: Pupillary responses to problem-solving in early multiple sclerosis patients. *Brain Behav.* 2017 May 17;7(7):e00717. doi: 10.1002/brb3.717. PMID: 28729927; PMCID: PMC5516595.
- [72] Stuart S, Galna B, Lord S, Rochester L. A protocol to examine vision and gait in Parkinson's disease: impact of cognition and response to visual cues. *F1000Res.* 2015 Nov 30;4:1379. doi: 10.12688/f1000research.7320.2. PMID: 27092242; PMCID: PMC4821288.
- [73] Barrionuevo PA, Nicandro N, McAnany JJ, Zele AJ, Gamlin P, Cao D. Assessing rod, cone, and melanopsin contributions to human pupil flicker responses. *Invest Ophthalmol Vis Sci.* 2014 Feb 4;55(2):719-27. doi: 10.1167/iovs.13-13252. PMID: 24408974; PMCID: PMC3915766.
- [74] Wroblewski D, Francis BA, Sadun A, Vakili G, Chopra V. Testing of visual field with virtual reality goggles in manual and visual grasp modes. *Biomed Res Int.* 2014;2014:206082. doi: 10.1155/2014/206082. Epub 2014 Jun 23. PMID: 25050326; PMCID: PMC4090491.
- [75] Panorgias A, Zawadzki RJ, Capps AG, Hunter AA, Morse LS, Werner JS. Multimodal assessment of microscopic morphology and retinal function in patients with geographic atrophy. *Invest Ophthalmol Vis Sci.* 2013 Jun 26;54(6):4372-84. doi: 10.1167/iovs.12-11525. PMID: 23696601; PMCID: PMC3694790.
- [76] Duque-Chica GL, Gracitelli CPB, Moura ALA, Nagy BV, Vidal KS, Paranhos A Jr, Ventura DF. Inner and Outer Retinal Contributions to Pupillary Light Response: Correlation to Functional and Morphologic Parameters in Glaucoma. *J Glaucoma.* 2018 Aug;27(8):723-732. doi: 10.1097/IJG.0000000000001003. PMID: 29965866.
- [77] Gracitelli CP, Duque-Chica GL, Moura AL, Nagy BV, de Melo GR, Roizenblatt M, Borba PD, Teixeira SH, Ventura DF, Paranhos A Jr. A positive association between intrinsically photosensitive retinal ganglion cells and retinal nerve fiber layer thinning in glaucoma. *Invest Ophthalmol Vis Sci.* 2014 Nov 18;55(12):7997-8005. doi: 10.1167/iovs.14-15146. PMID: 25406281.
- [78] Moura AL, Nagy BV, La Morgia C, Barboni P, Oliveira AG, Salomão SR, Berezovsky A, de Moraes-Filho MN, Chicani CF, Belfort R Jr, Carelli V, Sadun AA, Hood DC, Ventura DF. The pupil light reflex in Leber's hereditary optic neuropathy: evidence for preservation of melanopsin-expressing retinal ganglion cells. *Invest Ophthalmol Vis Sci.* 2013 Jul 2;54(7):4471-7. doi: 10.1167/iovs.12-11137. PMID: 23737476; PMCID: PMC4322722.
- [79] Stronks HC, Barry MP, Dagnelie G. Electrically evoked electroretinograms and pupil responses in Argus II retinal implant wearers. *Doc Ophthalmol.* 2016 Feb;132(1):1-15. doi: 10.1007/s10633-015-9522-x. Epub 2016 Jan 7. PMID: 26743880.

- [80] Alnæs D, Sneve MH, Espeseth T, Endestad T, van de Pavert SH, Laeng B. Pupil size signals mental effort deployed during multiple object tracking and predicts brain activity in the dorsal attention network and the locus coeruleus. *J Vis.* 2014 Apr 1;14(4):1. doi: 10.1167/14.4.1. PMID: 24692319.
- [81] Diaz G, Cooper J, Kit D, Hayhoe M. Real-time recording and classification of eye movements in an immersive virtual environment. *J Vis.* 2013 Oct 10;13(12):5. doi: 10.1167/13.12.5. PMID: 24113087; PMCID: PMC3795427.
- [82] Bueno APA, Sato JR, Hornberger M. Eye tracking - The overlooked method to measure cognition in neurodegeneration? *Neuropsychologia.* 2019 Oct;133:107191. doi: 10.1016/j.neuropsychologia.2019.107191. Epub 2019 Sep 12. PMID: 31521634.
