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Developing Robust Methods and Tools for Advancing Perceptual Learning Research

A Dissertation submitted in partial satisfaction
of the requirements for the degree of

Doctor of Philosophy

in

Psychology

by

Samyukta Jayakumar

June 2024

Dissertation Committee:
Dr. Aaron Seitz, Chairperson
Dr. Weiwei Zhang
Dr. Edward Zagha

The Dissertation of Samyukta Jayakumar is approved:

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Committee Chairperson

University of California, Riverside

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horizons and refine my skills. I consider myself incredibly fortunate to have benefited from the guidance of such an inspiring, and intellectually gifted mentor, whose unwavering belief in my potential has been the cornerstone of my academic journey at UCR. To you, I owe a debt of gratitude for providing a conducive environment for growth, and the opportunity to explore diverse domains of research. As I venture forth into new pursuits, I earnestly aspire to continue receiving your invaluable guidance and support.

DEDICATIONS

"Matha, Pitha, Guru, Deivam" - an ancient and popular Sanskrit phrase that stands for "Mother, Father, Teacher, God" and in that order, highlights the importance of the role that each of them has in the growth of an individual. Rightfully so, I wouldn't have accomplished my PhD without the unwavering support and strength that my parents have provided during the last 5 years from a hop, skip and jump of a few continents and thousands of miles away. I am incredibly grateful for having Sarada (my mom) and Jayakumar (my dad) as my parents and I dedicate my life's work to them. To my sister Samrakshita, thank you for being the best cheerleader and the best friend I could ever ask for. It would have been incredibly hard to have achieved this feat in my life without you by my side, assuring me that I can achieve whatever I set my mind to, and most importantly ensuring that everything and everyone will be fine during the pandemic. I dedicate my PhD to my loving grandmothers Kamalakshi and Parimala and my beloved grandfather, Balasubramanian, who I hope are proudly cheering for me as always from the stars.

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ABSTRACT OF THE DISSERTATION

Developing Robust Methods and Tools for Advancing Perceptual Learning Research

by

Samyukta Jayakumar

Doctor of Philosophy, Graduate Program in Psychology
University of California, Riverside, June 2024
Dr. Aaron Seitz, Chairperson

Perceptual Learning (PL) refers to experience-based changes enhancing the ability to extract sensory information from the environment leading to alterations in perceptual processing. A pivotal inquiry in this field investigates the potential for adult perceptual systems to undergo modifications through experience. While historically, research in the field has primarily delved into isolating and understanding individual visual processes, recent years have witnessed a growing interest in harnessing PL for therapeutic interventions in visual impairments. However, the translational potential of such interventions is impeded by methodological constraints, including small sample sizes, homogeneity within participant populations, and challenges in replications. The core objective of my dissertation is to advance our understanding of visual PL by designing

innovative methodologies and tools to explore its potential for translational applications. Each chapter of my dissertation contributes distinctively to this overarching aim: Chapter 1 provides a comprehensive review of extant PL literature, pinpointing prevailing limitations and gaps in the field; Chapter 2 introduces and validates PLFest, a cross platform open-source tool for PL research, fostering collaboration and data sharing within the scientific community; Chapter 3 introduces a gaze contingent display framework for PL research, utilizing simulated central vision loss as a model to assess specificity and generalizability of learning; and Chapter 4 examines the implications of a gamified visual rehabilitation strategy for promoting learning and designing targeted interventions for patients with schizophrenia. Through these multifaceted investigations, my thesis aims to deepen our understanding of visual PL dynamics and lay foundations for its broader application in clinical contexts.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

PL - Perceptual Learning
VPL - Visual Perceptual Learning
V1 - Primary visual cortex
MT - Medial temporal lobe
LIP - Lateral intraparietal cortex
PIT - Posterior inferior temporal cortex
LO - Lateral occipital cortex
FFA - Fusiform face area
IRT - Integrated Reweighting Theory
CS – Contrast Sensitivity
VA – Visual Acuity
AWS – Amazon Web Services
HIPAA – Health Insurance Portability and Accountability Act
MAR – Minimal Angle of Resolution
LOA – Limits of Agreement
LCD – Liquid Crystal Display
FrACT – Freiburg Acuity and Contrast Test
DDART – Democritus Digital Acuity Reading Test
API – Application Programming Interface
MD – Macular Degeneration
CVL – Central Vision Loss
s-CVL - Simulated Central Vision Loss
PRL – Preferred Retinal Locus
CRS – Cambridge Research Systems
CRT – Cathode Ray Tube
IR – InfraRed
MNRead – Minnesota Reading Task
RSVP – Rapid Serial Visual Presentation
URL – Untrained Retinal Locus
RT diff – Reaction Time difference
BCEA – Bivariate Contour Ellipse Area
KDE – Kernal Density Estimator
MAIA – Macular Integrity Assessment
SZ – Schizophrenia
NT – Neurotypical individuals
CI – Contour Integration
ERP – Event Related Potentials
fMRI – Functional Magnetic Resonance Imaging
CNTRICS – Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia
OJ – Orientation Jitter
IN – Inducer Number
dva – Degrees of visual angle
MM-ANOVA – Mixed Methods Analysis of Variance
RBC – Recognition by Components
EEG – Electroencephalogram

LIST OF FIGURES

LIST OF TABLES

Chapter 1: Introduction

A fundamental aspect of our day-to-day activities largely involves learning to process and interact with a rich set of incoming sensory input from the world. This leads to changes in perceptual systems across the lifespan of an individual (Seitz, 2021) and has broad implications for education, medicine, technology, and society (Seitz et al., 2023). These experience-based changes enhancing the ability to optimize the incoming sensory information is called Perceptual Learning (PL). PL occurs in all sensory modalities, including vision (Karni & Sagi, 1991), audition (Wright et al., 1997), touch (Dinse et al., 2003), smell (Chu et al., 2016), taste (Arvisenet et al., 2016), and multimodal combinations (B. Dosher & Lu, 2020), and can significantly improve performance (Karni & Sagi, 1991) and persist for years (Zhou et al., 2006). In laboratory settings, PL is typically studied by tracking performance improvements in perceptual tasks through practice or training.

Historical Significance and Background:

Visual perceptual learning (VPL) is one of the most extensively researched perceptual phenomena dating back to the end of the 19th century (Volkman,1858), however, it wasn't till the 1960s that PL was identified as an important subject for scientific inquiry until Eleanor Gibson put PL on the map. In the laboratory, this is typically studied using tasks such as orientation discrimination (Fiorentini & Berardi, 1980), line bisection (Poggio et al., 1992), texture discrimination (Karni & Sagi, 1991), motion direction discrimination (Ball & Sekuler, 1982) etc., (Figure 1.1), and have shown improved

performance as a result of training. A defining characteristic of VPL is its remarkable specificity, which extends to various aspects such as retinal location, eye, stimulus, and task. This has been well documented across a range of studies, including those focusing on contrast detection (Sowden et al., 2002), orientation discrimination (A. A. Schoups et al., 1995), texture discrimination (Karni & Sagi, 1991), motion-direction discrimination (Ball & Sekuler, 1987), depth from random-dot stereograms (O'Toole & Kersten, 1992), and localization tasks (Crist et al., 1997). Interestingly, while some tasks have shown specificity to the trained eye compared to the untrained eye (see (Karni & Sagi, 1991; Schwartz et al., 2002)), others have exhibited significant specificity to particular features of the trained stimulus, such as orientation (Ball & Sekuler, 1982; Fiorentini & Berardi, 1980; Poggio et al., 1992; Ramachandran & Braddick, 1973), spatial frequency (Huang et al., 2008; Sowden et al., 2002), and tasks themselves (Fiorentini & Berardi, 1980; Furmanski & Engel, 2000). While specificity of PL is critical for understanding the locus of plasticity in brain regions, it limits the benefits of training to the trained stimuli and tasks, making it difficult to generalize learning to other stimuli or tasks. Transfer of learning is also critical for real-world application of PL as well as for developing a well-rounded rehabilitation for vision related disorders.
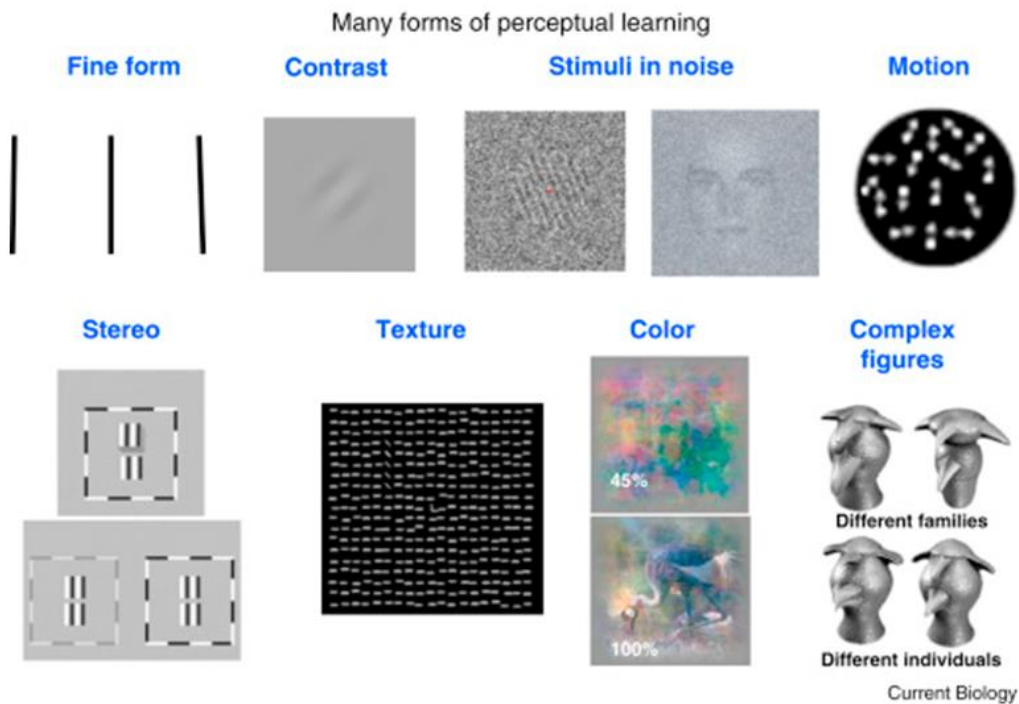
Figure 1.1. **Examples of characteristic stimuli used in Perceptual Learning research:** This figure is adapted from (Seitz, 2017) and showcases the different tasks used in PL research. Specifically, participants make judgments about the subtle details of the stimulus i.e., contrast, textures, direction of motion of dots, tilt of patterns or learning to discriminate collections of complex figures defined by multiple features.

A shift in perspective:

In recent years, a growing body of research has demonstrated that learning can indeed transfer to other retinal locations, tasks and stimuli. The extent of this transfer is contingent upon a multitude of factors such as task difficulty (Ahissar & Hochstein, 1997; Jeter et al., 2009; Liu, 1999; Meyer & Petrov, 2011; Petrov, 2009), duration of training (Jeter et al., 2010), engagement of attentional mechanisms (Donovan et al., 2015; Donovan & Carrasco, 2018; Hung & Carrasco, 2021; Roberts & Carrasco, 2022), uncertainty regarding stimulus features (Yashar & Denison, 2017), and cross training (Hung & Seitz, 2014; Xiao et al., 2008). Moreover, the acquisition of perceptual expertise

over extended periods of real-world task engagement has been documented (de Groot et al., 1996; Ericsson et al., 1993; Hoffman et al., 2013; Seitz, 2017; Tanaka et al., 2005). For instance, experienced radiologists are adept at identifying cancerous tissues/ growth amidst surrounding healthy tissues (Seitz, 2017), likely due to the nature of their profession, exposing them to diverse stimuli across various contexts. Similarly, expert weather forecasters excel in extracting and categorizing systematic patterns of visual and other features in satellite images (Hoffman et al., 2013). Interestingly, action video games provide another source of complex and variable training, and prior studies have shown that playing video games can improve a range of visual skills and transcend even to tasks such as laparoscopic surgery (Hogle et al., 2008). These improvements occur without altering the ocular characteristics of the eye (Polat et al., 2012) and are thought to be related to brain plasticity. Notably, while training with simple, uniform/ unvaried stimuli, and very precise judgements leads to specificity, training with more complex, naturalistic, and/or varied stimuli promotes broader generalization (Ahissar et al., 2009; Maniglia & Seitz, 2018).

In recent decades, research in VPL has increasingly focused on leveraging these training-induced changes to develop interventions catering to diverse populations, including athletes (Appelbaum & Erickson, 2018; Deveau et al., 2014), medical experts (Kellman, 2013), and individuals with visual impairments; such as amblyopia (Campana et al., 2014; Liao et al., 2016), myopia (Camilleri et al., 2016; Yan et al., 2015), presbyopia (Polat, 2009), macular degeneration (Chung, 2011; Maniglia, Cottereau, et al., 2016; Maniglia, Pavan, et al., 2016), age-related visual decline (Astle et al., 2015; DeLoss et al.,

2015; Mishra et al., 2015), autism (Mercado et al., 2016), dyslexia (Gori et al., 2016), and schizophrenia (Butler et al., 2017) among others.

Neural basis of Perceptual Learning:

These discoveries have spurred extensive inquiry into the neural substrates of PL, aiming to delineate the brain regions pivotal for this process. Initial evidence obtained from electrophysiological studies in animal models indicate that the plastic changes associated with PL are predominant within the primary visual cortex (V1), characterized by neurons have small receptive fields and are specialized in detecting fundamental stimulus features such as orientation (Hua et al., 2010; A. Schoups et al., 2001; Yang & Maunsell, 2004; Yotsumoto et al., 2008, 2009). Indeed, (Shibata et al., 2011) observed concomitant modifications in V1 activity alongside performance related improvements in orientation discrimination tasks with Gabors. Despite the prominence of V1 in PL research, other high-level visual processing areas also exhibit unique patterns of feature sensitivity involved in PL. Notably, there is robust evidence of learning induced alterations in V4 (Adab & Vogels, 2011; Yang & Maunsell, 2004), contrasting the mixed findings observed in V1 (Ghose et al., 2002), in animal studies.

Furthermore, several PL studies have incorporated a diverse array of stimulus features such as shapes, objects and faces (Bi et al., 2010; Furmanski & Engel, 2000; Gold et al., 1999; Sigman & Gilbert, 2000), indicating that plasticity in V1 alone may not comprehensively account for the observed learning outcomes on these tasks. Indeed, PL has been associated with alterations in response properties across multiple visual

processing areas, including motion in V3a (Chen et al., 2016), Medial Temporal (MT) cortex (Zohary et al., 1994) and Lateral Intraparietal (LIP) cortex (Law & Gold, 2008), orientation in V1 (A. Schoups et al., 2001), V4 (Adab & Vogels, 2011; Yang & Maunsell, 2004), and Posterior inferior temporal (PIT) cortex (Adab et al., 2014), contour in Lateral occipital (LO) cortex (Kuai et al., 2013), faces in Fusiform face area - FFA (Bi et al., 2014), among others.

An alternative avenue of investigation proposes that alterations in top-down attentional modulation might underlie the behavioral findings of PL. For instance, studies have demonstrated that visual learning augments V1 selectivity for task-relevant stimuli, thereby enhancing discriminability at the population level in mice (Poort et al., 2015). Moreover, changes in low-level response properties may result from top-down attentional modulation, facilitating the enhancement of target signals while suppressing responses to irrelevant features (C. Gilbert et al., 2000; C. D. Gilbert & Li, 2012; Mukai et al., 2011). Some other studies also suggest that PL relies on selective attention mechanisms with distinct temporal dynamics, encompassing attentional gain amplification and noise reduction (Bays et al., 2015; Itthipuripat et al., 2016). However, despite the potential explanatory power of attentional mechanisms for certain aspects of PL, studies controlling for attention (Adab & Vogels, 2011) or ones conducted without explicit attentional focus (Seitz & Watanabe, 2009) have still uncovered evidence of learning, indicating that attentional processes may not fully account for all PL phenomena.

Models of Perceptual Learning:

The investigation into the neural mechanisms underpinning PL has unveiled evidence indicating plasticity of brain regions engaged in representation of visual information. While empirical studies have shown plastic changes within V1 and other high-level areas, computational models propose that plasticity in visual representations may not be necessary to explain the specificity of PL (B. Dosher & Lu, 2017). This proposition hinges on the notion that even if the representations remain fixed during learning, most behavioral manifestations of PL can be attributed to changes in the read-out weights between the representation and decision areas. For example, Dosher and colleagues proposed an integrated reweighting theory (IRT), suggesting that changes in read-out weights between perceptual representation and decision areas can account for most behavioral findings of PL (B. A. Dosher et al., 2013), including transfer of learning to new retinal locations (Talluri et al., 2015).

Moreover, the reverse hierarchy theory (Ahissar & Hochstein, 2004) suggests that learning is a top-down guided process that begins at high-level areas and cascades backwards to the low-level input stages when necessary. This implies that learning is heavily dependent on the task demands i.e., learning of tasks that are easy or diverse occurs at high-level areas whereas more difficult tasks and stimuli are learned in low-level areas, thereby accommodating for both specificity and generalization of PL. Further modeling by (Wang et al., 2016) propose that PL operates at a 'conceptual level' where abstract rules pertaining to shared novel features across tasks are learnt, thus facilitating the transfer of learning to novel/ new tasks relying on similar features.

Thus, it is possible to conclude that a comprehensive model aimed at elucidating these diverse findings in the field necessitates components accounting for sensory representation, decision-making and learning processes, attentional modulation, reward mechanisms and even feedback (B. Dosher & Lu, 2017). Collectively, these findings suggest that since a myriad of systems undergo modifications as a result of learning, even in the simplest tasks, it is highly unlikely that PL is a singular process. Instead, PL likely relies on a distribution of plasticity across various brain regions, underscoring its multifaceted nature encompassing conceptual frameworks, learning dynamics and oculomotor processes, all contributing synergistically to the observed behavioral changes in PL.

