

PERCEPTUAL AND NEURAL MECHANISMS OF STATIC AND DYNAMIC STEREOPSIS IN BINOCULAR VISUAL IMPAIRMENTS

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PERCEPTUAL AND NEURAL MECHANISMS OF STATIC AND DYNAMIC STEREOPSIS IN BINOCULAR VISUAL IMPAIRMENTS

by

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Dedicated to

My Parents

“Money comes and goes, but morality comes and grows”

—Bhagawan Sri Sathya Sai Baba

Certificate

This is to certify that the thesis entitled “**Perceptual and Neural mechanisms of Static and Dynamic Stereopsis in Binocular Visual Impairments**” being submitted by **Ms. Kritika Lohia** to the Department of Electrical Engineering, Indian Institute of Technology-Delhi, for the award of the degree of **Doctor of Philosophy** is the record of the bonafide research work carried out by her under our supervision. In our opinion, the thesis has reached the standards fulfilling the requirements of the regulations relating to the degree.

The results contained in this thesis have not been submitted either in part or in full to any other university or institute for the award of any degree or diploma.

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Abstract

Vision is arguably the most vital sense for humans, providing a medium by which they perceive, interpret and interact with the world. It is the seamless association between the eyes, brain and several neural pathways that generates our perception of the surrounding environment. Central to this process is stereopsis, an ability to perceive 3-dimensional (3D) world based on the inputs received from both eyes simultaneously. Nevertheless, not everyone possesses an ideal association of the ocular and cerebral functions. Individuals having visual disorders such as eye misalignment (or squint or strabismus), lazy eye (amblyopia), cataracts and even refractive errors have disruptions in the accurate perception of depth. Consequently, to understand the perceptual and neural aspects of stereopsis, I utilize psychophysics and Functional Magnetic Resonance Imaging (fMRI) in patients with stereo-deficits and age-matched visually healthy population.

First, I redefine a crucial interval from birth to surgery for achieving stereopsis in patients with congenital cataract. For this, I use a systematic quantitative approach that integrates the results of existing studies to evaluate the presence of stereopsis post-cataract extraction. I take the study-specific proportions of stereopsis from 923 children using a random-effects model and stratify them based on the intervention age and the presence of strabismus. I find that birth to surgery interval of 4–6 months is crucial for stereopsis in congenital cataract. I also find that stereopsis drops by 9%–16% in congenital cataracts with pre-existing strabismus.

Then, I turn towards the creation of a random-dot stereogram (RDS) based stereoacu-

ity test for the detection and evaluation of stereopsis. In the current clinical scenario, the routinely used stereoacuity tests rely on expensive and imported printed books. These books are difficult to procure and fade over time involving recurrent costs. Therefore, I first create a digital stereoacuity test and perform a disparity plate-wise comparison with a clinical stereotest - TNO (The Netherlands Organization) in a wide range of stereo-deficit patients and visually healthy controls. Next, I extend this test by (i) adjusting for the ambient lighting and, (ii) incorporating a comprehensive and continuous framework for the detection and evaluation of stereopsis. I find that there are subtle changes in observed stereoacuity when the ambient lighting is not adjusted for, specifically in stereo-deficit patients. I also show that the overall test can be performed in significantly lesser time (approximately 5-10 minutes) compared to other research grade computer-based stereoacuity tests.

In the latter part of the thesis, I explore the neural mechanisms of the static and dynamic stereopsis. Under static stereopsis, I investigate causal mechanisms of coarse and fine binocular disparity processing using fMRI with a clinically validated, custom anaglyph-based stimulus with four disparity magnitudes, namely - 800 arc-sec, 480 arc-sec, 240 arc-sec and 120 arc-sec. Consequently, I use graph theoretical metrics such as degree and participation coefficient metrics representing rich and diverse properties of the brain network, respectively. Through experiments on visually healthy controls, I find that distinct rich and diverse clubs exist across different disparity magnitudes. Among all, the Middle Temporal (MT) brain region serves as the only common rich and diverse region across all disparity magnitudes and in both hemispheres. I also demonstrate that diverse clubs exhibit better performance in decoding disparity magnitudes, thereby providing further support to the growing evidence that diverse clubs are indeed the integrative core for processing disparities. Lastly, I show that there are subtle inter-hemispheric differences across different disparity conditions.

