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ORIGINAL ARTICLE

Structural and Functional Assessment of the Visual Analyzer in Acute Ischemic Optic Neuropathy

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Abstract

Acute ischemic optic neuropathy (AION) is a vision-threatening disorder characterized by sudden impairment of optic nerve perfusion, leading to structural damage of the visual pathway and rapid deterioration of visual function. It is one of the leading causes of acute optic nerve dysfunction in middle-aged and elderly individuals and is frequently associated with systemic vascular diseases such as hypertension, diabetes mellitus, atherosclerosis, hyperlipidemia, and cardiovascular disorders. The visual analyzer, which consists of the retina, optic nerve, optic chiasm, optic tract, lateral geniculate nucleus, optic radiations, and visual cortex, functions as an integrated system responsible for the perception and processing of visual information. Acute ischemic injury affecting any component of this pathway, particularly the optic nerve, disrupts signal transmission and leads to functional visual deficits that may become irreversible if treatment is delayed.

The optic nerve has one of the highest metabolic demands within the central nervous system because retinal ganglion cell axons require continuous oxygen and glucose delivery to maintain axonal transport and electrical conduction. Interruption of blood supply causes rapid depletion of intracellular adenosine triphosphate (ATP), resulting in failure of membrane ion pumps, intracellular calcium accumulation, mitochondrial dysfunction, oxidative stress, excitotoxic injury, inflammatory activation, and programmed cell death. These pathological mechanisms produce progressive degeneration of retinal ganglion cells and optic nerve fibers while simultaneously impairing conduction throughout the visual pathway.

Structural alterations within the visual analyzer are closely associated with measurable functional abnormalities. Morphological changes such as optic disc edema, retinal nerve fiber layer thinning, axonal degeneration, demyelination, retinal ganglion cell loss, and microvascular damage are accompanied by decreased visual acuity, visual field defects, impaired contrast sensitivity, delayed visual evoked potentials, reduced retinal electrophysiological activity, and diminished visual processing within central visual pathways. Simultaneous evaluation of structural and functional changes provides comprehensive information regarding disease severity, progression, and therapeutic response.

Recent advances in ocular imaging, electrophysiology, histopathology, immunohistochemistry, and digital morphometry have substantially improved the ability to investigate the relationship between structural injury and functional impairment in acute ischemic optic neuropathy. Comprehensive assessment of these alterations is essential for understanding disease mechanisms, establishing objective diagnostic criteria, and developing effective neuroprotective treatment strategies capable of preserving visual function.

Keywords: Acute Ischemic Optic Neuropathy (AION), Visual Analyzer, Structural Assessment, Functional Assessment, Optical Coherence Tomography (OCT), Visual Field Testing,

Optic Nerve Damage, Retinal Nerve Fiber Layer (RNFL), Visual Function, Ocular Imaging.

1. Introduction

The objective of this study was to evaluate structural and functional alterations of the visual analyzer following acute ischemic optic neuropathy by analyzing morphological changes in the retina and optic nerve together with functional abnormalities of visual signal transmission. The study also aimed to determine the relationship between tissue degeneration, retinal ganglion cell loss, optic nerve injury, electrophysiological dysfunction, and impairment of visual performance using comprehensive morphological and functional assessment methods.

2. Materials and Methods

The study was conducted using healthy adult Wistar rats maintained under standardized laboratory conditions with controlled environmental temperature, humidity, and a twelve-hour light-dark cycle. Animals received unrestricted access to food and water throughout the experimental period. All experimental procedures were approved by the institutional ethics committee and performed according to internationally accepted guidelines for laboratory animal research.

Acute ischemic optic neuropathy was induced by temporary elevation of intraocular pressure sufficient to produce reversible interruption of optic nerve head perfusion while avoiding direct mechanical injury to retinal structures. Following the ischemic interval, controlled reperfusion was established. A control group underwent identical anesthesia and experimental manipulation without induction of ischemia.