- [83] Chen Z, Fu H, Lo WL, Chi Z. Strabismus Recognition Using Eye-Tracking Data and Convolutional Neural Networks. *J Healthc Eng.* 2018 Apr 26;2018:7692198. doi: 10.1155/2018/7692198. PMID: 29854365; PMCID: PMC5944293.
- [84] Fernández G, Mandolesi P, Rotstein NP, Colombo O, Agamennoni O, Politi LE. Eye movement alterations during reading in patients with early Alzheimer disease. *Invest Ophthalmol Vis Sci.* 2013 Dec 30;54(13):8345-52. doi: 10.1167/iovs.13-12877. PMID: 24282223.
- [85] Joosten A, Girdler S, Albrecht MA, Horlin C, Falkmer M, Leung D, Ordqvist A, Fleischer H, Falkmer T. Gaze and visual search strategies of children with Asperger syndrome/high functioning autism viewing a magic trick. *Dev Neurorehabil.* 2016;19(2):95-102. doi: 10.3109/17518423.2014.913081. Epub 2014 May 27. PMID: 24866104.
- [86] Chrobak AA, Rybakowski JK, Abramowicz M, Perdziak M, Gryniewicz W, Tereszko A, Włodarczyk M, Dziuda S, Fafrowicz M, Czarnecki P, Sołtys Z, Siwek M, Ober JK, Marek T, Dudek D. Vergence eye movements in bipolar disorder. *Psychiatr Pol.* 2020 Jun 30;54(3):467-485. English, Polish. doi: 10.12740/PP/OnlineFirst/105229. Epub 2020 Jun 30. PMID: 33038881.
- [87] Hunfalvai M, Roberts CM, Murray NP, Tyagi A, Barclay KW, Bolte T, Kelly H, Carrick FR. Vertical smooth pursuit as a diagnostic marker of traumatic brain injury. *Concussion.* 2020 Jan 14;5(1):CNC69. doi: 10.2217/cnc-2019-0013. PMID: 32266081; PMCID: PMC7136983.
- [88] Donald A, Tan CY, Chakrapani A, Hughes DA, Sharma R, Cole D, Bardins S, Gorges M, Jones SA, Schneider E. Eye movement biomarkers allow for the definition of phenotypes in Gaucher Disease. *Orphanet J Rare Dis.* 2020 Dec 17;15(1):349. doi: 10.1186/s13023-020-01637-9. PMID: 33334373; PMCID: PMC7745364.
- [89] Roberts EO, Proudlock FA, Martin K, Reveley MA, Al-Uzri M, Gottlob I. Reading in schizophrenic subjects and their nonsymptomatic first-degree relatives. *Schizophr Bull.* 2013 Jul;39(4):896-907. doi: 10.1093/schbul/sbr191. Epub 2012 Jan 20. PMID: 22267532; PMCID: PMC3686437.
- [90] Raghuram A, Gowrisankaran S, Swanson E, Zurakowski D, Hunter DG, Waber DP. Frequency of Visual Deficits in Children With Developmental Dyslexia. *JAMA Ophthalmol.* 2018 Oct 1;136(10):1089-1095. doi: 10.1001/jamaophthalmol.2018.2797. PMID: 30027208; PMCID: PMC6583865.
- [91] Vrabič N, Juroš B, Tekavčič Pompe M. Automated Visual Acuity Evaluation Based on Preferential Looking Technique and Controlled with Remote Eye Tracking. *Ophthalmic Res.* 2021;64(3):389-397. doi: 10.1159/000512395. Epub 2020 Oct 20. PMID: 33080607.
- [92] Mourits DL, Hartong DT, van Beek JHM, Witte BI, Tan HS, Moll AC. A Novel Method to Measure Artificial Eye Motility. *Ophthalmic Plast Reconstr Surg.* 2017 Nov/Dec;33(6):413-418. doi: 10.1097/IOP.0000000000000804. PMID: 27811636.
- [93] Mazumdar D, Meethal NSK, Panday M, Asokan R, Thepass G, George RJ, van der Steen J, Pel JJM. Effect of Age, Sex, Stimulus Intensity, and Eccentricity on Saccadic Reaction Time in Eye Movement Perimetry. *Transl Vis Sci Technol.* 2019 Jul 30;8(4):13. doi: 10.1167/tvst.8.4.13. PMID: 31388465; PMCID: PMC6670042.