To explore dynamic stereopsis, I analyse the neural response of patients having Intermittent Exotropia (IDS) and age-matched visually healthy controls to a continu-

ously moving target in 3D Brownian motion. Specifically, I use One-vs-One Support Vector Classifier (OVO-SVC) to decode fronto-parallel (x & y) and depth (z) positions while the participants gaze at the moving target. In visually healthy controls, I find that both fronto-parallel and depth positions could be decoded with above chance accuracy, however, these depth positions are decoded slower compared to fronto-parallel counterparts. Notably, there is no such association in IDS patients.

In summary, the work presented in this thesis offer a comprehensive understanding of stereopsis in terms of both translational and fundamental visual science. It not only enables interactive assessment of stereopsis for ophthalmologists and optometrists but also contribute to advancing our knowledge of the neural mechanisms related to oculomotor behavior in both clinical and visually healthy populations.

सार

दृष्टि यकीनन मनुष्यों के लिए सबसे महत्वपूर्ण इंद्रिय है, जो उन्हें दुनिया को देखने, व्याख्या करने और उससे बातचीत करने का माध्यम प्रदान करती है। यह आंखों, मस्तिष्क और कई तंत्रिका मार्गों के बीच सहज जुड़ाव है जो हमारे आस-पास के वातावरण की धारणा को उत्पन्न करता है। इस प्रक्रिया का केंद्र स्टीरियोप्सिस है, जो एक साथ दोनों आंखों से प्राप्त इनपुट के आधार पर 3-आयामी दुनिया को देखने की क्षमता है। फिर भी, हर किसी के पास नेत्र और मस्तिष्क के कार्यों का एक आदर्श जुड़ाव नहीं होता है। जिन व्यक्तियों में दृश्य विकार जैसे कि आँख का गलत संरेखण (या भेंगापन), आलसी आँख (एम्ब्लियोपिया), मोतियाबिंद और यहाँ तक कि अपवर्तक त्रुटियाँ होती हैं, उनमें गहराई की सटीक धारणा में व्यवधान होता है। नतीजतन, स्टीरियोप्सिस के अवधारणात्मक और तंत्रिका पहलुओं को समझने के लिए, मैं स्टीरियो-घाटे वाली रोगियों और उम्र के हिसाब से स्वस्थ आबादी में साइकोफिजिक्स और फंक्शनल मैग्नेटिक रेजोनेंस इमेजिंग का उपयोग करती हूँ।

सबसे पहले, मैं जन्मजात मोतियाबिंद वाली रोगियों में स्टीरियोप्सिस प्राप्त करने के लिए जन्म से सर्जरी तक के महत्वपूर्ण अंतराल को फिर से परिभाषित करती हूँ। इसके लिए, मैं एक व्यवस्थित मात्रात्मक दृष्टिकोण का उपयोग करती हूँ जो मोतियाबिंद निष्कर्षण के बाद स्टीरियोप्सिस की उपस्थिति का मूल्यांकन करने के लिए मौजूदा अध्ययनों के परिणामों को एकीकृत करती हूँ। मैं यादृच्छिक-प्रभाव मॉडल का उपयोग करके 923 बच्चों से स्टीरियोप्सिस के अध्ययन-विशिष्ट अनुपात लेती हूँ और उन्हें हस्तक्षेप की उम्र और स्ट्रैबिस्मस की उपस्थिति के आधार पर स्तरीकृत करती हूँ। मुझे लगता है कि जन्मजात मोतियाबिंद में स्टीरियोप्सिस के लिए जन्म से सर्जरी के बीच 4-6 महीने का अंतराल महत्वपूर्ण है। मुझे यह भी लगता है कि पहले से मौजूद स्ट्रैबिस्मस के साथ जन्मजात मोतियाबिंद में स्टीरियोप्सिस 9%-16% तक कम हो जाता है।