Importance of Designing tools and methods for Perceptual Learning Research:

While these exciting directions in the field of PL have significantly enhanced our comprehension of the mechanisms governing specificity and generalization, neural substrates of learning, and the methodologies that boosts learning with a translational angle, the field to-date has been driven by novel findings leading to several inconclusive and/or confounding results (see (Ghose et al., 2002)), and suffers from numerous replication challenges (Aberg & Herzog, 2010; Hung & Seitz, 2011, 2014; Liang et al., 2015a, 2015b; Xiao et al., 2008; G.-L. Zhang et al., 2013; J.-Y. Zhang & Yu, 2016). These issues may be attributed to (1) methodological differences between different research labs aiming to isolate similar processes, (2) small sample sizes used in these studies, (3) variations in the hardware and software components between labs, (4) use of

homogenous participant samples, and (5) lack of publicly available and accessible datasets for cross-comparison of findings.

Therefore, to achieve more rigorous, reliable, representative and valid results, it is imperative to conduct large scale research studies using diverse population groups, and establish open-source platforms for transparent sharing of research findings in the field of PL (Seitz et al., 2023). Consequently, there is a pressing need for the development of more precise, efficient and accurate tools and methodologies to facilitate comprehensive investigations into the time course of learning and transfer effects in PL. Chapter 2 of my thesis will introduce and validate PLFest, a cross platform tool developed in our laboratory, with the objective of promoting open-science PL research practice, aiming to bridge these gaps in the field of PL.

While various PL models highlight the complex interplay and distribution of plasticity across various brain regions, to the best of our knowledge, there exists no single comprehensive framework within which one can study learning and transfer of said learning across different visual domains. This severely limits our understanding of the benefits of different PL strategies that have previously been shown to generalize. Without a unified framework, (1) it is challenging to measure and compare progress across different visual tasks, (2) training can be inefficient, requiring more time to achieve fewer comprehensive results, and (3) it could potentially lead to uneven skill development, where improvement in one area does not support or enhance skills in other areas. These issues are detrimental to the translational benefits of PL paradigms for structuring visual rehabilitation strategies for clinical populations. To address this need, Chapter 3 of my

thesis focuses on designing a comprehensive gaze contingent display framework for training and testing PL paradigms, using simulated central vision loss as a model. The importance of using such a model is two-fold: (1) it allows researchers to control and manipulate visual input precisely, providing insights into how different levels of visual processing interact and adapt to central vision loss, and (2) it informs the design of effective rehabilitation programs that help patients with central vision loss utilize their residual vision more effectively. Moreover, in this chapter we carefully address and account for the technical and design related limitations associated with developing such a comprehensive framework.

Previous studies in PL focusing on developing training strategies that can potentially increase the translational benefits in clinical populations have identified several key factors that promote transfer of learning such as the use of stimulus variety, enriched feedback, and adaptive difficulty in training tasks. Chapter 4 of my thesis extends this discourse by exploring a gamified contour integration training paradigm in patients with schizophrenia. While this body of work does not answer questions surrounding the generalizability of such a training strategy, it discusses novel findings regarding the nuances of mid-level visual processing deficits in these patients that can inform future studies aiming to leverage these findings to develop more comprehensive visual rehabilitation paradigms.

While the collective body of work in this thesis addresses the gaps in the field of PL research in very distinctive ways, it nevertheless opens up several exciting possibilities of research that can and are yet to be conducted in the field of PL, thereby largely informing

future studies aiming to address these long-standing questions in the field. As a final

remark, Chapter 5 will offer reflections on how this research will catalyze and chart the

trajectory for future investigations in PL.

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Chapter 2: PLfest: A cross-platform tool for open Perceptual Learning Research

The study presented in this chapter introduces a cross platform tool called PLFest developed in our laboratory to facilitate open science in PL research. Here, we perform reliability and validity testing of this platform (run on an iPad) by comparing performance of participants on two widely utilized perceptual tasks: Contrast Sensitivity (CS) and Visual Acuity (VA), on both the Tablet and conventional setups used in laboratories. These tasks were specifically chosen as they are sensitive to the display characteristics (like luminance and resolution of the screen) of the devices. Findings from our study indicate that the PLFest application run on the Apple iPad Pro tablets is indeed both reliable and consistent in measuring performance when compared to conventional display devices like the Cambridge Research System, Display++ and Liquid Crystal Displays (LCD) monitors used in vision science. We also briefly discuss the several perceptual and cognitive tasks that the platform currently supports. This platform is currently being used to collect data for a larger clinical trial study in collaboration with Dr. C. Shawn Green at the University of Wisconsin Madison aiming to identify the mediators and moderators of perceptual learning.

My contributions to this work encompassed several key aspects including (1) designing perceptual tasks and developing associated psychophysical paradigms supported by this platform, (2) experimental design for evaluating the reliability and validity of the platform, (3) overseeing data collection from human participants, and (4) conducting thorough data analysis and visualization.

Furthermore, I played a pivotal role in writing the manuscript and its subsequent

submission process. While my advisor (Dr. Aaron Seitz) primarily contributed to the

writing of the introduction section, I was also actively involved in drafting and revising

other sections of the manuscript, coordinated the submission process, and diligently

addressed the response to reviewers' post submission. The manuscript has currently been

accepted for publication in the Journal of Cognitive Enhancement.

Title: PLFest: A new platform for accessible, reproducible and open perceptual learning research

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ABSTRACT:

In recent decades, perceptual learning (PL) has witnessed significant advancements, but the field has faced questions regarding reliability, replication issues, and challenges in understanding individual differences, hindering accessibility to diverse populations. To address these issues, we introduce PLFest, a novel, cross-platform UNITY-based app designed to promote accessible, reproducible, and open PL research. PLFest supports a variety of training and assessment procedures, focusing on psychophysics and PL of contrast sensitivity. It facilitates data collection on computers, tablets, and smartphones, enhancing accessibility and portability, making it ideal for large-scale, multi-site studies. PLFest aims to promote open science, data sharing, and reproducible research, fostering collaboration within the research community. As a first step, to validate PLFest, we conducted tests on healthy participants, assessing visual acuity and contrast sensitivity on both desktop and tablet setups. These measures were specifically chosen as they represent fundamental assessments of visual functions in healthy and clinical populations and are also known to be sensitive to display characteristics. The results demonstrated that PLFest produces reliable measurements, in particular on Apple iPad tablets, suggesting that the app is appropriate for visual psychophysics. This validation supports PLFest as a robust platform for PL research, emphasizing its potential to overcome limitations associated with high-end desktop/monitor setups and ensuring its applicability across diverse hardware configurations.

INTRODUCTION:

Perceptual learning (PL) refers to experienced-based changes, typically improvements, in the ability to extract sensory information from the environment and encompasses the set of mechanisms through which experience with the environment gives rise to changes in perceptual processing (Lu & Dosher, 2022; Sagi, 2011; Seitz, 2017). PL is fundamental to perceptual development, formation of perceptual expertise, and rehabilitation after sensory damage (Lu et al., 2016; Maniglia & Seitz, 2018; Seitz, 2017). From a scientific perspective, PL represents one of the most examined training phenomena, with numerous studies showing that a wide range of visual abilities can improve with practice. This includes processing stimulus orientation (Hung & Seitz, 2011; Jehee et al., 2012; A. A. Schoups et al., 1995; A. Schoups et al., 2001) and contrast (Adini et al., 2002; Deveau, Lovcik, et al., 2014; Furmanski et al., 2004; Polat et al., 2012), resolving fine detail (i.e., acuity;(DeLoss et al., 2015; Deveau, Lovcik, et al., 2014; Deveau & Seitz, 2014; Polat et al., 2012), and higher-level visual abilities such as reading (Bernard et al., 2012; Chung et al., 2004; Deveau & Seitz, 2014; Lee et al., 2010; Polat et al., 2012; Yu et al., 2010). Beyond basic science, the field has generated numerous translational approaches (Deveau et al., 2013; Deveau & Seitz, 2014; Polat, 2009) aiming to exploit PL in interventions to enhance normal perceptual abilities (e.g., athletes (Appelbaum & Erickson, 2018; Deveau, Ozer, et al., 2014), medical experts (Kellman, 2013)), and to treat both purely perceptual (e.g., amblyopia: (Hussain et al., 2014; Levi & Li, 2009; Li et al., 2008; Polat et al., 2009), myopia: (Camilleri, Pavan, Ghin, Battaglini, et al., 2014; Camilleri, Pavan, Ghin, & Campana,

2014; Durrie & McMinn, 2007) presbyopia: (Deveau, Jaeggi, et al., 2014; Polat et al., 2012);, macular degeneration: (Chung, 2011; Maniglia, Cottereau, et al., 2016; Maniglia, Pavan, et al., 2016; Maniglia et al., 2020; Plank et al., 2014) and broader (e.g., ASD: (Harris et al., 2015) dyslexia: (Gori et al., 2016)) disorders. The potential broader impacts of PL are immense and careful research in this domain can greatly enhance our basic understanding of the perceptual systems and the plasticity of these systems.

However, despite its substantial potential impact, a major obstacle to a clearer understanding of the mechanisms underlying PL, and, consequently, more successful translation, is that the field, to date, has been strongly driven by "novel" and "provocative" findings, often demonstrated via small N studies, with few research projects utilizing the type of large and heterogeneous samples that are necessary to achieve robust and unbiased results. In turn, unsurprisingly, the field of PL, like many others in psychology, has suffered from numerous replication challenges (Aberg & Herzog, 2010; Hung & Seitz, 2011, 2014; Liang et al., 2015a, 2015b; Xiao et al., 2008; G.-L. Zhang et al., 2013; J.-Y. Zhang & Yu, 2016). This is undoubtedly exacerbated by the fact that PL researchers have largely examined the impact of their own paradigms via their own outcome measures, which frequently differ from those employed by other research groups in mostly unaccounted for ways. Such uncontrolled variability in approach severely hinders the field's ability to isolate the critical ingredients in successful PL (Hung & Seitz, 2011, 2014; Talluri et al., 2015).

As a glimpse into the inconsistencies within the existing PL literature, consider one of the more foundational results in the field - that PL of orientation discrimination is specific to the location of training and involves plasticity in primary visual cortex (V1) (A. A. Schoups et al., 1995; A. Schoups et al., 2001). Although this initial result is still considered seminal in the field, subsequent physiological data from Ghose et al (Ghose et al., 2002) failed to replicate the V1 finding, while other behavioral studies suggested that the observed degree of specificity is an artifact of pre-testing approaches . Together, these latter results appear to call the original findings into question. Yet, research by Seitz (Hung & Seitz, 2014) suggested that methodological differences, in particular in the adaptive procedures, could explain why later studies, such as (T. Zhang et al., 2010) did not show the same level of specificity observed in the original study.. In the case of (T. Zhang et al., 2010), the staircases included more easy trials, which in turn led to less specificity. Modeling by Seitz (Sotiropoulos et al., 2018; Talluri et al., 2015) showed that this methodological difference is sufficient to explain the discrepancies in behavioral findings across groups. Additional work by Seitz utilizing deep neural networks (Wenliang & Seitz, 2018) has shown that differences in training thresholds are sufficient to account for the differences in neural findings found between Schoups (A. A. Schoups et al., 1995; A. Schoups et al., 2001) and Ghose (Ghose et al., 2002). Critically, many of these various methodological differences across studies, which appear to substantially alter the learning outcomes, were not purposeful manipulations. They instead reflect unintended differences in lab-specific methodological practices.

These types of untracked and unaccounted for inconsistencies across studies abound in the literature.

It is a long-held field consensus that large-scale, multiple lab studies that include diverse individuals, regularize methods across labs, and use common account measures are necessary to advance rigor and reproducibility in the field. In 2008, the International Workshops on Perceptual Learning was formed (with the first meeting in Beijing) as a forum specifically for researchers in the field of perceptual learning. Here, the field established the goal of a PL "ModelFest" (with at least 10 additional PL ModelFest meetings held over the subsequent decade). This PL ModelFest (S. Klein et al., 2011) was originally meant to address the numerous surprising and minimally characterized findings in the field by replicating key PL results at multiple sites with conserved stimulus- and task-parameters and common outcome measures. These meetings identified a number of fundamental limitations of the field: 1) Small sample sizes (often $N < 12$ per condition); 2) The use of reasonably homogenous participant samples that might not allow extrapolation to other populations, in particular those of translational interest (e.g., the use of young adult participants, who are frequently well-trained psychophysical observers, that might not be good models of the impact of PL on older adults) 3) Lack of direct comparisons between training procedures; 4) Lack of consistent generalization outcome measures; 5) Lack of publicly available datasets upon which to advance models of PL; 6) Substantial hardware/software barriers to performing direct replications or extensions of existing work.

It was hoped that such a large-scale approach would clarify which methods show consistent results. However, a limitation of moving the project forward was a lack of appropriate tools to make the project convenient to participating labs. Indeed, labs can differ widely in terms of available hardware, software, and facilities, which in turn can make sharing and replication infeasible. In terms of hardware, for decades vision science has relied on cathode ray tubes (CRTs), which allowed for highly accurate timing of stimulus presentation. However with decreased production of these devices, researchers are turning towards using alternative equipment like liquid crystal displays (LCDs) for stimulus presentation (Rohr & Wagner, 2020; G.-L. Zhang et al., 2018). While these are increasingly well-adopted, they exhibit different spatial-temporal display characteristics than CRTs. For example, while CRTs present briefly flashed points of light, LCDs present light continuously and then have brief periods of changes to luminance/color at frame transitions (Ghodrati et al., 2015). Because many display properties have the potential to fundamentally alter participant performance in myriad ways, ensuring that results are reliable across hardware is a must. Then, in terms of software, tools like PsychToolBox and PsychoPy are most typical of PL studies. Although these tools are proven for lab-based research, they are challenging to share, and even more so to translate outside of the lab (especially to tablets and phones) as they require use of specific versions of MATLAB and Python (Nuutinen et al., 2018; Peirce et al., 2019). These hardware and software limitations pose a challenge when running studies across multiple sites, and even more so for replication.

Here we introduce a tool to help tackle these challenges: an app called PLFest that is designed to promote accessible, reproducible, and open PL research. This app takes advantage of the tremendous development of consumer tablet technology where, for example, current iPad Pros support a 120Hz screen refresh rate, over 300 pixels per inch, and 16 bits per color channel, making it a powerful psychophysical machine capable of ambulatory research and facilitating running many participants simultaneously. PLFest is innovative in a number of ways as it: (1) makes available a number of training approaches that are representative of those that have been used in research in the field to-date, (2) includes numerous outcome measures (Figure 2.1) by which to understand both near (e.g., to feature and task sets that have been trained) and far transfer effects (e.g., to features and task sets that are untrained, including a range of hearing, attentional and cognitive measures), (3) is highly configurable in a way that supports both easy reproduction of existing experiments and customization to support new experiments (including numerous built-in procedures and a scripting language to support more arbitrary procedures), and (4) is structured to be expandable to new methods (including both new task structures, stimulus sets, and use of peripherals such as eye-trackers, EEG systems, etc.). Importantly, with PLFest being built within the UNITY Game Engine, it is intrinsically cross-platform (it currently has been tested on iOS, Android, MacOS, and Windows), self-contained as a single app, and it does not rely upon versioning of other libraries and packages (unlike MATLAB and Python). Further, it supports easy configuration on multiple devices, including participant-owned

hardware, and is integrated with a HIPAA compliant Amazon Web Services (AWS) back-end, supporting both lab-based and at-home based research.

Data is saved in JSON file format, or can be exported to CSVs, that can be easily read using several different programming languages such as MATLAB, Python, R, etc. A sampling of the range of tasks that PLFest supports is shown in Figure 2.1. These include visual assessments (such as contrast sensitivity, contour detection, visual acuity and search), and cognitive assessments (such as matrix reasoning, N-back, Cancellation and Complex figure tasks). We note that there are many more tasks than the platform will allow, such as psychoacoustical tasks (pure tone thresholds, spectral, temporal and spectrotemporal sensitivity, binaural hearing, spatial release from masking, dichotic digits, etc.), neuropsychological testing (such as word lists, constructional praxis, Boston naming, trail-making, clock drawing etc.), as well as reading and vocabulary tasks. A novelty of the platform is that parameters such as task durations/ trial numbers, stimulus durations, target sizes and locations, and adaptive procedures can be customized through the graphic user interface within the application, or by directly editing configuration files. The platform additionally supports the creation and implementation of questionnaires in a standalone format or within each task. It is also possible to combine multiple different tasks as separate batteries within a single experiment, and include time-breaks, time-outs and password locked sessions for flexible administration. Features that are still in development include eye-tracking, ambient sound monitoring and communication with EEG systems. Furthermore, many other tasks, including those with moving stimuli are under development. PLFest is

currently in beta stage, and we encourage readers to contact the authors for instructions

on how best to use the application.
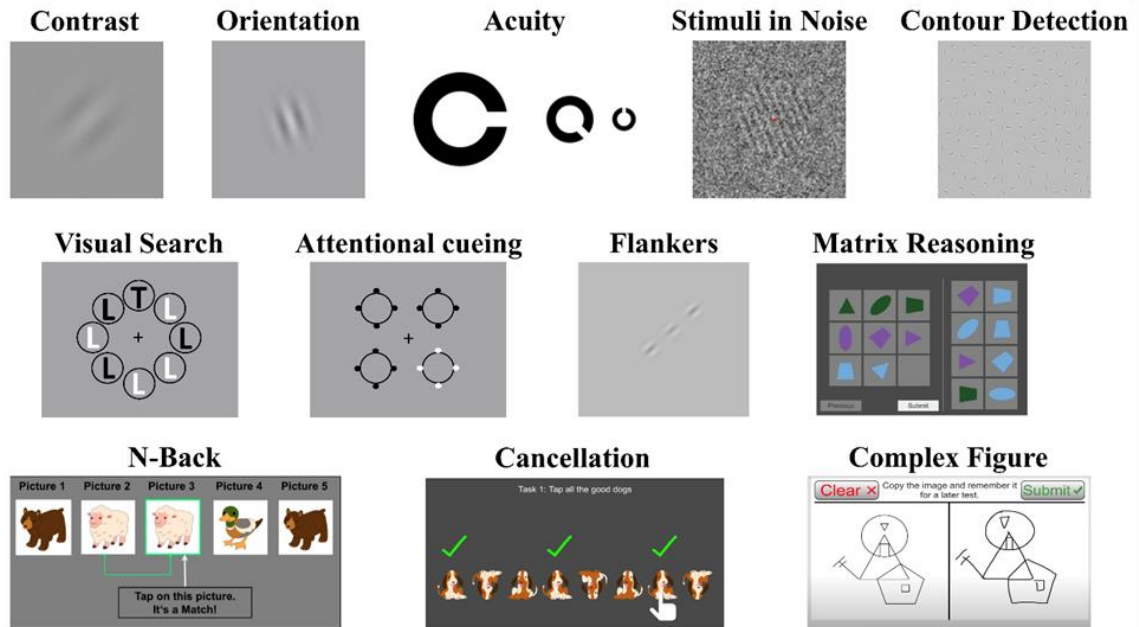
Figure 2.1. **Examples of tasks supported by the platform:** In addition to basic visual tasks, the application can support a wide range of cognitive tasks such as matrix reasoning, n-back working memory task, cancellation and complex figure tasks, among many others are not displayed in the figure.

