Pupillary Assessment for the Detection of Ischemic Stroke: Analysis of Multiform Pupil Shapes Using Bexel Irina Software

Bryan K. Marcia, Ph.D., Professor Emeritus

Abstract

Ischemic strokes, which occur when blood flow to the brain is obstructed, account for approximately 87% of all strokes and potential long-term disability. Prompt diagnosis and treatment of ischemic stroke are crucial for patient outcomes, and accurate and accessible diagnostic methods are needed for effective management of this condition.

Ischemic Stroke is ranked as the second leading cause of death worldwide with an annual mortality rate of about 5.5 million. Three types of ischemic strokes include Ischemic stroke, hemorrhagic stroke and Transient ischemic attack (TIA) [1].

The World Stroke Organization reports that there are more than 12.2 million new strokes annually worldwide, and one in four individuals over the age of 25 will experience a stroke during their lifetime [2].

Pupil assessment has been proposed as a potential diagnostic tool for ischemic stroke, as changes in pupil size, shape, and response to light can indicate neurological impairment.

Research Objectives

The aim of this study is to investigate the relationship between cerebral ischemic stroke and oval ellipse forms of the human pupil, and to assess the accuracy and reliability of pupillary assessment as a possible diagnostic tool for this condition.

Research Content:

This study provides a comprehensive review of pupillary assessment techniques, including biometric analysis and assessment, and compares various datasets studied to identify pupillary abnormalities in pre- and post-ischemic stroke case studies. The paper proposes an efficient and cost-effective model for detecting cerebral ischemic stroke using pupillary assessment tools.

This study investigates the potential of pupillary assessment as a reliable and accessible diagnostic tool for cerebral ischemic stroke, and provides important insights into the relationship between pupil abnormalities and neurological impairment. The findings of this study have important implications for the development of effective diagnostic and management strategies for ischemic stroke, and could ultimately improve patient outcomes and quality of life.

Introduction

The condition and placement of the pupil provide valuable insights into the operational status of the pupilomotor system and diverse brain structures. Typically, the pupil is circular and positioned at the center of the iris, with its placement determined by the equilibrium between the sympathetic and parasympathetic facets of the pupil-motor system. Nevertheless, the pupil may undergo deformation due to various factors such as local ocular maladies, surgeries, or illnesses impacting internal organs, all of which can affect the central nervous system.

Corectopia refers to the displacement of the pupil center from the center of the cornea and is linked with several ophthalmic conditions like iris coloboma, trauma, Axenfeld-Reiger anomaly, ectopia lentis et pupillae, hyperplastic pupillary membrane, persistent pupillary membrane, and high myopia. Post-operative cataract surgery has been associated with a 16% incidence of pupil abnormalities, according to one study [3].

According to A. Aliyev and Shulpina NB (1980), false variants of pupil deformations can also occur due to the melting of some sectors of the pupillary margin. They noted that the pigment fringe of the pupil depends on a person's age, and there is a progression with age, which can lead to the "melting" of pigment and false appearances of pupil deformations [4].

Accurately identifying the underlying causes of pupillary deformations is crucial for the correct diagnosis and effective treatment of associated conditions.

Authors Bremner Fion D., Drapkin Allan J. (2019) discuss clinical observations required to differentiate between a dynamic oval pupil and a static one. A dynamic oval pupil is an ominous prognostic sign due to midbrain dysfunction, and it occurs in association with severe impairment of consciousness. A dynamic oval pupil may be caused by various pathologies such as hemorrhage, ischemia, tumor, hypoglycemia, and head trauma. The responsible pathology results in major or minor impairment of the ascending reticular activating system. The possible location for the lesion responsible for producing a dynamic oval pupil might be in the area of the central mesencephalic reticular formation. Any damage to this area is expected to result in disinhibition of some of the preganglionic parasympathetic neurons [5].

C. Miller Fisher, M.D. (1980) summarizes a review of 17 patients who were found to have oval pupils in one or both eyes during a neurological examination. Among the 17 patients, 16 had serious cerebrovascular illnesses, such as cerebral hemorrhage, cerebral infarction, aneurysm rupture, or brainstem stroke, while one patient was recovering from an oculomotor palsy. Oval pupils usually indicate a transient and unstable phase in progressive injury to the oculomotor complex, and sometimes a transient phase of recovery [6].