फिर, मैं स्टीरियोप्सिस का पता लगाने और मूल्यांकन करने के लिए एक यादृच्छिक-डॉट स्टीरियोग्राम आधारित स्टीरियोएक्यूइटी परीक्षण के निर्माण की ओर मुड़ती हूँ। वर्तमान नैदानिक परिदृश्य में, नियमित रूप से उपयोग किए जाने वाले स्टीरियोएक्यूइटी परीक्षण महंगी और आयातित मुद्रित पुस्तकों पर निर्भर करते हैं।

इन पुस्तकों को प्राप्त करना मुश्किल है और समय के साथ ये फीकी पड़ जाती हैं और इसमें बार-बार खर्च होता है। इसलिए, मैं सबसे पहले एक डिजिटल स्टीरियोएक्यूइटी टेस्ट बनाती हूँ और स्टीरियो-डेफिसिट वाली मरीजों और दृष्टिगत रूप से स्वस्थ नियंत्रणों की एक विस्तृत श्रृंखला में एक क्लिनिकल स्टीरियोटेस्ट – टीएनओ (नीदरलैंड संगठन) के साथ असमानता प्लेट-वार तुलना करती हूँ। इसके बाद, मैं (क) परिवेश प्रकाश व्यवस्था के लिए समायोजन करके और (ख) स्टीरियोप्सिस का पता लगाने और मूल्यांकन के लिए एक व्यापक और निरंतर रूपरेखा को शामिल करके इस परीक्षण का विस्तार करती हूँ। मुझे लगता है कि जब परिवेश प्रकाश व्यवस्था के लिए समायोजन नहीं किया जाता है, तो विशेष रूप से स्टीरियो-डेफिसिट वाली मरीजों में देखी गई स्टीरियोएक्यूइटी में सूक्ष्म परिवर्तन होते हैं। मैं यह भी दिखाती हूँ कि समग्र परीक्षण अन्य शोध ग्रेड कंप्यूटर-आधारित स्टीरियोएक्यूइटी परीक्षणों की तुलना में काफी कम समय (लगभग 5-10 मिनट) में किया जा सकता है।

थीसिस के उत्तरार्ध में, मैं स्थिर और गतिशील स्टीरियोप्सिस के तंत्रिका तंत्र का पता लगाती हूँ। स्टैटिक स्टीरियोप्सिस के तहत, मैं चार असमानता परिमाणों के साथ एक चिकित्सकीय रूप से मान्य, कस्टम एनाग्लिफ़-आधारित उत्तेजना के साथ फंक्शनल मैग्नेटिक रेजोनेंस इमेजिंग का उपयोग करके मोटे और महीन द्विनेत्री असमानता प्रसंस्करण के कारण तंत्र की जांच करती हूँ, अर्थात् – 800 आर्क-सेकंड, 480 आर्क-सेकंड, 240 आर्क-सेकंड और 120 आर्क-सेकंड। नतीजतन, मैं क्रमशः मस्तिष्क नेटवर्क के समृद्ध और विविध गुणों का प्रतिनिधित्व करने वाले डिग्री और भागीदारी गुणांक मीट्रिक जैसे ग्राफ सैद्धांतिक मेट्रिक्स का उपयोग करती हूँ। नेत्रहीन स्वस्थ नियंत्रणों पर प्रयोगों के माध्यम से, मुझे पता चलता है कि अलग-अलग समृद्ध और विविध क्लब अलग-अलग असमानता परिमाणों में मौजूद हैं। इन सबके बीच, मध्य टेम्पोरल (एमटी) मस्तिष्क क्षेत्र सभी असमानता परिमाणों और दोनों गोलार्धों में एकमात्र आम समृद्ध और विविध क्षेत्र के रूप में कार्य करता है। मैं यह भी प्रदर्शित करती हूँ कि विविध क्लब असमानता परिमाणों को डिकोड करने में बेहतर प्रदर्शन करते हैं, जिससे बढ़ते सबूतों को और अधिक समर्थन मिलता है कि विविध क्लब वास्तव में असमानताओं को संसाधित करने के लिए एकीकृत कोर हैं। अंत में, मैं दिखाती हूँ कि विभिन्न असमानता स्थितियों में सूक्ष्म अंतर-गोलाद्धीय अंतर हैं। गतिशील स्टीरियोप्सिस का पता लगाने के लिए, मैं 3-आयामी ब्राउनियन गति में लगातार चलते लक्ष्य के लिए इंटरमिटेंट एक्सोट्रोपिया वाली रोगियों और आयु-मिलान वाले दृष्टिगत स्वस्थ नियंत्रणों की तंत्रिका प्रतिक्रिया का विश्लेषण करती हूँ। विशेष रूप से, मैं प्रतिभागियों द्वारा चलते लक्ष्य पर टकटकी लगाए रखने के दौरान फ्रंटो-समानांतर और गहराई स्थितियों को डिकोड करने के लिए वन-बनाम-वन सपोर्ट वेक्टर क्लासिफायर का उपयोग करती हूँ। दृष्टिगत रूप से स्वस्थ नियंत्रणों में, मुझे लगता है कि फ्रंटो-समानांतर और गहराई दोनों स्थितियों को संभावना से अधिक सटीकता के साथ डिकोड किया जा सकता है, हालाँकि, इन गहराई स्थितियों को फ्रंटो-समानांतर समकक्षों की तुलना में धीमी