- [94] Shi XF, Xu LM, Li Y, Wang T, Zhao KX, Sabel BA. Fixational saccadic eye movements are altered in anisometric amblyopia. *Restor Neurol Neurosci.* 2012;30(6):445-62. doi: 10.3233/RNN-2012-129000. PMID: 23001901.
- [95] Murray IC, Perperidis A, Cameron LA, McTrusty AD, Brash HM, Tatham AJ, Agarwal PK, Fleck BW, Minns RA. Comparison of Saccadic Vector Optokinetic Perimetry and Standard Automated Perimetry in Glaucoma. Part I: Threshold Values and Repeatability. *Transl Vis Sci Technol.* 2017 Sep 6;6(5):3. doi: 10.1167/tvst.6.5.3. PMID: 28900576; PMCID: PMC5588909.
- [96] Gitchev GT, Wetzel PA, Baron MS. Slowed saccades and increased square wave jerks in essential tremor. *Tremor Other Hyperkinet Mov (N Y).* 2013 Sep 3;3:tre-03-178-4116-2. doi: 10.7916/D8251GXN. PMID: 24116343; PMCID: PMC3779821.

- [97] Waisbourd M, Dhimi H, Zhou C, Hsieh M, Abichandani P, Pro MJ, Moster MR, Katz LJ, Hark LA, Myers JS. The Wills Eye Glaucoma App: Interest of Patients and Their Caregivers in a Smartphone-based and Tablet-based Glaucoma Application. *J Glaucoma*. 2016 Sep;25(9):e787-91. doi: 10.1097/IJG.0000000000000504. PMID: 27552513.
- [98] Shaikh AG, Factor SA, Juncos J. Saccades in progressive supranuclear palsy - maladapted, irregular, curved, and slow. *Mov Disord Clin Pract*. 2017 Sep-Oct;4(5):671-681. doi: 10.1002/mdc3.12491. Epub 2017 Aug 11. PMID: 29333474; PMCID: PMC5764187.
- [99] Brooks SH, Klier EM, Red SD, Mehta ND, Patel SS, Chuang AZ, Suescun J, Schiess MC, Sereno AB. Slowed Prosaccades and Increased Antisaccade Errors As a Potential Behavioral Biomarker of Multiple System Atrophy. *Front Neurol*. 2017 Jun 20;8:261. doi: 10.3389/fneur.2017.00261. PMID: 28676787; PMCID: PMC5476968.
- [100] Patel SS, Jankovic J, Hood AJ, Jeter CB, Sereno AB. Reflexive and volitional saccades: biomarkers of Huntington disease severity and progression. *J Neurol Sci*. 2012 Feb 15;313(1-2):35-41. doi: 10.1016/j.jns.2011.09.035. Epub 2011 Oct 21. PMID: 22018763; PMCID: PMC3254798.
- [101] Titchener SA, Kvangsakul J, Shivdasani MN, Fallon JB, Nayagam DAX, Epp SB, Williams CE, Barnes N, Kentler WG, Kolic M, Baglin EK, Ayton LN, Abbott CJ, Luu CD, Allen PJ, Petoe MA. Oculomotor Responses to Dynamic Stimuli in a 44-Channel Suprachoroidal Retinal Prosthesis. *Transl Vis Sci Technol*. 2020 Dec 18;9(13):31. doi: 10.1167/tvst.9.13.31. PMID: 33384885; PMCID: PMC7757638.
- [102] Ghasia FF, Wilmot G, Ahmed A, Shaikh AG. Strabismus and Micro-Opsoclonus in Machado-Joseph Disease. *Cerebellum*. 2016 Aug;15(4):491-7. doi: 10.1007/s12311-015-0718-0. PMID: 26306823.
- [103] Stephen JM, Coffman BA, Stone DB, Kodituwakku P. Differences in MEG gamma oscillatory power during performance of a prosaccade task in adolescents with FASD. *Front Hum Neurosci*. 2013 Dec 25;7:900. doi: 10.3389/fnhum.2013.00900. PMID: 24399957; PMCID: PMC3872294.
- [104] Surkar SM, Hoffman RM, Davies B, Harbourne R, Kurz MJ. Impaired anticipatory vision and visuomotor coordination affects action planning and execution in children with hemiplegic cerebral palsy. *Res Dev Disabil*. 2018 Sep;80:64-73. doi: 10.1016/j.ridd.2018.06.009. Epub 2018 Jun 22. PMID: 29940386.