Lawrence F. Marshall Et al., (1983) describes the clinical significance of oval pupils in relation to intracranial hypertension. The study involved 100 patients with intracranial hypertension, and 6% of them exhibited oval pupils. The authors conclude that the presence of an oval pupil is a reliable clinical indicator of intracranial hypertension, especially when other signs are absent. They also suggest that the oval pupil may be an early sign of uncal herniation, a potentially life-threatening condition [7].

E.S. Velchover (1990) proposed that an oval-shaped pupil in a horizontal orientation may indicate a disturbance in blood supply to the brain due to atherosclerosis or other pathological processes, and can serve as a warning sign of an impending stroke. This pupillary deformation may be observed in a variety of pathological conditions, whether inherited or acquired. Usually, changes in the pupil in one eye indicate a symptom of a disease, whereas changes in both eyes could be indicative of a genetic predisposition [8].

VA Smirnov (1953) found that various forms of pupil deformations, including flattened, oval, angular, pear, and multiform, are commonly associated with organic lesions of the central nervous system (67% of cases), peripheral nervous system (26%), alcohol and nicotine intoxication (64%), neurotic conditions (27%), and internal organ pathologies (38%) [9].

Velhover ES (1992) reported that pupillary deformations are common in various neurological diseases, with a prevalence ranging from 44% to 88%. The most frequent and pronounced deformations were observed in patients with epidemic encephalitis, with an incidence of 88% [10].

T. Kriege (1971) and Josef Deck (1985) both believed that the oval shape of the pupils in most cases points to an inherited or acquired predisposition to apoplexy states (stroke) [11], [12].

Rudolf Schnabel's (1925) observations suggest that the presence of vertically oriented oval pupils, where the major axis of the pupils is vertical, may indicate the risk of circulatory brain damage from stroke, which can have both hereditary and acquired causes. [13].

Overview of Methodologies

This study aimed to investigate the correlation between cerebral ischemic stroke and oval ellipse forms of the human pupil through biometric pupillary analysis. A dataset of 500 pupillary assessment case studies was analyzed, but 32 cases were excluded either due to incomplete history or duplication, resulting in 468 case studies consisting of 182 males and 286 females.

The pupillary assessment was conducted using a digital pupilometer or iriscope and images were captured in both scotopic and photopic conditions. The pupillary datasets were analyzed using Bexel Irina statistical software, and various parameters such as pupil size, shape, and symmetry were measured. The results were then compared to identify any significant differences in pupillary abnormalities. To further validate the accuracy of the pupillary assessment in the diagnosis of cerebral ischemic stroke, a receiver operating characteristic (ROC) analysis was performed. The area under the curve (AUC) was calculated to determine the diagnostic accuracy of the pupillary assessment method.

The use of medical professionals to submit case study histories and eye images is also a valuable addition to ensure accurate assessment and classification of the pupillary anomalies. All personal assessment data was HIPAA compliant.

The Bexel Irina software assesses the shape and size of the pupil by comparing it to a standard or "normal" pupil, and identifies any deviations as pupillary abnormalities.

According to R. Bourdiol (1975), pupillary ellipses or deformations, or changes in location that are greater than 3%, are considered clinically significant. It is important to note that the threshold of 3% for the oval ellipse is a clinical decision based on the analysis of the collected data [14].

Therefore, even if a large number of cases show an oval pupil, if it is less than 3%, it may not be clinically relevant. Thus, it is crucial to analyze the outcomes of the pupillary evaluation in relation to the particular threshold values and standards employed in the research.

The pupillary data results obtained from the assessment software used in this study includes several parameters related to the iris, pupillary border, pupil, and their relative positions. Some of these parameters include the size and shape of the pupil, position of the pupil within the iris, presence of any irregularities or abnormalities in the pupillary border, and the degree of ellipse in the pupil. These parameters are used to detect and quantify any abnormalities or deformations in the pupil that may be indicative of underlying pathology or disease. The information obtained from these assessments can be useful in diagnosing and monitoring various eye and systemic conditions.