Animals were evaluated at 24 hours, 72 hours, and seven days after reperfusion to investigate sequential structural and functional alterations. Ophthalmological examination included fundoscopy for assessment of optic disc morphology and retinal vascular appearance. Optical coherence tomography was performed to measure retinal nerve fiber layer thickness, ganglion cell complex thickness, and optic nerve head morphology.

Visual function was evaluated by measurement of visual evoked potentials (VEPs), flash electroretinography (ERG), pupillary light reflex, visual behavioral responses, and optokinetic tracking. VEP recordings were analyzed for latency and amplitude changes reflecting conduction through the visual pathway. Electroretinography assessed retinal electrical activity by measuring a-wave and b-wave amplitudes together with implicit times.

Following functional assessment, retinal tissue and optic nerves were collected for histological examination. Hematoxylin and eosin staining was used to evaluate general tissue morphology, while Luxol Fast Blue staining assessed myelin integrity. Cresyl Violet staining was performed to quantify retinal ganglion cells. Immunohistochemical analysis included glial fibrillary acidic protein (GFAP), ionized calcium-binding adaptor molecule-1 (Iba-1), cleaved caspase-3, vascular endothelial growth factor (VEGF), and hypoxia-inducible factor-1 alpha (HIF-1α). Transmission electron microscopy was used to evaluate ultrastructural alterations of retinal ganglion cells, axons, mitochondria, synaptic structures, and myelin sheaths.

3. Results

Acute ischemic optic neuropathy produced significant structural abnormalities throughout the visual analyzer. Fundoscopic examination demonstrated optic disc edema during the early stage of ischemia accompanied by narrowing of retinal arterioles and mild venous congestion. During later observation periods, progressive optic disc pallor became evident, indicating optic nerve atrophy secondary to neuronal degeneration.

Optical coherence tomography demonstrated a transient increase in retinal nerve fiber layer thickness during the acute stage due to intracellular and extracellular edema. As ischemic injury progressed, retinal nerve fiber layer thickness gradually decreased below normal values because of axonal degeneration and retinal ganglion cell loss. Significant thinning of the ganglion cell complex was observed seven days after ischemia, confirming progressive neuronal degeneration.

Histological examination demonstrated extensive structural damage within both retinal tissue and the optic nerve. Retinal ganglion cells exhibited cytoplasmic shrinkage, nuclear pyknosis, chromatin condensation, and formation of apoptotic bodies. Axonal swelling was followed by fragmentation of nerve fibers, disruption of neurofilament organization, vacuolar degeneration, and progressive demyelination. Luxol Fast Blue staining revealed marked disorganization and separation of myelin lamellae, indicating severe impairment of axonal insulation.

Immunohistochemical analysis demonstrated significant overexpression of GFAP within astrocytes, reflecting extensive reactive gliosis throughout the optic nerve and retina. Iba-1 immunoreactivity increased markedly due to activation and proliferation of microglial cells surrounding degenerating neurons. Cleaved caspase-3 expression confirmed widespread apoptosis of retinal ganglion cells, while increased HIF-1α expression indicated severe tissue hypoxia. VEGF expression increased during later observation periods, suggesting activation of compensatory angiogenic mechanisms.

Electron microscopy demonstrated profound ultrastructural abnormalities including swollen mitochondria with disrupted cristae, fragmentation of neurofilaments, degeneration of synaptic terminals, separation of myelin layers, endothelial swelling, and thickening of capillary basement membranes. These findings confirmed that ischemia affected both neuronal and vascular components of the visual analyzer.

Functional evaluation demonstrated substantial deterioration of visual performance. Visual evoked potentials showed significant prolongation of P100 latency together with marked reduction of response amplitude, indicating slowed conduction along damaged optic nerve fibers.

Electroretinography demonstrated reduced amplitudes of both a-wave and b-wave responses, reflecting impaired retinal function. Pupillary light reflexes became delayed, while behavioral visual tests demonstrated decreased visual orientation and impaired optokinetic responses.

Statistical analysis demonstrated a strong correlation between structural degeneration and functional impairment. Progressive reduction in retinal ganglion cell density and retinal nerve fiber layer thickness was closely associated with prolonged visual evoked potential latency, decreased electrophysiological responses, and worsening behavioral visual performance.