As a first step towards validation of the PLFest platform, here we examine reliability and

consistency measurements of Visual Acuity (VA) and Contrast Sensitivity (CS), two of the

most widely used tasks in PL. We tested these measures on a standard lab setup (monitor

driven by a laptop) and a tablet setup. Additionally, we also measured the performance in

the CS Task on a conventional display monitor (Cambridge Research Systems Display++)

driven by a tablet and contrasted it with the performance on the tablet setup. VA measures

the ability to distinguish fine structure of objects, usually at high contrasts, and is

considered a fundamental measure of spatial vision. CS meanwhile measures the ability to

identify differences between the luminance of the object and its background and is considered a fundamental measure of light sensitivity. VA and CS are foundational in evaluating visual performance in clinical and experimental settings and can be predictors of visual pathologies such as cataracts, glaucoma, diabetic retinopathy and macular degeneration (Brown et al., 2002; Howes et al., 1982; Klein et al., 1995; Lin et al., 2018; Ross et al., 1984; Sabour-Pickett et al., 2013). Critically, both tests are also particularly sensitive to display parameters, with visual acuity requiring high-pixel density and spatial precision, and contrast sensitivity requiring linearization display gammas and precision of luminance values. As we will see below, results showed equal-to-greater reliability of PLFest both on tests of acuity and contrast sensitivity on an iPad Pro compared to LCD display as well as good inter-device reliability of CS measures on all three displays. These data support the use of PLFest as a platform for perceptual learning research.

METHODS:

Participants: 50 undergraduate students (16 M, 1 Other; Mean age = 19.1 yrs [SD = 1.16]) at the University of California, Riverside (UCR) participated in the study comparing the tablet and a standard lab setup (LG monitor). For measuring the consistency across the tablet and Display++ devices we additionally recruited 48 undergraduate students (21 M; Mean age = 20.7 yrs [SD = 4.6]) at UCR. Written and informed consent was obtained from all participants in the study and all participants were given research credits for participation. All participants reported normal or correct to normal vision (= or > 20/40) and the study was approved by the IRB of UC Riverside.

Outlier Exclusion: Thresholds were calculated by taking the average of the last 6 reversal values of participant performance in the session phase for each task and on each device. We employed a 2-step outlier exclusion for the data collected in the study. The first step involved excluding participants whose thresholds were above 10% contrast (> -1 logCS) and 0.3 logMAR (translating to a Snellen acuity of 20/40) respectively. This was performed to exclude thresholds that were more likely due to attentional lapses or general issues with task comprehension and does not reflect task performance. The second step excluded participants based on the distance with respect to the dispersion of mean i.e., thresholds ± 3 SD of the mean were excluded. The total N for the two tasks after exclusions were 41 (for CS task) participants and 48 (for VA task) in the study comparing performance between the tablet and LG monitor. Three participants were excluded from the analyses comparing performance of participants between the tablet and Display++ device for the CS task.

Set up: Participants in the condition comparing the tablet and a standard lab setup performed the tasks on a Tablet (2021 Apple iPad pro-12.9'' with a resolution of 2048 x 2732 and refresh rate of 120Hz) and a Monitor (LG monitor with a resolution of 1920 x 1080 and refresh rate of 120Hz) driven by a separate laptop (Alienware, Dell Inc.). For participants in the condition contrasting a more conventional display device with the tablet, we measured performance on a Cambridge Research Systems Display++ that was driven directly by the 2021 Apple iPad Pro. Participants performed under low-light conditions, while the background luminance of both devices was matched (92.5 cd/m^2, background luminance of Display++ and iPad was matched at 74.7 cd/m^2). Head and chin rests were used with the devices to minimize discrepancies in viewing distance across participants.

The tablet was mounted on a stand and placed at a viewing distance of 50 cm, the LG monitor was placed at a distance of 67 cm and the Display++ screen at 91 cm in order to maintain equal size of the stimulus in visual angle across all devices. Participants were provided with headphones for auditory feedback, and they recorded their responses using the arrow keys on a keypad.

Procedure: Participants performed a 1-hour session where they were tested on two tasks: 1) CS and 2) VA. They performed two runs of each task on two devices: monitor (LG monitor or Display++) and tablet. Prior to performing the full session, participants were briefly exposed to each task on both devices in order to ensure they understood the tasks and knew what the stimuli would look like on both devices. The overall study design is shown in Figure 2.2.

Figure 2.2. **Overview of study design.** The red and black boxes denote specific devices (i.e., monitor and tablet), based on the order of each device presented to the participant). Prior to beginning the experiment, participants were required to practice both the tasks on each of the devices after which they completed Run 1 on each device before completing Run 2 on the devices. The order of the tasks performed was kept constant (i.e., CS followed by VA) throughout the study.

The order of devices was counterbalanced across participants. Participants always performed the CS task followed by the VA task during the practice and in each of the two runs.

Tasks: The details of the two tasks used in the study are as follows:

35

CS Task: This test uses centrally presented Gabor patches with a spatial frequency of 6 cpd tilted at either 45° or 135° to estimate contrast sensitivity (Figure 2.3A). Participants were required to indicate the direction of tilt of the Gabor using the left/ right arrow keys on the keypad. Participants first performed a 2-stage practice of this task on each device where the first stage consisted of a total of 10 trials during which the stimulus was presented with progressive difficulty starting at a value of -0.4 logCS with a step factor of 0.3 log units. This was followed by the second stage that consisted of a conventional 2 down 1 up staircase algorithm terminating after 20 trials, starting at a value of -0.1 logCS and a step size of 0.3 log units. Once practice was completed on both the devices, participants performed a longer version of this task. In order to mitigate the potential effects of cold-start performance as well as device and task switching effects, participants first performed the two-stage practice as mentioned above prior to engaging in the main task. The main task employed a 2-stage conventional 3 down/ 1 up staircase with a step factor of 0.3 log units until 3 reversals (stage 1), after which the step factor remained 0.1 log units (stage 2) until task completion.

When measuring the consistency between the iPad and Display++ devices, the general structure of the contrast task was the same as mentioned above. The only difference is that a blockwise staircase was used for the main task where 10 mini blocks of 6 trials were implemented with each of the 6 trials corresponding to 6 different orientations of the Gabor (22.5°, 45°, 67.5°, 112.5°, 135°, and 157.5°) in random order. Contrast of the Gabors stepped down (i.e., more difficult) when there were 1 or fewer errors within the block, stayed the same if there were 2 errors and stepped up (i.e., easier) when 3 or more errors

were made within each block. This allowed for maintaining the performance between 66%

and 83% as an average across the orientations. In this case data was averaged across the

blocks to ensure that there were adequate numbers of steps used to obtain a threshold.

Manipulations to the CS task structure were made such that it is consistent with a larger

clinical study that is currently ongoing in the lab. Of note, data depicting contrast

thresholds in both the Tablet and Display++ devices shown in Figure 6 was collected using

this structure of the CS task.

VA Task: In this test, a block letter C (Sloan Font) is presented in one of four orientations

(with the gap of the C facing up, down, right or left) as shown in Figure 2.3B. Participants

were required to indicate the side of the gap using the up, down, right/ left arrow keys on

the keypad. The structure of this task was slightly different from the CS task with two main

stages. In alignment with the CS task, participants first performed a 2-stage practice on

both the devices where the first stage comprised a total of 12 trials with progressive

difficulty (1.3, 1.1, 0.9, 0.7, 0.5, 0.4, 0.3, 0.2, 0.1, 0.0, -0.1, -0.2 logMAR units) followed

by a conventional 2 down 1 up staircase in the second stage with a starting value of 0.5

logMAR and a step factor of 0.2 log units that terminated after 20 trials. Post the

completion of practice on both the devices, participants performed the first stage of the

practice followed by the main task which employed a conventional 3 down 1 up staircase

that terminated after 60 trials. Similar to the CS task, here, the main task also consisted of 2

stages where we used a step factor of 0.2 log units until 3 reversals (stage 1) after which the

step factor remained at 0.1 log units (stage 2) until completion.
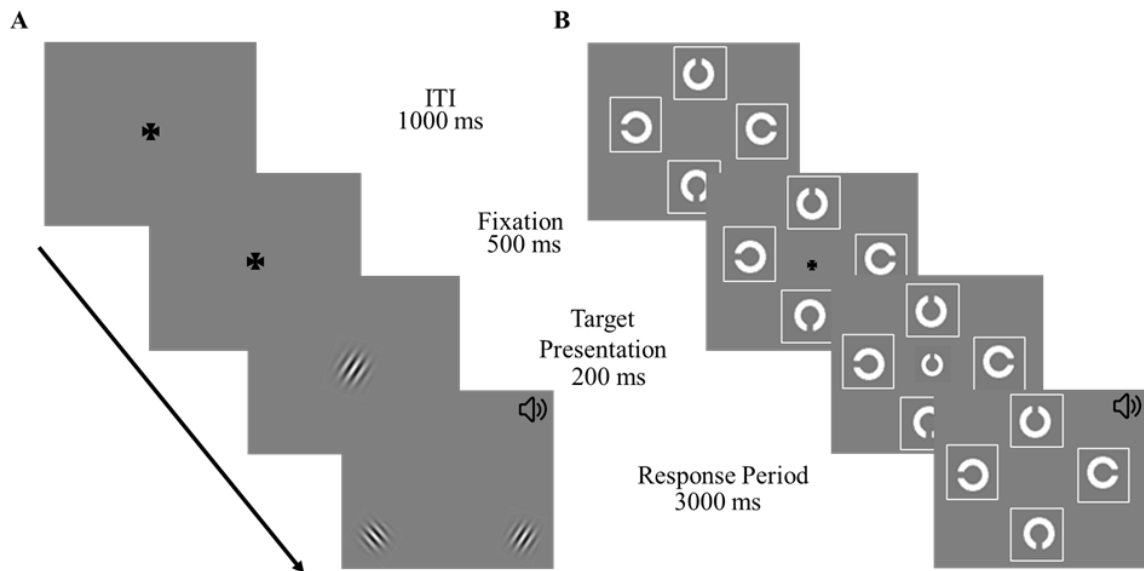
Figure 2.3. **CS (A) and VA (B) task paradigms**. Participants respond to the target orientation using the arrow keys on a keypad and receive auditory feedback based on the accuracy of their response i.e., high pitch pleasant tone for correct and a low beep for incorrect responses.

RESULTS:

We first examine within-device reliability (i.e., repeatability on the same device), followed by inter-device reliability (i.e., consistency of the measurements across platforms) on each of the tasks respectively.

Within–device Reliability:

The first question we asked was whether PLFest leads to reliable, repeatable measures within each device on which it is run.

Contrast Sensitivity: Within-device reliability of the CS task on the Monitor Figure 2.4A) and the Tablet (Figure 2.4B), respectively showed correlations of moderate magnitude for both devices $r_{Monitor} (39) = 0.72$, $p_{Monitor} < 0.001$; $r_{Tablet} (39) = 0.6$, $p_{Tablet} < 0.001$. To

understand these relationships in more detail, we examined Bland-Altman's limits of

agreement (LoA), which evaluates the difference in thresholds (Run 2 – Run 1) between

the two runs as a function of the average thresholds (mean of test-retest) across the two

runs (Altman & Bland, 2017; Bland & Altman, 1999). To illustrate the between-subject

variability of threshold estimation, the mean across runs is shown on the x axis to provide a

single point estimate for each participant in terms of their overall estimated threshold. To

display the within-subject variability of the predicted threshold, the difference between the

two runs is plotted on the y axis to provide a single point estimate of the extent of

divergence of performance between the two runs. The main point estimate of the

systematic bias in the measurement across sessions is represented by the distance between

the mean of these discrepancies, which is depicted as a straight line perpendicular to the y

axis and symbolizes zero (zero = perfect agreement). Plotted as dotted lines, the 95% LoA

[±1.96 SD (difference between sessions)] represents an estimate of the region in which

95% of the within-subject, between-run changes of threshold estimates are likely to be

seen. As observed from figures 2.4C and 2.4D, the mean difference between the runs were

close to 0 in all of the within-device comparisons indicative of less systematic bias within

the two devices. Overall, the data shows that CS tests were reliable on both platforms.

CONTRAST SENSITIVITY TASK

Figure 2.4. **Performance on CS Task within (A-D) and between (E & F) devices**. Participant thresholds in run 1 (x axis) are plotted against their thresholds in run 2 (y axis) on the Monitor (A) and Tablet (B) devices respectively. Bland-Altman LoA for within-device thresholds on the Monitor (C) and Tablet (D) tasks. The mean threshold across both runs (x axis) is plotted against the difference between the two runs (y axis). Solid line denotes the mean difference between runs and the dotted lines indicate 95% LoA. A negative value on the y axis denotes better performance on the second run for both tasks. Between device correlations and LoA plots can be observed in the right most panel (E & F) respectively. Here participant thresholds were averaged across both runs for each device and performance were correlated between the two devices (E). Bland-Altman LoA for between-device comparisons (F) shows the mean threshold across both devices (x axis) plotted against the difference between the two devices (y axis). Solid line denotes the mean difference between the devices and the dotted lines indicate 95% LoA. Here, a positive value on the y axis denotes better performance on the Tablet device.

Visual Acuity: Within-device reliability of the VA task on the Monitor (Figure 2.5A) and the Tablet (Figure 2.5B), respectively, showed a correlation of moderate magnitude in the Tablet (r_{Tablet} (46) = 0.7, $p_{Tablet} < 0.001$), but poor reliability on the Monitor for this task ($r_{Monitor}$(46) = 0.24, $p_{Monitor} = 0.1$). A closer examination of the LoA plots for test-retest