The observation of oval forms of the human pupil in relation to ischemic cerebral strokes was based on three recent case studies involving patients with a history of pre-ischemic and post-ischemic stroke. Among the three cases, two reported transient ischemic strokes, while one led to severe disability. In all three cases, there was a combination of oval-vertical and oval-diagonal forms observed in alternating eyes, which prompted further investigation.

It's important to note that while there were only 12 cases with a combination of oval-vertical and oval-diagonal forms in alternating eyes, 8 of these cases were verified to have ischemic stroke.

It's also interesting to see that there were three cases with no history of ischemic stroke and one case with an unverified stroke but a known history of liver cancer. This suggests that further investigation is needed to better understand the relationship between oval forms of the pupil and ischemic stroke. Unverified stroke represents no known strokes with no health case history updates reported from primary heath care giver.

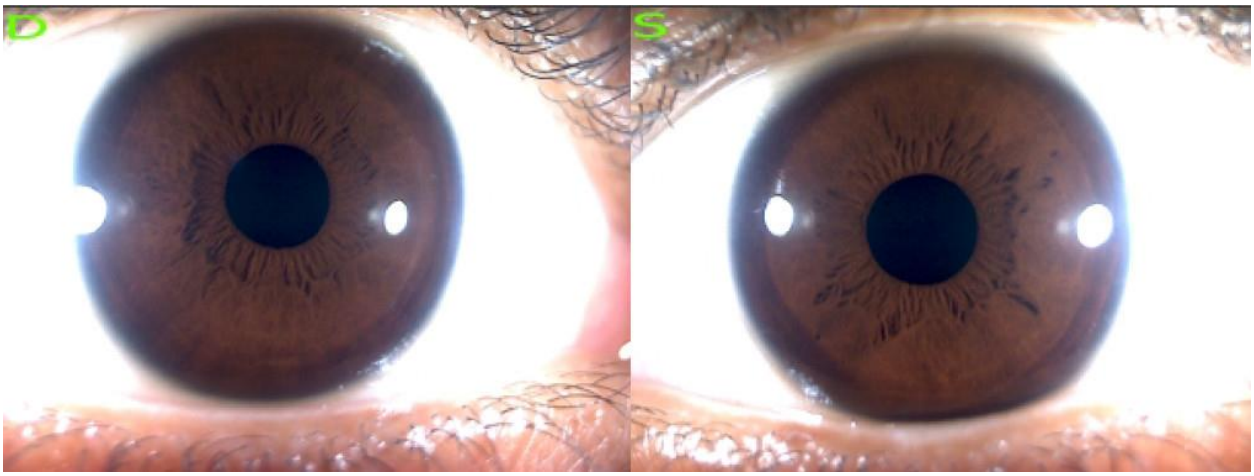
This study found that only one individual had pupils that could be classified as "normal" or "ideal" with minimal deformations under 3%. Additionally, among the participants, 70 individuals did not present with any oval-shaped pupils but did exhibit other types of pupillary deformations.

The Bexel Irina software was used to analyze 28 different types of pupillary deformations. Pupillary assessment results were indexed and classified into specific pupillary anomalies [tbl 1.]