- [105] Giacomelli G, Farini A, Baldini I, Raffaelli M, Bigagli G, Fossetti A, Virgili G. Saccadic movements assessment in eccentric fixation: A study in patients with Stargardt disease. *Eur J Ophthalmol*. 2021 Sep;31(5):2556-2562. doi: 10.1177/1120672120960336. Epub 2020 Oct 2. PMID: 33008267.
- [106] Gajardo AIJ, Madariaga S, Maldonado PE. Autonomic nervous system assessment by pupillary response as a potential biomarker for cardiovascular risk: A pilot study. *J Clin Neurosci*. 2019 Jan;59:41-46. doi: 10.1016/j.jocn.2018.11.015. Epub 2018 Nov 16. PMID: 30448298.
- [107] Kim SY, Moon BY, Cho HG, Yu DS. Comparison of image-based quantification methods in evaluating fixation stability using a remote eye tracker in abnormal phoria. *J Int Med Res*. 2022 May;50(5):3000605221098183. doi: 10.1177/03000605221098183. PMID: 35546441; PMCID: PMC9112722.
- [108] Ghasia F, Wang J. Amblyopia and fixation eye movements. *J Neurol Sci*. 2022 Oct 15;441:120373. doi: 10.1016/j.jns.2022.120373. Epub 2022 Aug 3. PMID: 36007287.
- [109] Lalanne C, Rateaux M, Oudre L, Robert MP, Moreau T. Extraction of Nystagmus Patterns from Eye-Tracker Data with Convolutional Sparse Coding. *Annu Int Conf IEEE Eng Med Biol Soc*. 2020 Jul;2020:928-931. doi: 10.1109/EMBC44109.2020.9175621. PMID: 33018136.
- [110] Chrobak AA, Rybakowski JK, Abramowicz M, Perdziak M, Gryniewicz W, Dziuda S, Fafrowicz M, Czarnecki P, Soltys Z, Ceglarek A, Ober JK, Marek T, Dudek D, Siwek M. Vergence eye movements impairments in schizophrenia and bipolar disorder. *J Psychiatr Res*. 2022 Dec;156:379-389. doi: 10.1016/j.jpsychires.2022.10.042. Epub 2022 Oct 20. PMID: 36323140.
- [111] García Cena C, Costa MC, Saltarén Pazmiño R, Santos CP, Gómez-Andrés D, Benito-León J. Eye Movement Alterations in Post-COVID-19 Condition: A Proof-of-Concept Study. *Sensors (Basel)*. 2022 Feb 14;22(4):1481. doi: 10.3390/s22041481. PMID: 35214383; PMCID: PMC8875414.
- [112] Taore A, Lobo G, Turnbull PR, Dakin SC. Diagnosis of colour vision deficits using eye movements. *Sci Rep*. 2022 May 11;12(1):7734. doi: 10.1038/s41598-022-11152-5. Erratum in: *Sci Rep*. 2022 Aug 2;12(1):13625. PMID: 35562176; PMCID: PMC9095692.
- [113] Elbaum T, Braw Y, Lev A, Rassovsky Y. Attention-Deficit/Hyperactivity Disorder (ADHD): Integrating the MOXO-dCPT with an Eye Tracker Enhances Diagnostic Precision. *Sensors (Basel)*. 2020 Nov 9;20(21):6386. doi: 10.3390/s20216386. PMID: 33182303; PMCID: PMC7664925.

- [114] Green CR, Mihic AM, Brien DC, Armstrong IT, Nikkel SM, Stade BC, Rasmussen C, Munoz DP, Reynolds JN. Oculomotor control in children with fetal alcohol spectrum disorders assessed using a mobile eye-tracking laboratory. *Eur J Neurosci.* 2009 Mar;29(6):1302-9. doi: 10.1111/j.1460-9568.2009.06668.x. PMID: 19302166.
- [115] Keller J, Gorges M, Aho-Özhan HE, Uttner I, Schneider E, Kassubek J, Pinkhardt EH, Ludolph AC, Lulé D. Eye-Tracking Control to Assess Cognitive Functions in Patients with Amyotrophic Lateral Sclerosis. *J Vis Exp.* 2016 Oct 13;(116):54634. doi: 10.3791/54634. PMID: 27768047; PMCID: PMC5092192.
- [116] Fabio RA, Giannatiempo S, Semino M, Capri T. Longitudinal cognitive rehabilitation applied with eye-tracker for patients with Rett Syndrome. *Res Dev Disabil.* 2021 Apr;111:103891. doi: 10.1016/j.ridd.2021.103891. Epub 2021 Feb 10. PMID: 33581477.