reliability on the Monitor (figure 2.5C) reveal a more dispersed distribution of differences in performance between the two runs with a low mean difference (bias = 0.01) whereas a more clustered distribution for the Tablet (figure 2.5D) device with a mean difference of 0.02. A possible explanation for this may be the lower resolution of the monitor compared to the tablet, however these data show that PLFest is producing reliable data on the tablet platform for visual acuity measures.
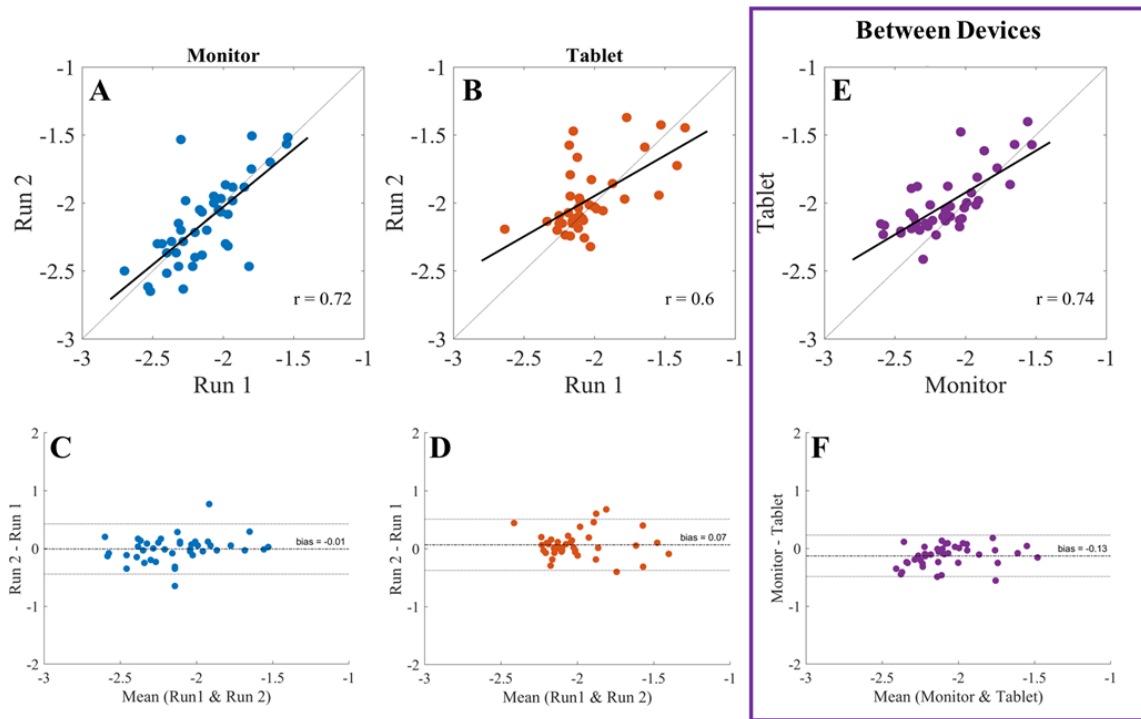
VISUAL ACUITY TASK
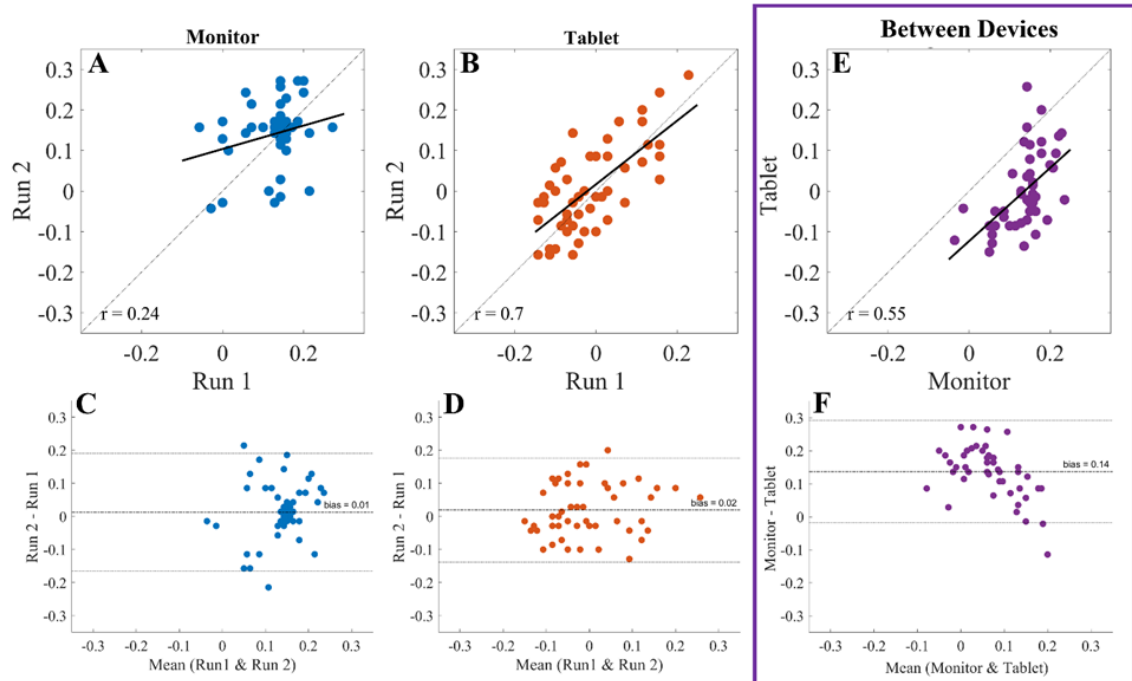
Figure 2.5. **Performance on VA Task within (A-D) and between (E & F) devices**. Participant thresholds in run 1 (x axis) are plotted against their thresholds in run 2 (y axis) on the Monitor (A) and Tablet (B) devices respectively. Bland-Altman LoA for within-device thresholds on the Monitor (C) and Tablet (D) tasks. The mean threshold across both runs (x axis) is plotted against the difference between the two runs (y axis). Solid line denotes the mean difference between runs and the dotted lines indicate 95% LoA. A negative value on the y axis denotes better performance on the second run for both tasks. Between device correlations and LoA plots can be observed in the right most panel (E & F) respectively. Here participant thresholds were averaged across both runs for each device and performance were correlated between the two devices (E). Bland-Altman LoA for between-device comparisons (F) shows the mean threshold across both devices (x axis) plotted against the difference between the two devices (y axis). Solid line denotes the mean difference between the devices and the dotted lines indicate 95% LoA. Here, a positive value on the y axis denotes better performance on the Tablet device.

Inter-Device Reliability

We next asked whether PLFest, when running on a tablet, assesses the same constructs as a traditional vision science setup using a desktop monitor. To examine this, we measured inter-device reliability (e.g. correlations between participants' performance across the two

devices) for CS (Figure 2.4E) and VA (Figure 2.5E). In this analysis, we averaged the

thresholds across both runs for each participant and task. We observed moderate

correlations for both CS ($r_{CS} = 0.74$, $p < 0.001$) and ($r_{VA} = 0.55$, $p < 0.001$) between the two

devices that are within range of the within-device reliabilities for each test. Figures 2.4F

and 2.5F show the Bland-Altman plots, for the CS and VA tasks respectively, to test for the

consistency in measuring the performance on both tasks between the two devices. To do

this, we averaged the thresholds across both runs for each participant and task. The x axis

shows the average thresholds of the participants across both the devices and the y axis

represents the difference in thresholds between the monitor and tablet. A positive bias in

both the CS and VA task is indicative of better performance on the tablet in comparison to

the monitor. From these graphs it can be observed that participants perform better on the

Tablet when compared to the Monitor on the VA task in contrast to the CS task ($bias_{CS} = -0.13$, $bias_{VA} = 0.14$, although the bias is small in both cases), perhaps due to the greater

spatial and luminance resolution on the tablet compared to the desktop display.

To further test whether running PLFest on a Tablet leads to reliable inter-device

performance, we compared PLFest on the tablet with a more conventional Display++

monitor used in vision science, and one that is specialized to produce high contrast depth.

To do this, we tested a modified version of the CS task as indicated in the methods. Figure

2.6A shows the moderate and significant correlations ($r_{CS} = 0.6$, $p < 0.001$) between the

thresholds on the Tablet and the Display++ devices. It can also be observed from the

Bland-Altman plots (figure 2.6B) as indicated by the small positive bias ($bias_{CS} = 0.02$) that

participants performed slightly better on the Tablet compared to the Display++. These

results suggest that the iPad can produce comparative data to the research grade Display++ system.

CONTRAST SENSITIVITY TASK
Between Device Reliability (Tablet vs Display++)
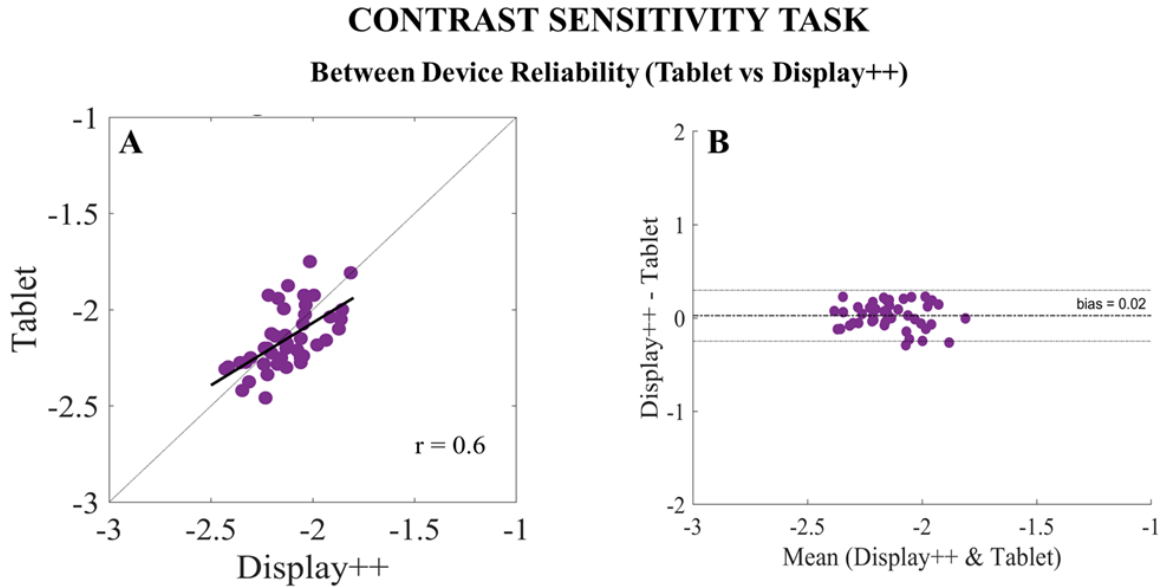
Figure 2.6. **Performance on CS Task between the Tablet and Display++ devices.** Between device correlations and LoA plots can be observed in the right most panel (A & B) respectively. Here participant thresholds were averaged across both runs for each device and performance were correlated between the two devices (A). Bland-Altman LoA for between-device comparisons (B) shows the mean threshold across both devices (x axis) plotted against the difference between the two devices (y axis). Solid line denotes the mean difference between the devices and the dotted lines indicate 95% LoA. Here, a positive value on the y axis denotes better performance on the Tablet device.

DISCUSSION:

The goal of this study was to introduce and validate PLFest, a novel, cross-platform app to support perceptual learning research. Here we found that measures of Contrast Sensitivity and Visual Acuity show acceptable within-device reliability when tested on an iPad tablet. Further tests of inter-device reliability show that the iPad produces results that are consistent with those found on consumer grade LCD and the research grade Display++

system (although both systems have lower spatial resolution than the iPad). These results show that PLFest is a reliable platform for visual psychophysics and can support PL research.

Over the last several years, multiple tests measuring CS and VA have been developed on multiple platforms such as computer devices and made commercially available for testing. However, it was only until recently that these tests were created for use on remote devices such as iPads and Tablets (Habtamu et al., 2019; Kollbaum et al., 2014; Labiris et al., 2023). For example, (Habtamu et al., 2019) developed and validated a smartphone-based CS test employing the tumbling E Pelli-Robson CS test and PeekCS test on Android phones and observed high test-retest correlations. Similarly, (Kollbaum et al., 2014) validated an iPad-based Letter CS test and compared it to the Pelli-Robson test and Freiburg Acuity and Contrast Test (FrACT) and observed good repeatability. On the other hand, (Labiris et al., 2023) recently validated a web based Democritus Digital Acuity and Reading test (DDART) against conventionally used distance vision charts across multiple sites with high n (543 participants) and noticed reliable measurements in both normal and low vision patients. While all of these studies show reliable measures akin to ours, our platform offers a one-stop solution to conduct multiple vision-based tests on a single platform. Further, it is structured to facilitate both testing and perceptual learning training within the same platform.

The development of PLFest builds upon other developments cropping out from the COVID-19 pandemic emphasizing the need for reliable and remote testing platforms

worldwide (Collins et al., 2022; Yaghoubi et al., 2022) and telehealth approaches more generally. This has led our research group to develop several tools to measure several different auditory (Lelo de Larrea-Mancera et al., 2020) and cognitive functions (Pahor et al., 2022, 2019) on tablet-based devices that are reliable and portable to reach more diverse populations and adequately support comparisons across different approaches developed by different research groups. PLFest is built within the same test framework as these other tasks and while in the current paper we emphasized measurements of basic visual functions, the app is capable of doing more than just measuring VA and CS. Indeed, the current version of PLFest includes visual search tasks, orientation discrimination, contour integration, numerous psychoacoustic tasks, cognitive and neuropsychological tasks, for visual, auditory perceptual learning and cognitive training.

While these results are encouraging, there are also some limitations to the current study. First, we notice that a few participants were outliers (i.e., had unreliable scores/contrast thresholds above 10%). This is most likely due to issues with task instructions or lapses of attention. This is not uncommon in psychophysical research with undergraduate students; however, it emphasizes the importance of uniform instructions across participants, sufficient breaks between tasks and potentially employing performance cutoffs during practice that could be informative of and further mitigate such occurrences. These issues are being addressed in versions of PLFest currently being developed, specifically via the implementation of animated tutorials and automatic checks for outlying performance. Closer examination of the data from the VA task data suggests that the tablet might be more reliable than the monitor, which is likely a consequence of the lower poor resolution

on the monitor screen compared to the iPad. This could have led to the pixel density not being high enough to capture an acuity better than 20/25, thus contributing to poor VA thresholds when measured on this device. Future use of PLFest in combination with desktop monitors should use displays of higher resolution (or have participants at a further distance).

The PLFest app is currently validated on iPad devices, due to their high resolution and refresh rate, allowing for high quality rendering of the stimuli. In terms of field of view, at the distance (50 cm) it was tested in the current study, the screen subtended approximately 32 x 24 degrees of visual angle and it can be placed as close as 35 cm (subtending approximately 46 x 34 degrees of visual angle) without sacrificing conform and usability. Further, the app is cross-platform and can also run on Mac and PC Desktops and also other iOS and Android tablets and even phones, and we plan future studies to validate across a larger range of platforms. While the platform currently does not include visual assessments with moving stimuli, these are planned for future studies, and given the high spatial and temporal resolution of tablets and phones (catering users that expect high-fidelity movies) we are confident that psychophysics related to visual motion can be conducted with psychophysical precision on mobile platforms. Further, with remote use in mind, next steps will include moving beyond the present study's in-lab setting and assess reliability and consistency of PLFest in remote testing conditions that are susceptible to several uncontrolled environmental factors such as lighting, viewing distance, screen brightness etc. We note that this has already been accomplished in the case of psychoacoustics (Lelo

de Larrea-Mancera et al., 2022), which is also quite sensitive to the perceptual environment in which testing is conducted.

Overall, PLFest shows great promise as a reliable cross-platform tool to promote open research in perceptual learning. As it is publicly available and a free to use platform, PLFest opens up a multitude of opportunities to conduct a wide range of vision science experiments both in-in-lab as well as in remote settings, which can facilitate research in underserved communities. Further the platform supports straightforward localization to different languages. PLFest is structured both to facilitate easy reproducibility of perceptual learning research, as well as comparisons across studies through the use of common outcome measures. Further the platform can support modeling both through its standardization of data structures as well as through APIs to directly interact with models that are currently under development. Overall, PLFest can open up new possibilities for studying vision and perceptual learning and help address the long-standing issues of replicability and reproducibility in the field.

Ethical Approval:

This study has been approved by the University of California, Riverside, Institutional Review Board (IRB). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Author Contribution:

All authors contributed to the study conception and design. Data collection, analysis and interpretation as well as manuscript preparation were performed by SJ and MM. Data interpretation and manuscript preparation were performed by CSG and ARS. Additionally, both CSG and ARS secured funding for this study from the National Eye Institute (NEI R01 EY031226 grant).

Data Availability:

Data will be made available upon request. Please direct all requests to the corresponding author at samyukta.jayakumar@email.ucr.edu.

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Chapter 3: Gaze contingent display framework for Perceptual Learning Research

This chapter is a methodological paper discussing in detail the development of a gaze contingent display framework to conduct perceptual learning and oculomotor research in healthy individuals with simulated central vision loss (s-CVL) as a model. s-CVL is an excellent model to test PL paradigms as it serves as a blank canvas for testing specificity and generalizability of perceptual training paradigms. Here, we elaborate on the design and methodological considerations for the implementation and testing of a wide range of perceptual tasks within this framework. Specifically, we describe in detail (1) the hardware and software requirements for designing this framework, (2) experimental design for priming oculomotor behavior under modified viewing conditions of s-CVL, and (3) methodological considerations pertaining to the design of psychophysical adaptive procedures for measuring performance on a wide range of perceptual tasks within this framework. We show representative results delineating the perceptual and oculomotor behavioral performance of two participants using this model. Additionally, we describe how this framework can be adapted for vision rehabilitation in patients with age-related macular degeneration. The primary goal of this chapter is to inform future studies aiming to conduct and/or use gaze contingent displays for the study of spontaneous and training-induced compensatory oculomotor strategies in conditions of central vision loss with a translational angle. Currently, we are in the process of collecting data from participants as a part of a clinical study investigating the behavioral and neural underpinnings of training related specificity and transfer of PL, in

collaboration with Dr. Kristina. M. Visscher at the University of Alabama at

Birmingham.

My contribution to this work largely involves designing this framework and ensuring its

adaptability and flexibility for supporting an array of perceptual paradigms. This work is

currently in the process of being submitted to the Journal of Visualized Experiments, and

while there are several co-authors listed as a part of the manuscript preparation, I am the

sole contributor towards the preparation and writing of this chapter as a part of my

dissertation.

Title: A Gaze Contingent Display Framework for Perceptual Learning Research with Simulated Central Vision Loss

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ABSTRACT:

Age-related Macular Degeneration (MD) is one of the leading causes of vision impairment in the western world. While there exist several interventions for visual rehabilitation in MD patients, a growing body of research focuses on simulating central vision loss in healthy individuals using gaze contingent paradigms. Research in normal sighted individuals with simulated central vision loss (s-CVL) offers a new perspective into designing rehabilitation for MD due to similarities in the oculomotor and compensatory behavior observed in the healthy individuals and patient population. The current paper focuses on the design and development of a comprehensive framework for conducting gaze contingent studies for perceptual learning in s-CVL. Specifically, we focus on highlighting the (1) hardware considerations (i.e., combined latency of the eye-tracker, operating systems and display screens), and (2) methodological considerations (i.e., training participants to view with central vision occluders, providing precise task directives, and tailored adaptive psychophysical procedures) for designing a wide range of perceptual tasks in healthy young individuals with s-CVL. We also briefly discuss several oculomotor metrics that can be used to both qualitatively and quantitatively analyze eye-movement and fixation strategies under these modified viewing conditions as well as discuss how this framework can be adapted for testing MD patients.