Table 1: Results of detected pupil anomalies in 468 case studies

Pupillary Assessments				
	Total	**Male**	**Female**	**%**
Total Case Studies	468	182	286	%
Deformations (8 Types)	**Total**	**Male**	**Female**	**Total %**
Frontal Flatness (Upper central)	162	67	95	34.6%
Middle-temporal flatness	122	49	73	26.1%
Middle-nasal flatness	114	42	72	24.4%
Basal Flatness (Lower Basal)	27	16	11	5.8%
Lower temporal flatness	18	5	13	3.8%
Lower nasal flatness	14	4	10	3.0%
Upper nasal flatness	13	8	5	2.8%
Upper temporal flatness	11	5	6	2.4%
Decentrations (5 Types)				
Upper-nasal decentralization	308	107	201	65.8%
Middle-nasal decentralization	126	66	60	26.9%
Middle-upper nasal decentralization	58	16	42	26.9%
Frontal decentralization	38	14	24	12.4%
Upper-temporal decentralization	5	2	3	1.1%
Protusions (8 types)				
Basal protrusion	213	75	138	45.5%
Middle-temporal protrusion	171	69	102	36.5%
Middle-nasal protrusion	162	36	54	34.6%
Lower nasal protrusion	86	32	54	18.4%
Lower temporal protrusion	60	23	37	12.8%
Frontal protrusion	51	21	30	10.9%
Upper nasal protrusion	38	11	35	8.1%
Upper temporal protrusion	31	8	35	6.6%
Drawing In (2 types)				
Frontal (top) drawing in	82	28	54	17.5%
Basal (Bottom) drawing in	29	14	15	6.2%
Ellipse Multiformaties (3 types)				
Ellipse of one or both pupils	396	183	285	84.6%
Oval-horizontal form	172	70	102	36.8%
Oval-vertical form	124	54	70	26.5%
Oval-diagonal form	100	41	59	21.4%
Pupil Size in relation to age (two types)				
Mydriasis	80	25	55	17.1%
Anisocoria	67	24	43	14.3%
Normal Pupils				
No Ellipse with deformations or decentrations	70	31	39	15.0%
No Ellipse with no significant deformations or decentrations	1	0	1	0.2%

Normal Pupils



Numerical Data Analysis

PARAMETERS OF THE IRIS :	S	D
Diameter (pix) =	406	404
Area (pix)	129462	128190
PARAMETERS OF THE PUPILLARY BORDER :		
Diameter (pix)	100	94
Diameter of the pupil in relation to iris (%)	24	23
Normal for current age 23-32%	Normal	Normal
Pupil border deformation degree (normal:0%...5%)	6	12
PARAMETERS OF THE PUPIL RELATIVE TO THE IRIS :		
Distance between the pupil and iris centers (%)	3.45	3.96
Normal (lower than 5% of above) or pathology	Normal	Normal
PARAMETERS OF THE APPROXIMATE ELLIPSE		
Ellipseness degree of the pupil (normal: 95% ... 100%)	100	98
	Normal	Normal
Pupil form type	circle	circle
	Normal	Normal
PARAMETERS OF THE PUPILLARY MARGIN :		
Type of the form -	regular	regular
	Normal	Normal

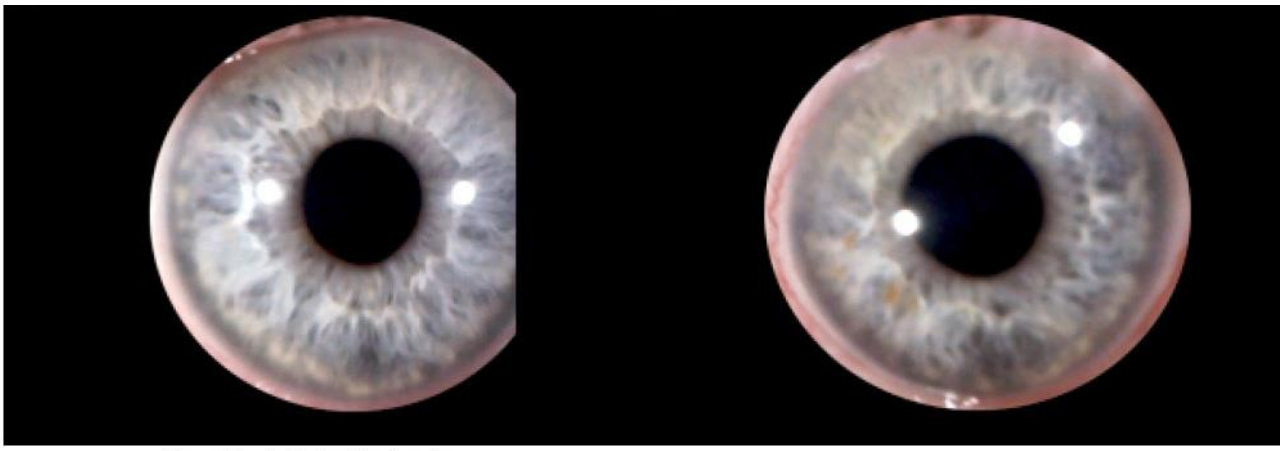
Diagnosis

S : Upper nasal drawing in (10:40 - 11:48) - 2.00 %
S : Lower temporal protrusion (3:56 - 5:06) - 2.00 %
S : Decentralization of the pupil is normal.
S : Ellipseness of the pupil is normal.