- [117] Gantz L, Caspi A. Synchronization of a Removable Optical Element with an Eye Tracker: Test Case for Heterophoria Measurement. *Transl Vis Sci Technol.* 2020 Jun 29;9(7):40. doi: 10.1167/tvst.9.7.40. PMID: 32832245; PMCID: PMC7414612.
- [118] Camargo MVZA, Pais MV, Bellan AFR, Tahira AC, Dos Santos B, Sant'Ana LCFG, Radanovic M, Forlenza OV. Impact of Cognitive Demand on Eye Movement Pattern in Patients with Alzheimer's Disease. *J Alzheimers Dis.* 2022;90(1):85-95. doi: 10.3233/JAD-220385. PMID: 36093694.
- [119] Kołodziej P, Tuszyńska-Bogucka W, Dzieńkowski M, Bogucki J, Kocki J, Milosz M, Kocki M, Reszka P, Kocki W, Bogucka-Kocka A. Eye Tracking-An Innovative Tool in Medical Parasitology. *J Clin Med.* 2021 Jul 4;10(13):2989. doi: 10.3390/jcm10132989. PMID: 34279473; PMCID: PMC8268455.
- [120] Chainey J, Elomaa AP, O'Kelly CJ, Kim MJ, Bednarik R, Zheng B. Eye-Hand Coordination of Neurosurgeons: Evidence of Action-Related Fixation in Microsuturing. *World Neurosurg.* 2021 Nov;155:e196-e202. doi: 10.1016/j.wneu.2021.08.028. Epub 2021 Aug 13. PMID: 34400325.
- [121] Bin Zahid A, Hubbard ME, Lockyer J, Podolak O, Dammavalam VM, Grady M, Nance M, Scheiman M, Samadani U, Master CL. Eye Tracking as a Biomarker for Concussion in Children. *Clin J Sport Med.* 2020 Sep;30(5):433-443. doi: 10.1097/JSM.0000000000000639. PMID: 30095503.
- [122] Szpisjak L, Szaraz G, Salamon A, Nemeth VL, Szepfalusi N, Veres G, Kincses B, Maroti Z, Kalmar T, Rydzanicz M, Ploski R, Klivenyi P, Zadori D. Eye-tracking-aided characterization of saccades and antisaccades in SYNE1 ataxia patients: a pilot study. *BMC Neurosci.* 2021 Feb 1;22(1):7. doi: 10.1186/s12868-021-00612-9. Erratum in: *BMC Neurosci.* 2021 Mar 10;22(1):16. PMID: 33526008; PMCID: PMC7852103.
- [123] Russell LL, Greaves CV, Convery RS, Bocchetta M, Warren JD, Kaski D, Rohrer JD. Eye movements in frontotemporal dementia: Abnormalities of fixation, saccades and anti-saccades. *Alzheimers Dement (N Y).* 2021 Dec 31;7(1):e12218. doi: 10.1002/trc2.12218. PMID: 35005203; PMCID: PMC8719345.
- [124] Putcha D, Ross RS, Rosen ML, Norton DJ, Cronin-Golomb A, Somers DC, Stern CE. Functional correlates of optic flow motion processing in Parkinson's disease. *Front Integr Neurosci.* 2014 Jul 8;8:57. doi: 10.3389/fnint.2014.00057. PMID: 25071484; PMCID: PMC4086480.
- [125] Bhowmik S, Arjunan SP, Sarossy M, Radcliffe P, Kumar DK. Pupillometric recordings to detect glaucoma. *Physiol Meas.* 2021 May 11;42(4). doi: 10.1088/1361-6579/abf05c. PMID: 33740779.
- [126] Kirchner J, Watson T, Lappe M. Real-Time MRI Reveals Unique Insight into the Full Kinematics of Eye Movements. *eNeuro.* 2022 Jan 7;9(1):ENEURO.0357-21.2021. doi: 10.1523/ENEURO.0357-21.2021. PMID: 34876474; PMCID: PMC8751851.
- [127] Ballae Ganeshrao S, Jaleel A, Madicharla S, Kavya Sri V, Zakir J, Garudadri CS, Senthil S. Comparison of Saccadic Eye Movements Among the High-tension Glaucoma, Primary Angle-closure Glaucoma, and Normal-tension Glaucoma. *J Glaucoma.* 2021 Mar 1;30(3):e76-e82. doi: 10.1097/IJG.0000000000001757. PMID: 33394842.