INTRODUCTION:

Age - related Macular Degeneration (MD) is the main cause of vision impairment in the western world, and it is projected to affect 248 million people worldwide by 2040 (Wong et al., 2014). Late-stage MD is characterized by damage to the photoreceptors in the center of the visual field (fovea) which often leads to a retinal scotoma (Figure 1A), with detrimental effects on day-to-day tasks that rely on intact vision, such as navigation (Bowers et al., 2005), reading (Bullimore & Bailey, 1995) and recognizing faces (Bernard & Chung, 2016), impacting the quality of life of these individuals (Šiaudvytytė et al., 2012). MD patients, deprived of their central vision, rely on their visual periphery to perform any visual task (Figure 3.1A and C). The large majority of patients with MD spontaneously develop compensatory strategies like the adoption of a peripheral retinal region in substitution of the fovea (Figure 3.1C). This region, referred to as the *preferred retinal locus* (PRL) (Fletcher & Schuchard, 1997; Mackensen, 1966), is often systematically used by patients in tasks involving fixation, reading, face recognition, and effectively takes over the functionality of the fovea as the fixation and oculomotor reference. However, loss of central vision deprives the visual system not only of its retinal region with the highest resolution, but also of its oculomotor and attentional reference. Indeed, there is evidence that the PRL, in patients with a long history of MD, takes over the oculomotor referencing duties of the fovea (White & Bedell, 1990; Whittaker & Cummings, 1990). Additionally, neuroimaging data suggests that consequences of central vision loss (CVL) can alter the functional connectivity between early visual cortex and the parietal, frontal and cognitive control networks relying on

vision (Sabbah et al., 2017). Taken together, these pieces of evidence suggest that loss of

central vision has far-reaching consequences in the brain, well beyond visual resolution
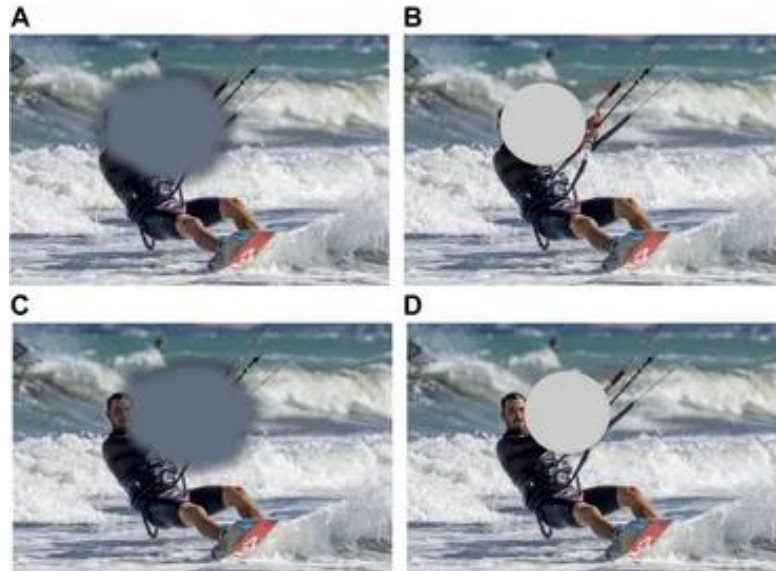
and the early visual cortex.

Figure 3.1. **Visual representation of the scotoma:** A) representation of the visual field of a
patient with CVL. B) an example of a simulated scotoma with visible boundaries. A spontaneous
compensatory strategy is the development of a preferred retinal locus (PRL), an eccentric
peripheral region close to the border of the scotoma, for fixating, viewing and solving visually
demanding tasks. (C & D) a possible location where the patient's (C) and artificial (D) scotoma
might be placed in order to reveal the surfer's face. Of note, the clear and visible boundaries of
the artificial scotoma might contribute to the speeded development of PRLs (Walsh & Liu, 2014).
Figure adapted from (Maniglia et al., 2021).

Promising solutions for MD come from disciplines such as optometry and vision science,

and generally fall under two broad categories: oculomotor and perceptual. Oculomotor

approaches focus on teaching patients to improve eye movement control and

coordination, including teaching them to use a more adequate PRL (Morales et al., 2020;

Nilsson, n.d.; Nilsson et al., 2003; Verdina et al., 2013, 2020) while perceptual

interventions focus on improving the general peripheral visual abilities or vision within

the PRL, helping with alleviating the limitation of peripheral vision (Chung, 2011; Maniglia et al., 2016; Maniglia, Soler, et al., 2020; Plank et al., 2014; Tarita-Nistor et al., 2014). Prior studies focused on oculomotor interventions have found improvements in reading speed, fixation stability and visual acuity in MD patients, where patients were trained with the help of eye tracking technology or computerized programs (Morales et al., 2015, 2020; Nilsson et al., 2003; Verdina et al., 2013, 2020). However, in these approaches, the mechanisms of neural plasticity are not well studied, and these interventions vary greatly based on the expertise and subjective approach of therapists. On the other hand, literature in perceptual interventions stem from the Perceptual Learning (PL) field which focuses on improving perceptual skills through task practice (Sagi, 2011). Visual training in this domain has shown improvements in visual acuity, contrast sensitivity and crowding in the PRL of MD patients (Chung, 2011; Maniglia et al., 2016; Maniglia, Soler, et al., 2020; Plank et al., 2014). While this approach is promising, to date they have only shown moderate effectiveness in patients, particularly when considering generalization of learning, which is a fundamental outcome for clinical interventions.

Recent years have seen the emergence of a paradigm for the study of eye movements in central vision loss that makes use of eye-tracking based gaze contingent displays (Aguilar & Castet, 2011; Barraza-Bernal et al., 2017; Bertera, 1988; Chen et al., 2019; Costela et al., 2020; Fine & Rubin, 1999; Kwon et al., 2013; Liu & Kwon, 2016; Maniglia et al., 2019; Maniglia, Jogin, et al., 2020; Xie et al., 2020). This approach, which utilizes a simulated scotoma (i.e., an opaque (or blurry) occluder to obstruct the central region of

the visual field) in healthy individuals (Figure 3.1B and D), has several advantages: it allows for combining some targeted insights from vision science and optometry; and, it addresses issues of recruitment and compliance of clinical research, thereby offering a promising alternative to the direct involvement of MD patients. While there exist several differences between CVL and simulated scotoma, some of the oculomotor behavior observed in the former can be seen in the latter (Kwon et al., 2013; Walsh & Liu, 2014), suggesting that some aspects of compensatory oculomotor strategies can be elicited by the gaze-contingent paradigm.

This methodological paper presents in detail the design, development and use of a gaze contingent framework that encompasses a multidimensional approach of perceptual learning (Figure 3.2). By extracting multiple oculomotor metrics that we developed (Maniglia, Jogin, et al., 2020), we can better understand mechanisms of PRL development, allowing for the design of personalized training tailored to the profile of each patient, and potentially identify strategies observed in healthy individuals that can be taught to patients. This approach particularly focuses on developing training strategies and assessing visual functions that takes into account the multitude of systems and networks affected by CVL, as shown in Figure 3.2 (adapted from (Maniglia, Jogin, et al., 2020)). The proposed intervention operates on all levels of visual processing affected by CVL, specifically low-level vision, oculomotor control, and cognitive control. Preliminary tests conducted using a modified version of this integrated approach in both healthy controls and patient population showed evidence of statistically reliable gains on visual acuity (for more details on experimental design and results, refer to (Maniglia et

al., 2021). With these observations in mind, we have made several modifications to the training and assessment tasks discussed in this paper (i.e., adding more comprehensive training and assessment tasks, designing mindful strategies for introduction of healthy individuals to the modified viewing conditions, implementing uniform instructions, and meticulously addressing psychophysical demands of different tasks). It is important to note however, that there are differences between pathological and simulated scotomas. Particularly, the simulated scotomas are usually uniform and have visible boundaries (Van der Stigchel et al., 2013; Walsh & Liu, 2014), whereas in patients, the shape and size of these scotomas often expand with time and are irregular in shape (Fletcher et al., 2012; Safran & Landis, 1999). The current paper aims at describing this framework and showcasing how this model of gaze contingent central vision loss can be used to test a multitude of perceptual, oculomotor, and attentional performances in healthy individuals and, with some modifications, in MD patients. A novel aspect of our paradigm is its ability to support a wide range of training and assessment tasks within a single framework for perceptual learning research in both healthy and patient populations.
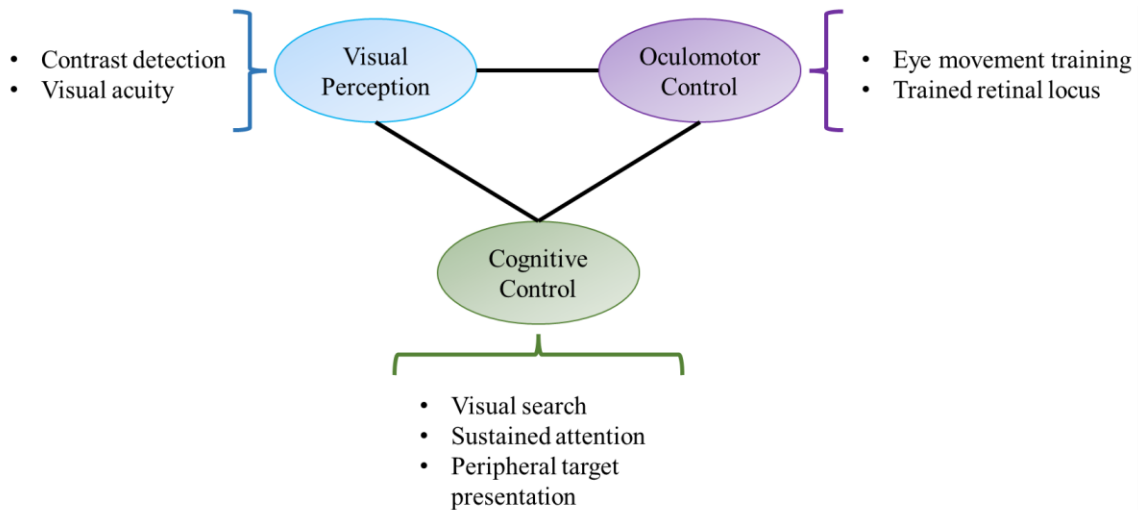
Figure 3.2. **Multidimensional approach to vision rehabilitation in MD**. This figure illustrates how interconnected dimensions such as visual perception, oculomotor and cognitive control contribute to effective vision. (Adapted with permission from Maniglia et al, 2021).

In designing such a framework, it is important to consider the technical and psychophysical limitations that accompany it. Particularly relevant are the technical challenges due to the large variety of display devices, eye trackers, and operating systems available to design such a framework (Bridges et al., 2020; Lin et al., 2022; Rohr & Wagner, 2020). Gaze contingent display relies on the perception of a smooth, short latency movement of the scotoma, to convey the perception of central vision obstruction. Thus, it is crucial that 1) the resolution of the monitor and its refresh rate are high, 2) the eye tracker is fast and accurate, and 3) the overall latency, from eye position information registered by the eye tracker to the updated rendering of the scotoma, is short.

Each of the hardware systems that concur to generate the gaze contingent display independently adds latency to the rendering of the scotoma on the computer screens. While this is a known issue in the field (i.e., (Aguilar & Castet, 2011) propose strategies

to reduce overall latency, accommodate blinks, and slow eye movements, and (Saunders & Woods, 2014) observed large latencies contributed by different displays), to date, there has not been an exhaustive investigation of the relationship between the participants' gaze, and the rendering of the actual gaze contingent scotoma across different combinations of systems used in these studies. In the current study, we first characterized the latencies of different displays (CRT, Cambridge Research System Display++ monitor), eye trackers (Eyelink 1000 and VPixx), and operating systems (Mac iOS and Windows OS), using a method proposed by (Saunders and Wood, 2014), to identify the combination of systems that introduce the least latency for displaying gaze contingent scotomas.

Finally, a systematic evaluation of performance within this framework requires a meticulous approach to the design of various assessment and training tasks. PL literature in general shows a large discrepancy in terms of adaptive procedures used to obtain measures of performance, as well as verbal and/or written instructions provided to the participants, both of which affect the participants performance on a given set of tasks (Marcus et al., 1996). In order to obtain reliable estimates of performance, it is important that healthy individuals are provided with clear and uniform instructions about the tasks, and engage in practice with simulated scotomas, as they are not experienced in using their peripheral vision to make judgements. Additionally, when designing a framework that supports a wide range of perceptual assessments and training, it is important to keep in mind specific demands of the tasks themselves (such as implementation of practice blocks and adaptive staircase procedures), that inturn reflect the performance of

participants within this paradigm. The proposed framework and accompanying methodologies aim to target these limitations by carefully considering specific parameters and outcome measures across multiple tasks.

Overall, the current paper describes a comprehensive framework for the use of gaze contingent displays to study and train perceptual, oculomotor, and attentional performance in peripheral vision in healthy individuals, with a translational angle. We highlight the design-related and practical challenges associated with gaze contingent studies and propose some approaches to overcome such limitations. We also discuss methods to extract several metrics of oculomotor behavior in a cohort of healthy individuals trained in their peripheral vision, with a specific lens on aiding future studies aiming to develop such a framework for conducting PL research in simulated central vision loss.

EXPERIMENTAL DESIGN:

Measuring system latency:

Gaze contingent displays rely on efficient transmission of information from the eye tracker to the stimulus generation software, in a continuous loop. The short latency of this setup is paramount to generate the perception of gaze contingency and approximate the visual experience of patients with CVL. Hardware and software constraints concur in limiting the use of gaze contingent display to specific combinations of equipment that constitute the ideal working system with the least combined latency to conduct such

experiments. As a first step, we measured the latency of different combinations of systems to identify the one which adds least latency for rendering gaze contingent scotomas. To do so, we employed the method described in (Saunders & Woods, 2014).

Equipment:

We used an Apple iPhone 12 with a refresh rate of 240 Hz for recording the screen during testing along with an InfraRed (IR) illuminator that effectively disrupts the IR signals of the eye tracker. Particularly the goal was to measure the time to the disappearance of the gaze contingent scotoma controlled by a participant (in this case, the author M.M) from the start of the IR illuminator. Two eye trackers (Eyelink 1000 and VPixx), two display devices (Cathode Ray Tube (CRT) monitor (refresh rate = 100 Hz) and Cambridge Research system (CRS), Display++ (refresh rate = 120 Hz)) along with two operating systems (Windows 10 and Mac iOS) were used in the experiment.

Methods:

The participant was seated in front of the eye tracker which is initially calibrated and validated using a standard 9-point calibration system. A gaze contingent scotoma of 10 degrees of visual angle (dva) in size appears on the screen and is controlled by the participants eye movements. The experimenter then holds the IR illuminator close to the eye tracking camera lens. The illuminator when turned on causes an instantaneous loss of tracking which is displayed as the disappearance of the gaze contingent scotoma on the screen. The time between the switching on of the IR illuminator and the disappearance of

the scotoma was recorded (in frames and converted to milliseconds) across 20 trials for different combinations of systems. We first measured the latency of the more commonly used setup i.e., Eyelink 1000 along with a CRT monitor using Mac iOS (System 1). However, given the lack of further manufacturing of CRT monitors and an increasing number of vision science experiments conducted using linearized Display++ screens, we measured the latency for the same setup, substituting the CRT with a CRS Display++ monitor (System 2). We additionally tested the latency of the Eyelink 1000 with the CRS Display ++ monitor using the Windows OS (System 3). Lastly, we tested if the latency can be further reduced using a more sophisticated eye tracker i.e., VPixx system with the CRS Display++ monitor driven by Windows OS (System 4).

Figure 3.3 shows the average latency measurements in milliseconds across 20 trials for each of the 4 combinations of systems. A One-Way ANOVA revealed significant differences between the different systems ($F(3,76) = 147.46$, $p < 0.001$). Post hoc comparison using t-test with Bonferroni correction indicated that the average latency of the Eyelink 1000 using CRS Display++ screen driven by MaciOS (Mean = 72.71, SD = 12.79, $p < 0.001$) was significantly larger than the other 3 systems. Further, the average latency of the Eyelink 1000 using CRT screen, driven by MaciOS (Mean = 44.37, SD = 8.58, $p < 0.001$) was significantly larger than both the Eyelink 1000 (Mean = 28.75, SD = 2.99, $p < 0.001$) and VPixx eye trackers (Mean = 25, SD = 3.02, $p < 0.001$) coupled with CRS Display++ screen and driven by Windows OS respectively. While this indicates that using the Windows OS significantly improves latency compared to Mac iOS (consistent with prior studies, refer to (Bridges et al., 2020)), we did not observe any significant

improvements on latency as a function of the eye tracker used (i.e., no significant

differences between the Eyelink 1000 and VPixx), despite a qualitative shorter latency of

the latter (Vpixx). Therefore, for designing our gaze contingent framework we used the

VPixx eye tracker with the CRS Display++ screen and Windows OS.

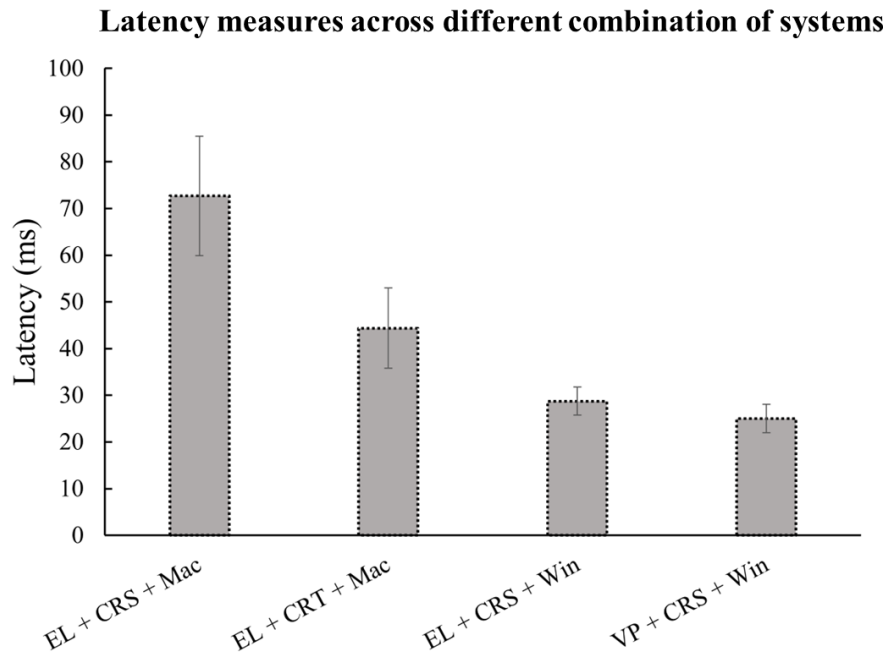**Latency measures across different combination of systems**

Figure 3.3. **Latency across different systems:** Average Latency measures across 20 trials in 4 combinations of systems in milliseconds (ms). EL → Eyelink, CRT → Cathode Ray Tube, CRS → Cambridge Research System, Display ++, Mac → Mac iOS, Win → Windows 10 OS.