D : Decentralization of the pupil is normal.
D : Ellipseness of the pupil is normal.

FIG 1: Pupillary parameter results for normal pupil. The parameters of this pupil are considered to be near-perfect. Less than 3% deformation or decentration of pupils may not have any clinical significance according to R. Bourdiol (1975) [14].

Two pre-ischemic case studies were of particular interest. One individual, male, 65 years old experienced ischemic stroke two years after initial pupillary assessment [FIG. 2].



Numerical Data Analysis

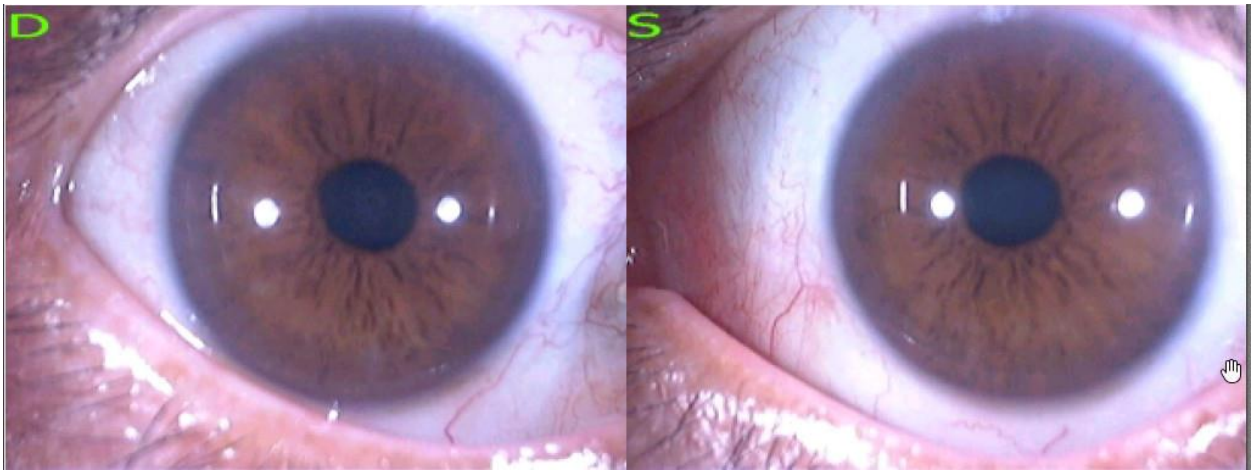
PARAMETERS OF THE IRIS :	S	D
Diameter (pix) =	354	366
Area (pix)	98423	105209
PARAMETERS OF THE PUPILLARY BORDER :		
Diameter (pix)	120	104
Diameter of the pupil in relation to iris (%)	33	28
Normal for current age 21-25%	Mydriasis	Mydriasis
Pupil border deformation degree (normal:0%...5%)	2	0
PARAMETERS OF THE PUPIL RELATIVE TO THE IRIS :		
Distance between the pupil and iris centers (%)	9.60	6.01
Normal (lower than 5% of above) or pathology	Pathology	Pathology
PARAMETERS OF THE APPROXIMATE ELLIPSE		
Ellipseness degree of the pupil (normal: 95% ... 100%)	92	94
	Pathology	Pathology
Pupil form type	ellipse	ellipse
	Pathology	Pathology
PARAMETERS OF THE PUPILLARY MARGIN :		
Type of the form -	regular	regular
	Normal	Normal

Diagnosis

S : Lower nasal flatness (6:22 - 10:04) - 20.00 %
S : Frontal decentralization.
S : Oval-diagonal form of the pupil.
D : Middle-temporal flatness (8:04 - 9:36) - 7.69 %
D : Basal protrusion (5:16 - 6:46) - 5.77 %
D : Upper-nasal decentralization.
D : Oval-vertical form of the pupil.
ANISOCORIA (S>D) = 5 %.