4. Discussion

The present investigation demonstrates that acute ischemic optic neuropathy simultaneously produces profound structural damage and functional impairment throughout the visual analyzer. Structural degeneration of retinal ganglion cells and optic nerve fibers directly compromises transmission of visual information from the retina to higher visual centers, thereby explaining the rapid deterioration of visual function observed during the experimental period.

One of the earliest structural alterations identified in this study was optic disc edema accompanied by swelling of retinal nerve fibers. This change resulted from disruption of axonal transport and intracellular accumulation of water secondary to failure of ATP-dependent ion transport mechanisms. Although edema initially represents a reversible response, persistent tissue swelling compresses surrounding capillaries, further reducing blood supply and accelerating neuronal injury.

The progressive reduction in retinal nerve fiber layer thickness observed during later stages reflects irreversible axonal degeneration. Retinal ganglion cell death inevitably leads to loss of optic nerve fibers because these neurons constitute the sole source of optic nerve axons. Consequently, structural degeneration of retinal tissue closely parallels deterioration of optic nerve integrity. The strong correlation identified between retinal nerve fiber layer thickness and visual evoked potential abnormalities demonstrates that anatomical preservation is essential for maintenance of normal visual conduction.

Electrophysiological findings further confirmed functional impairment of the visual analyzer. Prolonged visual evoked potential latency indicates delayed transmission of electrical impulses through damaged optic nerve fibers, whereas reduced response amplitude reflects decreased numbers of functioning axons. Simultaneous reduction of electroretinographic responses demonstrates that ischemic injury extends beyond the optic nerve and influences retinal neuronal activity as well.

Reactive gliosis and microglial activation contributed substantially to secondary neuronal injury. Although astrocytes initially support neuronal survival by maintaining extracellular homeostasis and providing metabolic support, prolonged activation promotes glial scar formation that limits axonal regeneration. Activated microglia release inflammatory cytokines, reactive oxygen species, and

proteolytic enzymes that amplify neuronal degeneration beyond the primary ischemic lesion. Ultrastructural mitochondrial damage identified in this study further explains the progressive deterioration of visual function. Mitochondrial disruption impairs ATP synthesis, increases oxidative stress, and activates apoptotic pathways responsible for retinal ganglion cell death. Preservation of mitochondrial integrity therefore represents a promising therapeutic target for maintaining both structural and functional integrity of the visual analyzer.

The close relationship observed between morphological alterations and electrophysiological dysfunction emphasizes the importance of combined structural and functional assessment in experimental studies of acute ischemic optic neuropathy. Integration of optical coherence tomography, electrophysiological testing, histopathology, immunohistochemistry, and electron microscopy provides a comprehensive evaluation of disease progression and allows objective assessment of potential neuroprotective therapies.

5. Conclusion

Acute ischemic optic neuropathy produces extensive structural and functional abnormalities affecting every major component of the visual analyzer. Progressive degeneration of retinal ganglion cells, optic nerve fibers, myelin sheaths, and microvascular structures is accompanied by deterioration of visual acuity, delayed electrophysiological responses, impaired retinal function, and reduced visual performance. The severity of functional impairment closely reflects the extent of structural damage. Comprehensive assessment combining morphological examination, ocular imaging, electrophysiological testing, and ultrastructural analysis provides reliable evaluation of disease progression and establishes a strong relationship between anatomical injury and visual dysfunction. These findings demonstrate that structural degeneration and functional impairment develop simultaneously and interact continuously throughout the course of acute ischemic optic neuropathy. Early identification of structural alterations before irreversible neuronal loss occurs may significantly improve therapeutic outcomes. Future research should focus on the development of advanced diagnostic biomarkers, neuroprotective treatment strategies, mitochondrial preservation, reduction of inflammatory responses, enhancement of microvascular circulation, and stimulation of neuronal regeneration in order to maintain both structural integrity and functional performance of the visual analyzer following acute ischemic optic neuropathy.

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