Simulating Central Vision Loss:

The VPixx eye tracker records participants' gaze using a 2kHz binocular IR sensitive

camera (TrackPixx3). The eye tracker sends out a near IR light that is reflected in the

participants eyes and captured continuously using the camera to extract pupil size and

corneal reflections. This information is then transmitted to the DataPixx box connected to

the computer and processed using MATLAB. Before any data is collected, it is imperative for the participants to undergo a nine-point calibration/ validation until the error is smaller than 1° on average. The DataPixx box receives triggers and timing signals from MATLAB Psychophysics ToolBox and precisely controls the timing of stimulus presentation. This continuous gaze information from the eye tracker is then used to draw the artificial simulated scotoma on the experimental monitor (CRS Display++) at a refresh rate of 120 Hz, where the participants gaze position corresponded to the center of the scotoma. The scotoma (6°-10° in size for different tasks, consistent with the range used in previous studies) is then drawn for every frame of the display thus allowing for the perception of a smooth moving central vision occluder. There is, however, a possible concern that the eye-tracking technology may not have at all times presented the artificial scotoma properly, perhaps allowing participants to get foveal glimpses of the target. To address this concern, we have implemented calibration checks within and between each task. In the event that the eye tracker loses the participant's eye information (due to unexpected head movements away from the chin rest, or other technical issues), the calibration/ validation procedure is triggered and needs to be completed before continuing the task. This allows for the continued perception of s-CVL throughout task completion during both assessment and training.

Addressing experimenter bias:

Healthy individuals with intact foveal vision are seldom experienced in performing tasks using the visual periphery. While the concept of a central scotoma is simple to

experimenters, the same might not be true for naive participants. Therefore, clear instructions need to be provided to participants regarding the scotoma and the task itself. In our study, we aim to assess and train participants across a wide range of perceptual tasks encompassing different stimuli warranting for different viewing behaviors from participants. While verbal instructions by the experimenter have been provided in the past, prior studies in the field of psychology in general have shown significant effects of experimenter bias in these cases (Bridgeman et al., 1991; Rosenthal & Fode, 1963). Thus, to minimize this bias and provide participants with a more holistic understanding of the task, we designed instructional videos for each assessment and training task that highlight the sequence of events that takes place within a given trial (i.e., what the scotoma looks like, whether fixation is required, the nature of the stimulus presented, task difficulty, and how to respond to the stimulus). We particularly note that these instructional videos do not prime the participant to a specific viewing strategy or influence their behavioral performance but were only designed to explain the instructions to the participant in a visual format, circumventing discrepancies in verbal instructions provided.

In addition to providing clear and uniform instructions, participants are also subjected to practice blocks (5-10 trials) before performing each assessment or training task (including but not limited to instances when any aspect of the stimuli or task demands changes) for familiarization and to allow for any clarifications regarding the task demands. Moreover, we ensure a double-blind assignment of each participant to different training conditions and also counterbalance the order of the assessment tasks across participants.

Implementation of the gaze contingent scotoma to test behavior:

In healthy individuals, the oculomotor system continuously brings targets of interest to the fovea using ballistic eye movement called saccades. The fovea typically serves both as the locus for fixations and oculomotor reference for saccades (Kwon et al., 2013). However, in the case of simulated central vision loss, this ability is severely impaired due to the presence of an artificial scotoma occluding the fovea. Hence, it is important to allow participants to adapt and familiarize themselves to the "new viewing conditions". A critical component is the ability to form stable fixations to maintain a clear and stable image on the retina for processing visual information. To aid the participants in fixation we utilized "fixation wedges", that fanned out from the center of the screen along with a fixation box (white central box) within which the scotoma must be placed. Together, these aids ensure the fixation of the scotoma in the center so that the stimulus is presented at fixed eccentricities throughout all the tasks that require fixation. While these fixation aids are a modified version of the aids used in previous studies (Falsini et al., 2007; Kasten et al., 2010; Maniglia et al., 2018; Nilsson & Nilsson, 1986; Rosengarth et al., 2013), it provides an added benefit for MD patients to recenter and acquire fixation owing to their compromised vision extending into the periphery (i.e., patient's scotoma of specific shape and size that may not be circular as in s-CVL). Therefore, as a first step we design a fixation task that is simple and trains the participants to fixate within a central white box on the screen. Participants are required to direct the artificial scotoma (controlled using the eyes) to land within a central white box (fixation window, as shown in Figure 3.4) and maintain fixation for a specific duration while ignoring distracting

stimuli that might appear during a given trial (Figure 3.4). The size of the fixation

window and durations are varied between trials to reduce anticipatory effects.

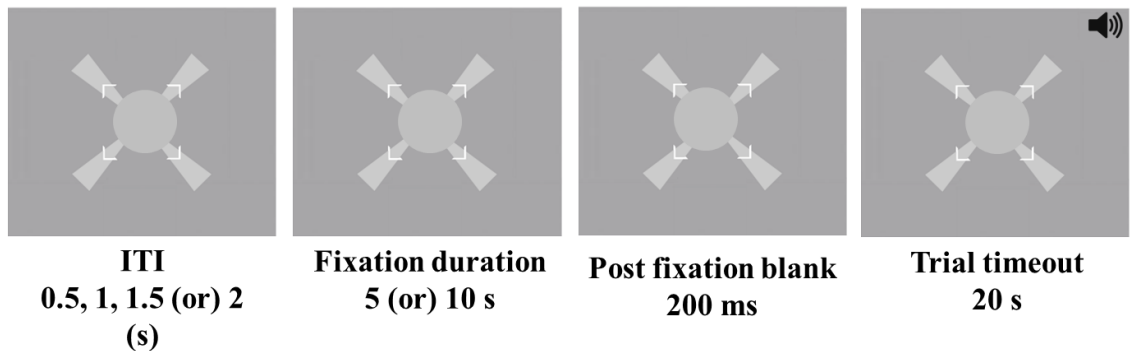| ITI | Fixation duration | Post fixation blank | Trial timeout |
| 0.5, 1, 1.5 (or) 2 (s) | 5 (or) 10 s | 200 ms | 20 s |

Figure 3.4. **Fixation training Task:** Here participants are required to maintain fixation of the artificial scotoma within the central white box presented on the screen. The intertrial intervals and fixation durations are jittered across trials. Once fixation conditions are satisfied, the participant is provided with auditory feedback indicating the end of the current trial and the beginning of the next.

Secondly, in order to investigate the adaptive eye movements and fixation strategies

developed in healthy individuals, it is important to first identify the PRL. Prior studies

using the simulated central vision loss paradigm have observed the rapid development of

PRLs in healthy individuals within a 1-hr session (Kwon et al., 2013). The benefits of

jumpstarting the oculomotor behavior by identifying PRLs is two-fold: (1) it allows for

participants to rereference their saccades to the PRL location allowing for better

perception of targets, (2) it is rapid and offers us the ability to track performance of

participants within the PRL (used for training) and at other untrained peripheral locations.

Prior to participants performing any behavioral assessment or training tasks, we subject

them to an induction task to allow for and analyze the development of PRLs. Participants

are initially presented with visual instructions in the form of task videos prior to

commencing the task. Following this, they engage in a brief practice session consisting of 10 trials, during which they are encouraged to seek clarification on the task and ask any pertinent questions before proceeding to the main task. Here we used a 10° scotoma that occluded the participants' fovea. A target made up of four Landolt C's with different orientations appeared within a circle (Figure 3.5) extending 3° radially from the border of the scotoma. Participants are required to fixate within a box at the beginning of the trial until they hear an auditory tone that indicates the disappearance of the fixation box and the appearance of a white circular target. They are then required to direct the scotoma towards the target to reveal the C's. Participants respond using ResponsePixx box to indicate the overall orientations of all the C's (i.e., using the green button to indicate left and a red button to indicate right orientations respectively). Auditory feedback (different from the auditory tone) is provided to indicate the accuracy of the responses, wherein a high pitch auditory tone indicates a correct response and low pitch tone indicates an incorrect response. Participants are required to complete a total of 150 trials spanning 30 minutes, and prior research has shown the development of PRLs within this window.

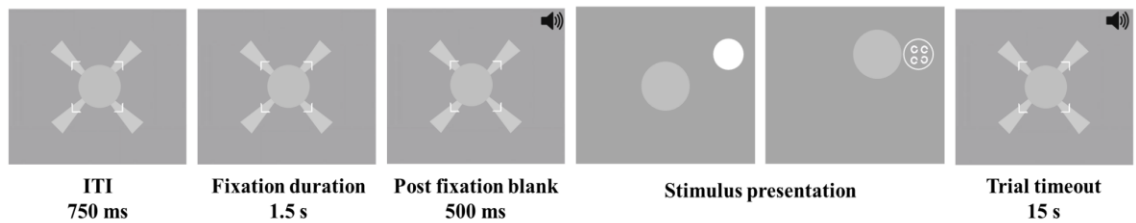|ITI|Fixation duration|Post fixation blank|Stimulus presentation|Trial timeout|
|750 ms|1.5 s|500 ms||15 s|

Figure 3.5. **PRL Induction Task:** Participants are required to fixate within a central box for 1.5 s after which they are presented with an auditory cue indicating the appearance of the target. The target is occluded with a white circle until the participant directs the scotoma close to the target boundaries. The stimulus is made up of four Landolt - C's and the participants are required to report the overall orientation of the C's (in this case, right red button on the response box). Auditory feedback is provided to indicate the accuracy of the response. Stimulus remains on the screen until either the participant makes a response or is timed out of the trial after 15 s.

Designing perceptual tasks within the framework:

Training participants to fixate within a central box and identifying PRL sets the stage to design and measure performance across a wide range of assessments including but not limited to acuity, contrast sensitivity, visual search and reading (see Figure 3.6 for visual representation and short description of the different assessment tasks implemented). The following sections will highlight the design considerations for measuring behavior across a wide range of perceptual tasks, to measure peripheral looking strategies through perceptual learning. Specifically, we emphasize the considerations for size of the scotoma and the adaptive staircases used to measure performance across these tasks.

The perceptual tasks (Figure 3.6) designed within this framework are broadly divided into two main categories: (1) Free eye movement tasks and (2) Fixed eye movement tasks. As the name indicates, in fixed eye movement tasks, participants are required to maintain fixation within a central white box throughout the task and use their periphery to

make judgements, whereas in the free eye movement tasks, participants are allowed to

make eye movements across the screen to identify targets appearing at random locations
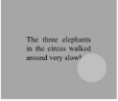
on the screen (or read texts).

Oculomotor Demands	Task Figures	Task Description
Free eye movement Tasks	**Fixation Stability**	Measures the ability to maintain stable fixation of a flickering target (O) within the PRL.
	MNRead	Minnesota Reading Task to measure reading speed, acuity and accuracy.
	Trail Making	Measures visual search skills, Here participants are required to connect consecutive numbers (or letters and numbers) in ascending order (or alternating order of numbers and letters i.e., 1-A-2-B etc)
Fixed eye movement Tasks	**Visual Acuity & Contrast Sensitivity**	Measured using Landolt-C stimulus where the size (acuity task) and contrast (contrast sensitivity task) of the letter C is manipulated.
	Crowding	Measured by manipulating the gap between the target (C) and flankers (O's) both in radial and tangential orientations.
	Contour Integration	Measures the ability to integrate and identify shapes made up of collinear fragments embedded in a background of distractors. Individual orientation of the gabor elements that make up the shape is manipulated.
	Exogenous Attention	Measures covert attention by presenting visual cues (congruent or incongruent) for 50 ms prior to target presentation (Landolt – C).
	Endogenous & Sustained Attention	Measures both overt and sustained attention using a rapid serial visual presentation (RSVP) task. Here an endogenous visual cue (white arrow; congruent or incongruent) is presented for 133 ms prior to target presentation (Landolt – C) followed by rapid presentation of C's and O's at the location

Figure 3.6. **Perceptual Tasks:** A visual representation of different assessment tasks designed using our framework. The tasks are broadly categorized into Free eye movement tasks where the scotoma follows the eye movements of the participants to view targets freely (top panel); and Fixed eye movement tasks where the scotoma needs to be placed within a central white box throughout the task (bottom panel).

81

While certain tasks such as MNRead and Trail Making can be completed in under six minutes, others like contour integration, crowding and attention tasks require more extensive time commitments, exceeding 15 minutes. Consequently, it is paramount to factor in the task complexities, visual strain, and participants fatigue during task execution. To address this, the tasks are distributed across two 90-minute sessions, with one session held per day. Tasks are strategically grouped and interleaved between days, alternating between easy and difficult tasks. To mitigate visual strain and fatigue, breaks lasting one minute are incorporated within each task (between blocks), with two additional three-minute breaks scheduled during each assessment day between tasks. These breaks allow participants to rest and stretch as needed, with calibration and validation procedures conducted after each break.

A critical aspect to the implementation of different assessments is the ability to estimate performance thresholds quickly and successfully in a subset of these tasks (specifically visual acuity, contrast sensitivity, crowding and contour integration). While it is possible to design these tasks using conventional 3 down 1 up staircases, this procedure takes several hundred trials to obtain thresholds causing fatigue and thereby taking several sessions to complete. To circumvent this, we implemented a two-stage adaptive staircase method to estimate performance of participants in these tasks. The first stage utilized a 2 down 1 up staircase that terminated after 3 downward reversals (i.e., direction of stimulus change, from down (hard) to up (easy), also refer to representative results section), followed by the second stage that consisted of a conventional 3 down 1 up staircase that ended after 60 trials. Pilot studies conducted in our lab indicated that this staircase was

sufficient to get reliable performance thresholds for the visual acuity, crowding and contrast sensitivity tasks, but not the contour integration task. Therefore, we used a slightly modified version of the adaptive staircase for this task (for details on the modification to the adaptive staircase procedure refer to contour integration task below). The section below discusses in detail the design of different perceptual assessment tasks using this framework.

Fixation Assessment:

This task measures the ability to make eye movements such that the to-be-attended object falls on the location of the retina corresponding to the PRL. This involves improving the capacity to maintain the eye at that location for extended duration required to process the stimulus ("fixation stability"). Attention to targets involves planning saccades to land at a given location. Post-training, eye-movements can be planned so that saccades land with a target directly on the PRL. The ability to remap eye-movements to consistently land so that the target appears within the PRL is called "saccadic precision". Standard approaches have limitations in examining eye-movements after training in MD, in that they mix temporal epochs of fixation, making it difficult to separately examine saccadic precision and fixation stability (Crossland et al., 2005).

Here, we design a new method (Maniglia et al., 2019) to overcome this limitation. We test the eye-movement components using a basic task where the participants make and hold an eye-movement such that their PRL lands on a 2° target (O). The target appears in 1 of 10 equally eccentric locations 15° from the center of the white fixation box (also

center of scotoma) as illustrated in Figure 3.7. Once the participants make the eye-movement towards the target and hold the scotoma near it, the target begins to flicker for 3-5 seconds (randomized across trials). Participants are required to stably maintain fixation until the flickering stops accompanied by auditory feedback (high pitch tone for correct and low pitch tone for incorrect responses). A new trial begins by redirecting the scotoma to the white fixation box and satisfying the fixation condition (maintain fixation within the box for 500 ms) to trigger the appearance of a new target. Prior to performing the full task consisting of 80 trials, participants are presented with visual instructions and also perform a practice block comprising 10 trials with one trial per location.
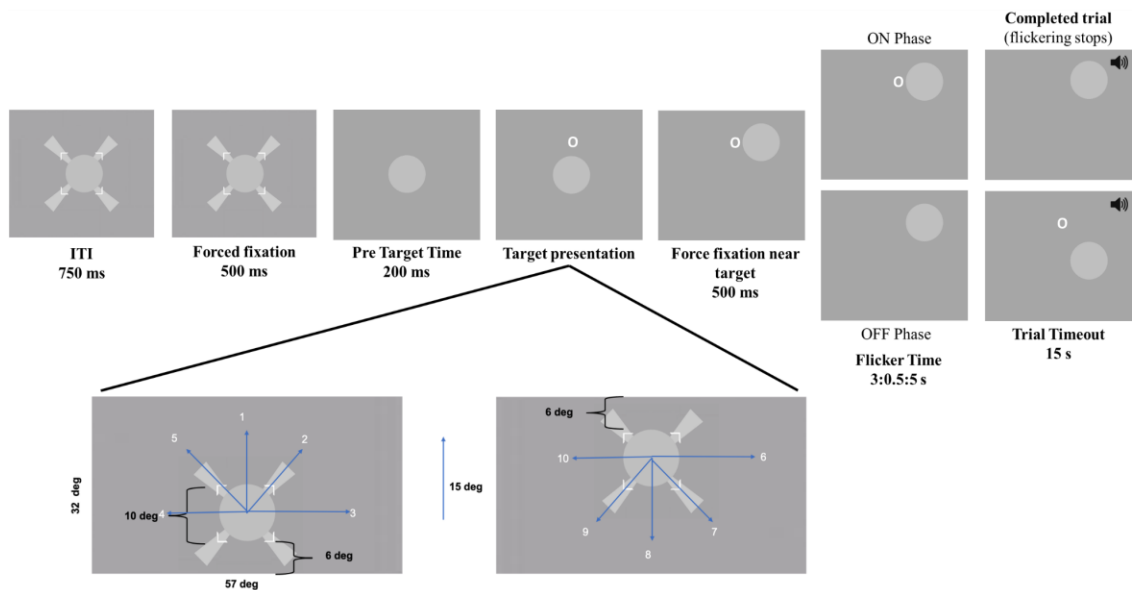
Figure 3.7. **Fixation Assessment Task:** Here, participants were required to maintain fixation within a white box at the beginning of each trial for 500 ms. Once they satisfied this condition, the fixation box disappeared, and white O (target) appeared on the screen in one of eight locations shown (bottom panel). They then had to make an eye-movement towards the target and hold the scotoma near the target to trigger the flickering of the target. If the participant moves their eyes away from the target, the flickering stops and will only begin after reacquiring the fixation close to the target. Auditory feedback is provided once the fixation stops to indicate the completion of a trial.