FIG 2: Initial pre-stroke pupillary parameters for 65 years old male in 2018 whom experienced ischemic stroke in 2020. A re-assessment in 2022 revealed no anisocoria and normal ellipse of the right eye. While the resolution of the anisocoria and return to normal pupillary shape on the right side is encouraging, it does not necessarily indicate complete resolution of the underlying pathology.

Male, 50 years old at the time, experienced severe ischemic stroke three years later. The pupil images of his 5-year-old son were also analyzed, and oval-vertical forms were detected in both pupils, indicating the potential for hereditary factors. [Fig 3].



Numerical Data Analysis

PARAMETERS OF THE IRIS :	S	D
Diameter (pix) =	412	404
Area (pix)	133317	128190
PARAMETERS OF THE PUPILLARY BORDER :		
Diameter (pix)	78	80
Diameter of the pupil in relation to iris (%)	18	19
Normal for current age 21-25%	Miosis	Miosis
Pupil border deformation degree (normal:0%...5%)	55	32
PARAMETERS OF THE PUPIL RELATIVE TO THE IRIS :		
Distance between the pupil and iris centers (%)	7.28	6.44
Normal (lower than 5% of above) or pathology	Pathology	Pathology
PARAMETERS OF THE APPROXIMATE ELLIPSE		
Ellipseness degree of the pupil (normal: 95% ... 100%)	87	91
	Pathology	Pathology
Pupil form type	ellipse	ellipse
	Pathology	Pathology
PARAMETERS OF THE PUPILLARY MARGIN :		
Type of the form -	regular	regular
	Normal	Normal

Diagnosis:

S : Basal protrusion (5:30 - 7:18) - 5.13 %
S : Frontal protrusion (10:54 - 12:00) - 5.13 %
S : Upper-nasal decentralization.
S : Oval-vertical form of the pupil.
D : Upper-nasal decentralization.
D : Oval-diagonal form of the pupil.

FIG 3: Pupillary parameter results from 50-year-old pre-ischemic stroke study. According to authors, E.S. Velchover (1988) [16] and V-Krivenko (1995) [17], oval-vertical form pupils with major axes diverging above, reflects a predisposition to bleeding in the brain. In 468 case studies, bilateral "oval-vertical" pupils occurred in 39 cases (8.3%).

Related Findings

The results of the pupillary assessment revealed that 60 case studies showed "circulatory cerebral disturbance with danger of ischemic variation". In all these cases, either one or both pupils displayed a combination of horizontal, vertical, and diagonal ellipse, which represented 12.82% of the total 468 case studies. These findings suggest that there may be a possible link between pupillary abnormalities and circulatory problems that can lead to ischemic events in the brain.

Further analysis found that there was no significant difference in the predominance of oval-vertical and oval-diagonal forms in either the right or left pupil. The distribution was split evenly at 50% for both the right and left pupils.

The pupillary assessment data also revealed six additional cerebral anomalies in the database, namely: disturbance in cerebral blood circulation disturbances (178 cases - 38.03%), decreased basal cerebral circulation (9 cases - 1.8%), circulatory cerebral disturbance with risk of spastic variation (63 cases - 12.6%), discirculatory encephalopathy (94 cases – 18.8%), neurocirculatory dystonia (17 cases - 3.4%) and risk of blood cerebral hemisphere vessel spasm (22 cases - 4.7%) [tbl. 2].

Pupillary Neurocirculatory Findings in 468 Clinical Case Studies			
	Total	**Male**	**Female**
Total Case Studies	468	182	286
Findings			
Blood cerebral circulation disturbance	178	74	106
Basal cerebral circulation is decreased	9	2	7
Circulatory cerebral disturbance with danger of ischemic variation	60	42	31
Circulatory cerebral disturbance with risk of spastic variation	63	19	44
Discirculatory encephalopathy. Depression.	94	41	54
Neurocirculatory dystonia	17	9	8
Risk to blood cerebral hemisphere vessel spasm	22	10	12

Table 2: Bexel data results for neurocirculatory pathologies related to the pupil.

The researcher observed an even distribution of oval-vertical and oval-diagonal forms between the left and right pupils in the 12 case studies that exhibited both types of pupillary deformation [tbl. 3].