- [128] Yang B, Tan F, Xu SZ, Liu LQ, Zheng XJ. [Analysis of Characteristic Eye Movement Behaviors of Young Adults with Different Degrees of Myopia]. *Sichuan Da Xue Xue Bao Yi Xue Ban.* 2022 Sep;53(5):911-915. Chinese. doi: 10.12182/20220960303. PMID: 36224696.
- [129] Wright IH, Sekar A, Jensen MT, Hodgson M, Bancroft MJ, Koohi N, Lees AJ, Morris HR, Kaski D. Reflexive and volitional saccadic eye movements and their changes in age and progressive supranuclear palsy. *J Neurol Sci.* 2022 Dec 15;443:120482. doi: 10.1016/j.jns.2022.120482. Epub 2022 Oct 28. PMID: 36356484.
- [130] Carbone F, Ellmerer P, Ritter M, Spielberger S, Mahlknecht P, Hametner E, Hussl A, Hotter A, Granata R, Seppi K, Boesch S, Poewe W, Djamshidian A. Impaired Inhibitory Control of Saccadic Eye Movements in Cervical Dystonia:

An Eye-Tracking Study. *Mov Disord.* 2021 May;36(5):1246-1250. doi: 10.1002/mds.28486. Epub 2021 Jan 8. PMID: 33416199; PMCID: PMC8247854.

- [131] Donald A, Tan CY, Chakrapani A, Hughes DA, Sharma R, Cole D, Bardins S, Gorges M, Jones SA, Schneider E. Eye movement biomarkers allow for the definition of phenotypes in Gaucher Disease. *Orphanet J Rare Dis.* 2020 Dec 17;15(1):349. doi: 10.1186/s13023-020-01637-9. PMID: 33334373; PMCID: PMC7745364.
- [132] Khaldi A, Daniel E, Massin L, Kärnfelt C, Ferranti F, Lahuec C, Seguin F, Nourrit V, de Bougrenet de la Tocnaye JL. A laser emitting contact lens for eye tracking. *Sci Rep.* 2020 Sep 9;10(1):14804. doi: 10.1038/s41598-020-71233-1. PMID: 32908167; PMCID: PMC7481179.
- [133] Zhu G, Wang J, Xiao L, Yang K, Huang K, Li B, Huang S, Hu B, Xiao B, Liu D, Feng L, Wang Q. Memory Deficit in Patients With Temporal Lobe Epilepsy: Evidence From Eye Tracking Technology. *Front Neurosci.* 2021 Sep 7;15:716476. doi: 10.3389/fnins.2021.716476. PMID: 34557066; PMCID: PMC8453169.
- [134] Rempe T, Dastgheyb N, Miner A, Palomino M, Kinkel R, Liston D, Graves JS. Quantification of smooth pursuit dysfunction in multiple sclerosis. *Mult Scler Relat Disord.* 2021 Sep;54:103073. doi: 10.1016/j.msard.2021.103073. Epub 2021 Jun 5. PMID: 34214878.
- [135] Vrabič N, Juroš B, Tekavčič Pompe M. Automated Visual Acuity Evaluation Based on Preferential Looking Technique and Controlled with Remote Eye Tracking. *Ophthalmic Res.* 2021;64(3):389-397. doi: 10.1159/000512395. Epub 2020 Oct 20. PMID: 33080607.
- [136] Hunfalvay M, Roberts CM, Murray NP, Tyagi A, Barclay KW, Bolte T, Kelly H, Carrick FR. Vertical smooth pursuit as a diagnostic marker of traumatic brain injury. *Concussion.* 2020 Jan 14;5(1):CNC69. doi: 10.2217/cnc-2019-0013. PMID: 32266081; PMCID: PMC7136983.
- [137] Guerrero-Molina MP, Rodríguez-López C, Panadés-de Oliveira L, Uriarte-Pérez de Urabayen D, Garzo-Caldas N, García-Cena CE, Saiz-Díaz RA, Benito-León J, Gonzalez de la Aleja J. Antisaccades and memory-guided saccades in genetic generalized epilepsy and temporal lobe epilepsy. *Epilepsy Behav.* 2021 Oct;123:108236. doi: 10.1016/j.yebeh.2021.108236. Epub 2021 Aug 19. PMID: 34419714.
- [138] Ting WK, Perez Velazquez JL, Cusimano MD. Eye movement measurement in diagnostic assessment of disorders of consciousness. *Front Neurol.* 2014 Jul 29;5:137. doi: 10.3389/fneur.2014.00137. PMID: 25120529; PMCID: PMC4114324