MNRead:

The Minnesota Reading task (MNRead) is a standardized task employed in vision science as a test of reading skills (Legge et al., 1989). This test relies on acuity and provides a more ecological measure of visual sensitivity, where participants are free to move the eyes when reading sentences (unlike the visual acuity task that requires participants to fixate in the center). We adapt this task for testing reading skills under simulated central vision loss. Participants are first presented with visualized instructions on what to expect in the task and how to respond to the stimuli that appears, after which they perform 5 practice trials with the scotoma where the font size decreases, prior to performing the whole task. Here we use a 10° scotoma where, in each trial, the participant reads out loud a sentence (made up of 7-10 words) while the font size decreases with consecutive trials until the font is too small to successfully read the text (Figure 3.8). In addition to measuring the acuity, we can also extract measures of reading speed, critical print size and accuracy.
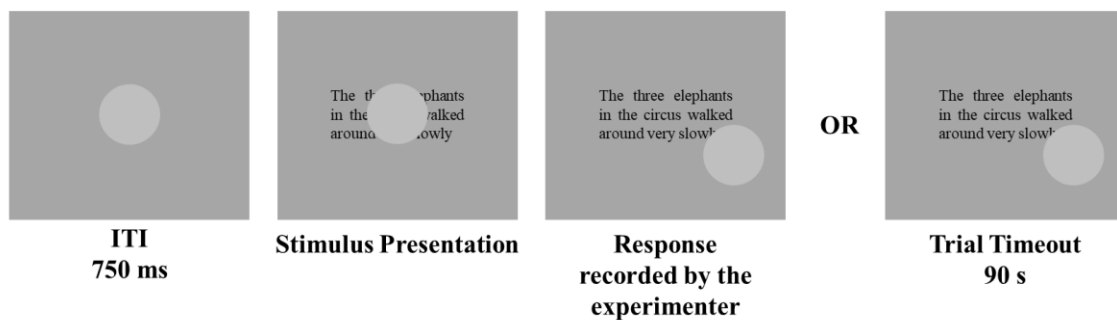

Figure 3.8. **MNRead Task:** Participants are presented with sentences of decreasing font size in consecutive trials and are required to read out the sentence loudly while the experimenter checks for accuracy of the response. The task ends when the font size is too small for the participant to read words in a sentence correctly or if they time out after 90 seconds.

85

Trail Making Task:

The trail-making task is a test typically employed to measure visual search abilities and has been adapted for use with the current framework (Tombaugh, 2004). Here, participants are required to connect a sequence of consecutive target numbers (1-2-3-), and numbers and letters (1-A-2-B-3-C-) displayed across the screen. This necessitates the visual search for subsequent numbers or letters in the sequence (see Figure 3.9). To ensure optimal task performance, the numbers and letters are arranged on the screen in a manner that prevents overlap or crossover of the connecting lines, facilitating accurate identification of sequential targets using peripheral vision. Participants are initially provided with visual instructions, followed by a practice session where they perform the task once without a scotoma, and then with the scotoma on a truncated version of the task. This ensures that participants comprehend the task demands before performing it under modified viewing conditions. Performance is evaluated based on the reaction time to identify targets and complete the sequence.
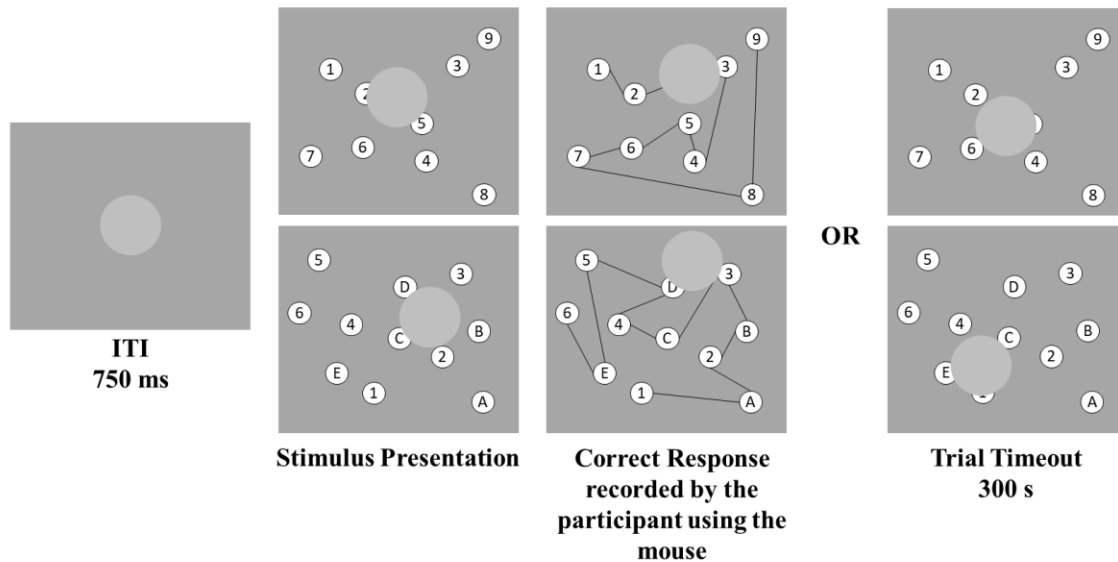
Figure 3.9. **Trail Making Task:** Participants are presented with either numbers (top panel) or numbers and letters (bottom panel) in different blocks and are required to click on numbers (or number and letters) in sequence of ascending order (i.e., 1-2-3 or 1-A-2-B-3-C) using the mouse. Auditory feedback is provided if the participant clicks on the correct number in the sequence and the trial ends after 300 seconds.

Visual Acuity and Contrast Sensitivity:

These tasks are designed to measure the ability to resolve fine details and are typically an important measure of low-level visual processing. It is important to note that the detection of a small gap (like a Landolt-C) is limited by the retinal mosaic compared to other tasks like vernier acuity tasks are limited by cortical processes (Levi et al., 1985; Thomas & Olzak, 1997). Both visual acuity and contrast sensitivity decreases with eccentricity and therefore using a large central scotoma produces a greater reduction that is too large to measure accurately, thereby impeding the ability to determine the true impact of the scotoma. Therefore, to effectively measure the performance with s-CVL we use a scotoma of 6° in size.

Here, we use the Landolt-C stimuli to measure acuity, where participants make judgements about the orientation of the gap of the C (left, right, up or down) while the size (for visual acuity task) and contrast (for contrast sensitivity task) of the C is manipulated (Figure 3.10). Prior to beginning the tasks, participants are presented with visualized instructions and practice trials at each location. At the beginning of each trial, participants are presented with a central square (fixation box) slightly larger than the scotoma. Each trial begins with an inter - trial interval of 750 ms followed by a fixation duration of 500 ms during which participants are presented with a visual cue (i.e., white dot) indicating the appearance of the upcoming target. Participants are required to satisfy the 500 ms fixation in order for the target to appear. If the scotoma moves outside the fixation box, the duration resets until the participant acquires stable fixation. This is implemented to ensure that the participant is stably fixating at the center of the screen to aid in perceiving the upcoming target effectively. Once fixation is acquired, the target stimuli i.e., Landolt – C appears for 200 ms. The contrast was fixed at 1 and the initial size of the letter C was 1° in the visual acuity task whereas the size of the C was fixed at 1° and the initial contrast was 0.35 units for the contrast sensitivity task. Both the size and contrast of the C was manipulated using a 2 staged staircase in the acuity and contrast sensitivity tasks respectively. Participants report the orientation of the C using one of four buttons on the response box (green → left, red → right, yellow → up, blue → down). Auditory feedback is provided to indicate the accuracy of the response, where correct responses are paired with a high pitch tone and incorrect responses are paired with a low pitch tone respectively. If the participant fails to acquire fixation or respond to the target

within 8 seconds, the trial is terminated. The task comprises a total of 120 trials with

trials blocked per location (60 trials on the left and 60 trials on the right of the central
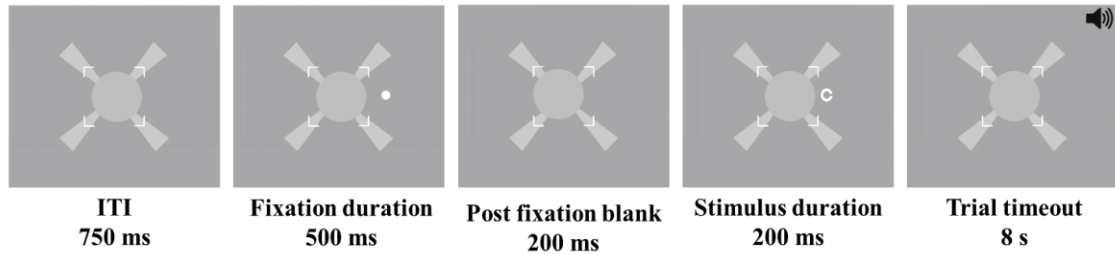
fixation).

Figure 3.10. **Visual Acuity and Contrast sensitivity Task:** Sequence of events in a given trial. Participants respond to the orientation of the C using the keys on the response box. In the figure, the correct response to the target is the red button, corresponding to the right orientation of the C. Auditory feedback is provided to indicate the accuracy of response.

Contour Integration:

Contour Integration is the ability to bind locally fragmented elements to form a

perceptual shape and is considered to involve mid-level visual processing i.e., binding

multiple low-level features (Field et al., 1993; Nothdurft, 1991). This task shares the

structure of the visual acuity test, but the stimuli used are contours of different shapes i.e.,

alphanumeric characters (letters "d" and "p") and egg-shaped contours (refer to

supplementary material for all stimuli figures). The target stimulus is a 15x15 grid made

up of Gabor elements of 3 cycles per degree and 1° in size as shown in Figure 3.11. The

stimulus is blocked per location (left and right) and shape (eggs and p/d) with participants

completing a total of 60 trials per block. Thus, the total number of trials in this task is

240. Difficulty in the task is manipulated by implementing an adaptive staircase on the orientation jitter of the individual Gabor elements that make up the shape.

There are a few things to keep in mind when designing this task: *Firstly*, the task in itself is considerably harder to perform in the periphery because of the low acuity and contrast as we move away from the fovea compounded by more inhibitory interactions in the periphery, making it harder for the visual system to compensate for eye movements and maintain a stable image of the contours (Kuang et al., 2012; Kwon et al., 2012). Therefore, we enforce a practice session that must be completed before performing each block of the task. The practice block consists of 12 trials with increasing jitter levels (0°-5° jitter) to familiarize the participants with the task and expose them to different difficulty levels. Participants must achieve a minimum of 70% accuracy (minimum of 9 correct responses) in order to move to the actual task (60 trials per location and shape). *Secondly,* pilot studies on this task in our lab revealed that the adaptive staircase procedure implemented for the acuity and contrast task was insufficient to obtain reliable estimates of performance on this task. Therefore, we implemented a slightly different 2 stage staircase procedure to get multiple outcome measures. Difficulty was manipulated using a progressive staircase where the orientation jitter (0°, 1°, 2°, 4°, 6°, 8°, 10°, 12°) increased every three trials for a total of 24 trials. A conventional 3 down/ 1 up adaptive staircase was then implemented until completion i.e., 60 trials. This allows us to measure the accuracy and reaction time of the participants in the first 24 trials as well as calculate the thresholds from reversals in the adaptive staircase stage.
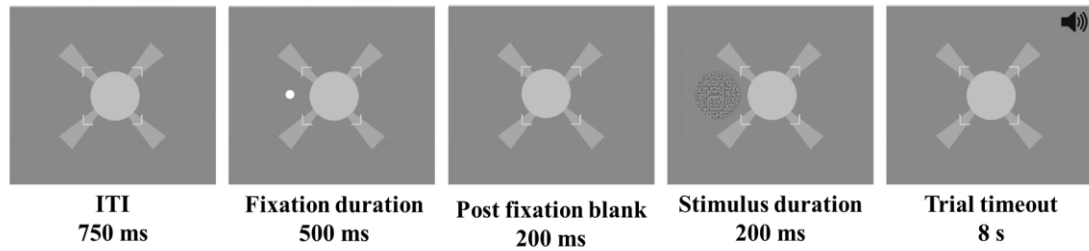
Figure 3.11. **Contour Integration Task:** Participants are presented with contour shape pairs (p/d and eggs) and are required to respond to the correct shape that appeared. For example, participants press the green button (left) if a "d" is presented and the red button (right) if a "p" is presented indicating the direction of the larger portion of the letter. Trial-by-trial auditory feedback is provided to indicate accuracy.

Crowding:

The crowding task complements the contour integration task as it measures the ability to avoid integration of background features. We designed this task using a procedure recently validated in MD patients (Greenlee et al., 2018), where the stimulus consists of a Landolt C flanked by O's on either side. A notable property of spatial crowding is the radial tangential asymmetry in which the effect of crowding is much more severe for items in the radial (horizontal) line compared to items arranged tangentially (vertical) with regard to a center fixation (Chambers & Wolford, 1983; Toet & Levi, 1992). Therefore, to test this asymmetry in the case of s-CVL we present the target C flanked by O's in both radial and tangential orientations as shown in Figure 3.12. The spacing between the C and O's are manipulated using the two stage adaptive staircase procedure (separate staircases for radial and tangential targets). The size of the C subtends 0.8° and the task comprises 4 blocks (radial vs tangential and left vs right locations) with each block consisting of 60 trials. Auditory feedback is provided to indicate accuracy of the

participants. We used a scotoma of 6° to ensure that the radial flankers aren't obstructed by the presence of a large scotoma (i.e., 10° as used in other tasks). Similar to the other tasks, participants are presented with visual instructions followed by practice trials at each location and orientation before performing the full task (i.e., 60 trials).
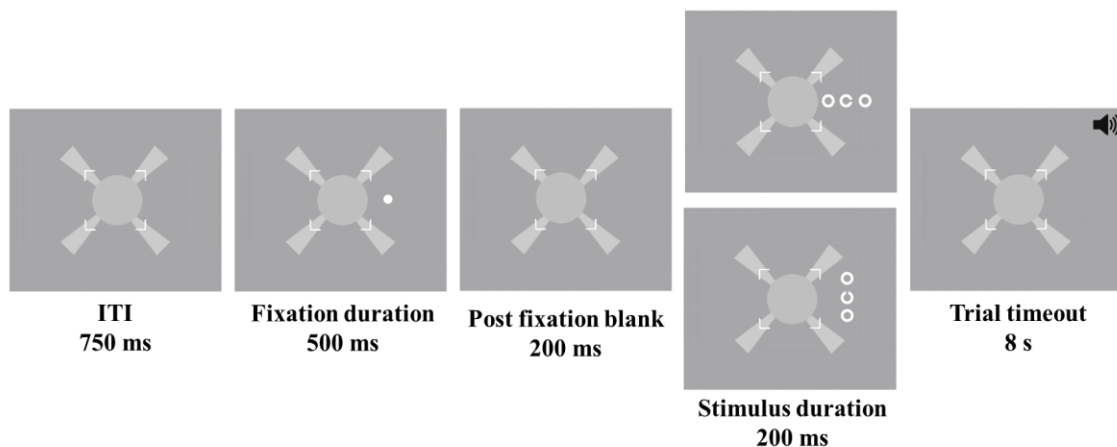

Figure 3.12. **Crowding Task:** Participants are presented with a radial (top panel) and tangential (bottom panel) target made up of Landolt - C flanked by two O's on either side, once they have satisfied the fixation condition, and are required to respond to the orientation of the C using the keys on the response box. For example, the participant responds using the red (right) button for the radial target and the yellow (up) button for the tangential target. Trial-by-trial auditory feedback is provided to indicate the accuracy of the response.

Exogenous Attention:

Exogenous (or covert) attention is an involuntary system that corresponds to an automatic orienting response to a location where sudden stimulation has occurred (James, 1918; Müller & Rabbitt, 1989; Nakayama & Mackeben, 1989). It is measured by presenting a visual cue and measuring the observer's reaction to a target that appears at the cued location (or an uncued location). Here, we design an exogenous attention task using the Landolt-C stimuli as indicated in Figure 3.13. Participants are required to fixate in a

central white box and must be prepared to pay attention to one of the two target locations (left and right eccentricities of the fixation box). The target locations are indicated with four black dots making up a square box. A cue is presented either at the target location (congruent) or at the location opposite to the appearance of the upcoming target (incongruent) indicated by the change in color of the four black dots at either location. Here, we used a low contrast Landolt-C stimulus (contrast = 0.35) as opposed to a high contrast C (contrast > or = 0.5) to ensure that the attentional effects observed are not simply due to differences in the physical properties of the stimuli (Boynton et al., 1999; Carrasco, 2011; Nachmias, 1967). For instance, if a target stimulus is presented with high contrast, participants may be able to detect the orientation of the C due to the contrast alone, without tapping into the attentional processes. By using a low contrast stimulus, we rule out this possibility and ensure that the attentional effects are not due to the physical properties of the stimulus itself. Participants need to report the orientation of the C using one of the four response buttons. Auditory feedback is provided to indicate the accuracy of the response during each trial. The task is divided into 4 blocks per cue type (congruent, incongruent) and location (left, right) with each block comprising 60 trials. Prior to performing the full task encompassing a total of 240 trials, participants are presented with instructional task video followed by 10 practice trials.
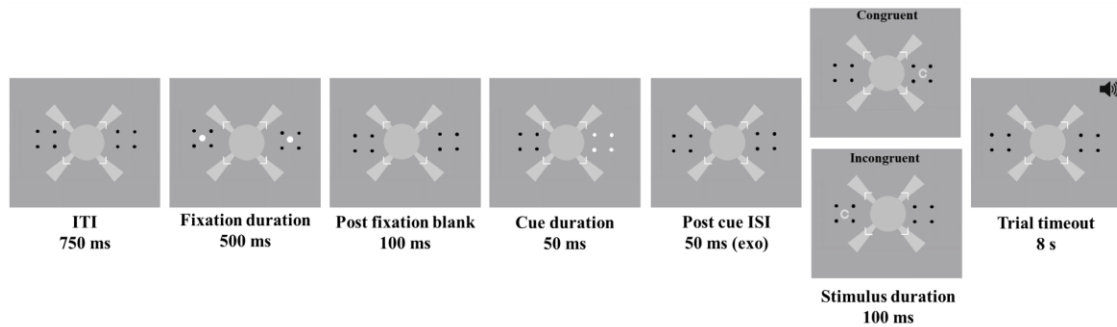
Figure 3.13. **Exogenous Attention Task:** Participants are presented with a target either on the left or right side of the central fixation box. A cue briefly flashes on the screen for 50 ms duration turning the 4 black dots on one of the locations to white. Landolt-C stimulus appears on either the cued (top panel) or uncued (bottom panel) location and the participants are required to make a response indicating the orientation of the gap of the C. For example, in the above task, participants correctly respond to the target using the red button (right) and auditory feedback is provided during each trial.