गति से डिकोड किया जाता है। उल्लेखनीय रूप से, गतिशील स्टीरियोप्सिस रोगियों में ऐसा कोई संबंध नहीं है।

संक्षेप में, इस थीसिस में प्रस्तुत कार्य अनुवादात्मक और मौलिक दृश्य विज्ञान दोनों के संदर्भ में स्टीरियोप्सिस की व्यापक समझ प्रदान करता है। यह न केवल नेत्र रोग विशेषज्ञों और ऑप्टोमेट्रिस्ट के लिए स्टीरियोप्सिस के इंटरैक्टिव मूल्यांकन को सक्षम बनाता है, बल्कि नैदानिक और दृष्टिगत रूप से स्वस्थ आबादी दोनों में ऑकुलोमोटर व्यवहार से संबंधित तंत्रिका तंत्र के बारे में हमारे ज्ञान को आगे बढ़ाने में भी योगदान देती है।

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Abbreviations

3D	3-Dimensional
AIC	Akaike Information Criterion
AIIMS	All India Institute of Medical Sciences
AGC	Adaptive Gamma Calibration
BCVA	Best Corrected Visual Acuity
CDOT	Changing Disparity over time
CI	Confidence Interval
CL	Contact Lens
D	Degree
DOF	Degrees of Freedom
DST	Digital Stereo Test
DT	Decision Tree
e-RDS	electronic Random Dot Stereogram
FEF	Frontal Eye Field
FOV	Field of View
fMRI	Functional Magnetic Resonance Imaging
FST	Fundus of Superior Temporal Sulcus
GC	Granger Causality
BOLD	Blood Oxygen Level Dependent Signal
HVS	Human Visual System
IA	Induced Anisometropia
ICC	Intra Class Correlation
IDS	Intermittent Divergent Squint or Intermittent Exotropia

IIT	Indian Institute of Technology
IOL	Intraocular Lens
IOVD	Inter Ocular Velocity Differences
IPS	Intraparietal Sulcus
IT	Inferior Temporal
LO	Lateral Occipital
MAR	Multivariate Auto Regression
MOG	Middle Occipital Gyrus
MT	Middle Temporal
OVO-SVC	One-vs-One Support Vector Classifier
PC	Participation Coefficient
PCN	Precuneus
PEF	Precentral Eye Field
PMd	Dorsal Premotor
PRISMA	Preferred Reporting Items for Systematic Review and Meta Analyses
PROSPERO	International prospective register of systematic reviews
RDS	Random Dot Stereogram
ROI	Region of Interest
SMA	Supplementary Motor Area
SN	Scrambled Noise
ST	Stereoacuity Testing
TE	Echo Time
TNO	The Netherlands Organization
TP	Time Point
TPO	Temporo-Parieto-Occipital junction
TR	Repetition Time
V2v	Ventral V2
V3d	Dorsal V3
VIP	Ventral Intraparietal