Pupil Ellipse Location	Form	Right Pupil	Left Pupil
Right Pupil -	Oval-vertical form	6	
Left Pupil	Oval-vertical form		6
Right Pupil	Oval-diagonal form	6	
Left Pupil	Oval-diagonal form		6

Table 3: Pupil deformation location for oval-vertical and oval-diagonal forms.

Discussion

Pupillary examination is not as commonly used in modern medical practice as it once was, due in part to the availability of more sophisticated diagnostic tools such as CT and MRI. However, these imaging techniques may not always be readily available, particularly in developing countries and rural areas, making pupillary assessment a potentially valuable diagnostic tool in these settings.

While modern imaging technology has greatly improved our ability to diagnose and monitor neurological diseases, there are still limitations and challenges to access in certain regions and populations. The use of pupillary assessment as a non-invasive, low-cost, and easily accessible diagnostic tool may have the potential to improve healthcare outcomes for individuals in these areas. However, as with any diagnostic tool, it's important to continue to evaluate and validate its effectiveness through scientific investigation.

This study aimed to investigate the relationship between pupillary abnormalities and ischemic cerebral strokes. The researcher used the Bexel Irina pupillary assessment software to analyze 468 case studies and found that combinations of oval-vertical and oval-diagonal forms in alternating eyes were present in 12 cases, with eight cases verified as ischemic stroke.

Two pre-ischemic case studies were notable in that both individuals exhibited both oval-vertical and oval-diagonal pupil forms in their initial pupillary assessments before experiencing cerebral ischemic strokes.

The results of this study indicate that there may be an association between certain types of pupillary multiform conditions, specifically the combination of oval-vertical and oval-diagonal forms in alternating eyes, and ischemic cerebral strokes. While the overall prevalence of these conditions in the studied population was relatively low, it is noteworthy that all three cases of stroke in the study presented with this combination of pupillary forms.

It should be emphasized that the accuracy of pupillary assessment results can be greatly influenced by the lighting conditions and patient positioning. A pre-stroke case study presented a false positive result of 20.00% lower nasal flatness in the left pupil due to the light source obstructing the pupil border between 6:22 and 10:04. This underscores the importance of standardized procedures and equipment to ensure consistent and reliable pupillary assessments. [fig 2].

The results of this study suggest that further investigation into the relationship between pupillary multiform conditions and ischemic strokes is warranted. This highlights the importance of pupillary assessments in identifying potential underlying health conditions affecting the eyes and the nervous system.

Additionally, the development of new pupillary assessment software using machine learning techniques may lead to higher accuracy and the discovery of new pupillary signs with diagnostic significance.

Conclusion

The study concludes that pupillary abnormalities could potentially be used as an early indicator of ischemic cerebral strokes and that further research in this area is needed. The researcher also suggests that the development of new pupillary assessment software with machine learning techniques could lead to higher accuracy in detecting pupillary abnormalities and potentially identifying new unknown pupillary signs of diagnostic significance.

Overall, this study highlights the potential value of pupillary assessment in the diagnosis and management of neurological conditions, particularly in resource-limited settings where advanced imaging techniques may not be readily available in underdeveloped countries.

It's important to note that while the pupillary assessment software used in the study can detect anomalies in the pupil, it is not a substitute for a medical diagnosis or examination by a qualified healthcare professional. The results of the study should be interpreted with caution and not used to make any medical decisions or diagnoses.

Further Research

Further research and development includes the integration of machine learning techniques that can potentially enhance the accuracy and reliability of pupillary assessment in diagnosing various neurological conditions. Machine learning algorithms can be trained on large datasets of pupillary images, allowing for the detection of subtle patterns and anomalies that may not be discernible to the human eye.

Additionally, the use of artificial intelligence may allow for real-time analysis and interpretation of pupillary data, potentially reducing the time and resources required for diagnosis. As technology continues to advance, it is likely that pupillary assessment will become an increasingly important tool in the diagnosis and treatment of neurological disorders.

Conflict of Interest Statement

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Keywords: human pupils, oval-vertical pupil, oval-diagonal pupil, ischemic stroke, neurology

Author: Bryan K. Marcia, Ph.D. Professor Emeritus (2006), Dept. of Natural Medicine, Capital University of Integrative Medicine

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