Endogenous and Sustained Attention:

In contrast to exogenous attention, endogenous (or overt) attention is a voluntary attentional process where the observer moves their eyes to attend to a specific spatial location often characterized by eye movement to the attended location (Carrasco, 2011). Endogenous attention is also known as "sustained" attention as the observers seem to be able to sustain the voluntary deployment of attention to a given location for as long as is needed to perform a task (Carrasco, 2011). Therefore, here we design a single task to measure both endogenous and sustained using the Rapid serial visual presentation (RSVP) paradigm. Participants are first presented with visual instructions of the task followed by 10 practice trials on the task before moving into the full task. Here, participants are required to keep their gaze steady within the central white fixation box and report the side of the gap of the Landolt-C stimuli (Figure 3.14). The target can appear in one of three peripheral locations. At the onset of each trial participants are

presented with three circles (one at the PRL and two control locations) as shown in the figure. The task comprises a total of 144 trials with 40 congruent and 8 incongruent trials per location. At the start of each block, trials are self-initiated by the participant's response to the target presented in one of three circles. This triggers the onset of the sustained attention task where a RSVP stream of 6 - 16 targets (3-5 C's) and distractors (3-11 O's) are presented. Each presentation of a target is followed by the presentation of n distractors to ensure that the response to the target C's is temporally spaced to measure accuracy during the sustained attention. Participants respond and report the orientation of the C for each target while ignoring the distractors. At the end of the trial, the participants are presented with an endogenous cue (white arrow) indicating the location of the appearance of the next target. The target then either appears at the cued location (congruent) or at any one of the uncued locations (incongruent). Performance is measured as a function of both accuracy and reaction times on this task across three locations. Sustained attention is estimated as the reaction times to the C's presented in the RSVP stream during each trial and endogenous attention is estimated as the reaction time and accuracy of response when switching to new locations between congruent and incongruent trials.
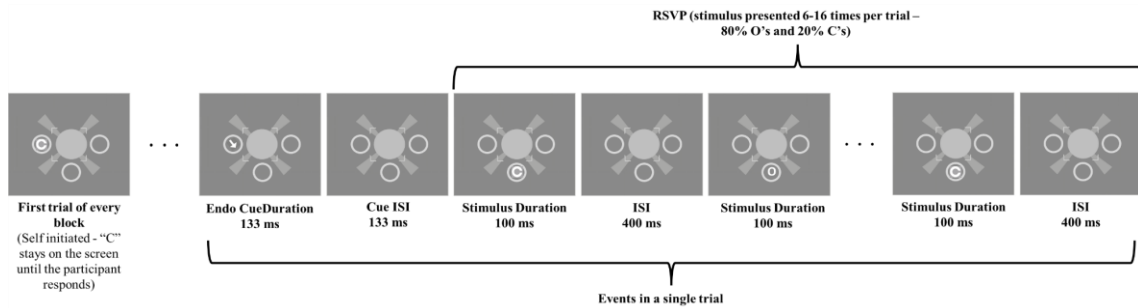
Figure 3.14. **Endogenous and Sustained Attention RSVP Task:** Participants respond to a stream of targets (C's) interleaved with distractors (O's) in this task. Each block is self-initiated by the participant's response to the orientation of a C present in one of three locations indicated by the three empty circles. Each trial ends with the presentation of an endogenous cue (arrow) pointing towards the location of the next target. The figure above illustrates a congruent trial where the target appears at the cued location. Throughout the task, participants are required to maintain fixation within the central white box and eye movements away from the center will immediately halt the stream of stimulus presentation until fixation is reacquired.

OCULOMOTOR METRICS:

While the perceptual tasks mentioned above encompass all levels of visual processing, it is also imperative to evaluate oculomotor behavior within these tasks. Previous research on understanding peripheral viewing strategies after CVL largely focused on analyzing fixation distributions to estimate fixation stability and the location of PRL. However, these approaches do not dissociate how gaze patterns differ between trials. While for some individuals, there is a single well-defined PRL, there exist inhomogeneities in peripheral looking strategies that may lead to more than one PRL and sometimes even partial PRLs. To effectively characterize the oculomotor behavior in a subset of training and assessment tasks mentioned above, we recently developed six different metrics to better understand more complex strategies to help quantify the use of PRL(s) (Maniglia, Visscher, et al., 2020). These metrics look at: (1) *Saccadic re-referencing* - whether the first saccade after target presentation places the target outside of the scotoma, (2)

96

Saccadic precision - whether the first eye movement placing the target outside the scotoma lands in a consistent location, (3) *First Saccade landing dispersion* - the dispersion of the landing location of the first saccade after target presentation, (4) *Fixation stability* - whether the eyes keep this position stable within each trail, (5) *Latency of Target acquisition* - how long does it take to bring the target to a location outside the scotoma and (6) *Percentage of useful trials* - percentage of trials where some fixations occurred with the target outside the scotoma. A visual representation of these metrics in the event of multiple PRLs is illustrated in Figure 3.15 below (adapted from (Maniglia, Visscher, et al., 2020)). Refer to the sections below for detailed description on the estimation of the six different metrics highlighted.
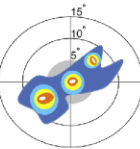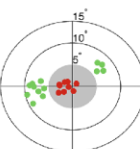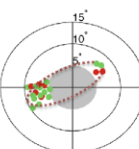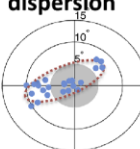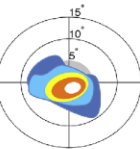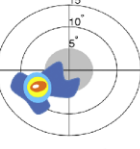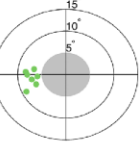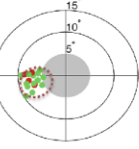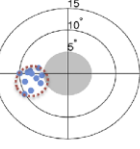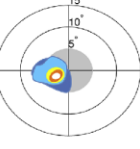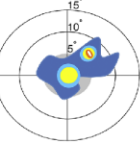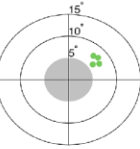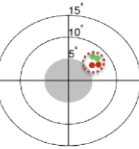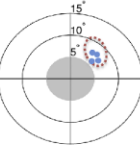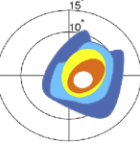
	Fixation Distribution	Saccadic Re-referencing	Saccadic Precision	First saccade landing dispersion	Fixation stability	Latency of target aquisit.	% of trials useful
PRL agnostic metrics	65 deg²	50%	60 deg²	55 deg²	6.5 deg²	0.4 s	95%
Identify candidate PRLs			PRL 2 / PRL 1				
PRL 1 specific metrics	36 deg²	60%	BCEA: 20 deg²	BCEA: 18 deg²	3 deg²	0.45 s	85%
PRL 2 specific metrics	50 deg²	10%	15 deg²	21 deg²	7 deg²	0.3 s	10%

Figure 3.15. **Overview of Oculomotor Metrics** adapted from (Maniglia, Visscher, et al., 2020)**:** Classification of eye movements first involves analyzing PRL agnostic metrics (first row) from the whole dataset to define PRLs. If multiple PRLs emerge, these metrics are calculated separately for trials where each PRL is used (bottom two rows, PRL specific). Metrics are shown from left to right: probability density map of fixation distributions, Saccadic re-referencing: proportion of trials where landing point of first saccade places the target outside the scotoma, Saccadic precision: dispersion of landing point of first saccade that places target outside of the scotoma, First saccade landing dispersion: dispersion of the end point of first saccade, Fixation stability: mean dispersion of eye positions after first saccade across trials, Latency of target acquisition: average time taken for a saccade to place target outside the scotoma, and % useful trials: how often participants place target outside of the scotoma (% of dots in saccadic precision relative to total trials) and in the case of multiple PRLs this informs us about the proportion of trials in which the participants used the specific PRL location first.

Saccadic Re-referencing:

This metric is calculated as the proportion of initial fixations per trial occurring outside the scotoma, representing the percentage of initial fixations that position the target in a visible location. Here, fixations are operationally defined as instances of eye stability

(characterized by eye velocity < 10 deg/s) lasting at least 150 ms and occurring at least

100 ms subsequent to target presentation. A value of 100% suggests negligible reliance

on the fovea for initial fixation on the target, while 0% indicates consistent placement of

the fovea on the target, thus obstructing its visibility. Notably, this assessment remains

unaffected by the presence or absence of designated PRL(s) outside the foveal region.

Saccadic Precision:

Saccadic precision quantifies the spatial distribution of initial fixations landing outside

the scotoma within a trial. These fixations may include the first, second, third, etc.,

wherein the target remains perceptible. The assessment is delineated by the size of the

Bivariate Contour Ellipse Area (BCEA) fitted around these fixation coordinates. BCEA is

computed to encompass a specified proportion ($p = 0.68$) of the total fixations, aligning

with established methodologies (Chung, 2013; Crossland et al., 2004; Kwon et al., 2013).

Notably, we differentiate "absolute" initial fixations (depicted as green dots) that also

happen to be the first fixation of the trial that places the target outside the scotoma from

other fixations (red dots) following initial fixations to the scotoma.

First Saccade landing dispersion:

This measure assesses the uniformity of initial saccadic landing locations across trials by

computing the area encompassing these locations (regardless of whether or not the

scotoma covered the target). The dispersion of initial saccadic landing positions was

evaluated using BCEA. Both measures of initial saccadic landing dispersion and saccadic

re-referencing delineate the deviation from foveal fixation in distinct manners. While saccadic re-referencing quantifies the frequency of initial saccades toward the target is within or outside the scotoma, the first saccade landing dispersion elucidates the spatial spread of these saccades, including potential involvement of multiple PRLs.

Fixation Stability:

Fixation stability characterizes the dispersion of eye positions within individual trials while controlling for variations in fixation locations across trials. Initially, this metric involves identifying all eye positions subsequent to the initial fixations within each trial, as outlined in the saccadic re-referencing section. Subsequently, a Kernel Density Estimator (KDE) is applied to these positions, weighted by their duration (i.e., KDE / duration of the trial in frames). The position of each trial's KDE is then normalized relative to the estimated across-trial PRL location. This PRL location is determined as the average center of single-trial BCEAs, normalized by the position of the first fixation, and centered on the average center of the single-trial BCEAs.

Latency of Target acquisition:

This metric is determined as the temporal duration from target presentation to the initial fixation outside the scotoma (the same fixation utilized in the saccadic precision analysis), expressed in seconds.

<u>Percentage of useful trials:</u>

This indicates the percentage of trials wherein at least one saccade landed the target outside the scotoma (referred to as "useful" trials denoting instances where the target was visible outside the scotoma). It is presented as a proportion relative to the total number of trials.

In addition to these metrics, please refer to (Maniglia et al., 2023) for more details on extracting oculomotor behavior in MNRead and Trail Making tasks.

REPRESENTATIVE RESULTS:

In this section we show representative results for each of the tasks discussed above. This section is largely divided into four categories to showcase (1) the adaptive staircases, (2) measures of attention, (3) performance on ecologically valid tasks, and finally (4) oculomotor metrics of fixation distributions, from two participants. Prior to data collection, participants were consented, and the study was approved by the IRB of University of Alabama, Birmingham.

Performance on tasks with adaptive staircases:

Figures 3.16 and 3.17 showcase the performance trajectory of the two participants on the visual acuity (panel A), contrast sensitivity (panel B), contour integration (panel C) and crowding tasks (panel D), respectively. The staircases are color coded based on the location of the appearance of the target (i.e., performance on the left location indicated in green and on the right location indicated in purple). Thresholds were estimated by

calculating the average of the last 6 reversals per location (and per shape or orientation in the contour integration and crowding tasks, respectively) and are indicated by a dotted line perpendicular to the y axis for each task. Lower values on the y axis indicate better performance for the visual acuity, contrast sensitivity and the crowding tasks, whereas higher values on the y axis indicate better performance for the contour integration task.
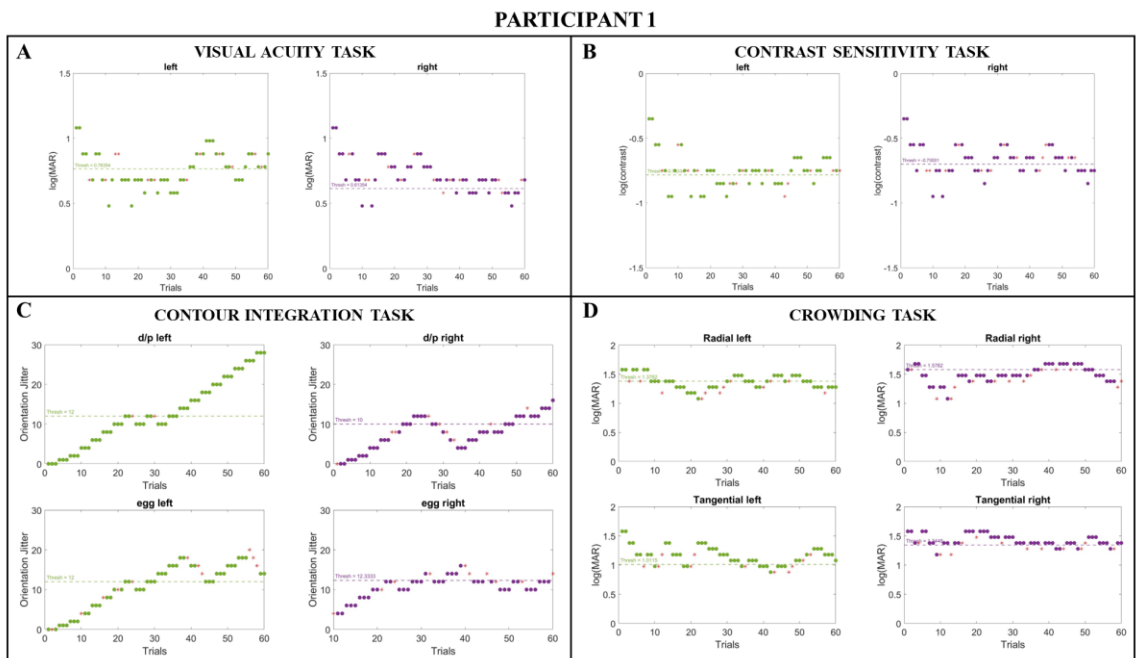
Figure 3.16. **Performance of Participant 1 in tasks with adaptive staircases:** Panel A, B, C, and D represent the performance of the participant on the visual acuity, contrast sensitivity, contour integration and crowding tasks respectively. Green dots indicate performance of the participant on the left location, whereas purple dots indicate performance of the participant on the right location. Red stars indicate incorrect responses on trials and thresholds are represented as dashed lines perpendicular to the y axis.
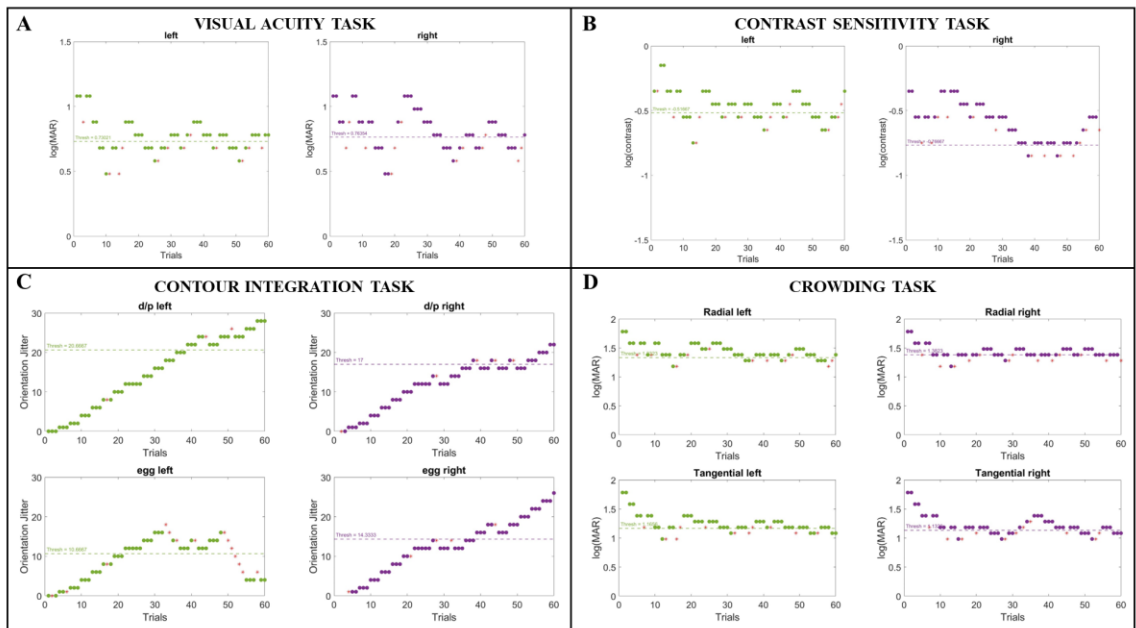
Figure 3.17. **Performance of Participant 2 in tasks with adaptive staircases:** Panel A, B, C, and D represent the performance of the participant on the visual acuity, contrast sensitivity, contour integration and crowding tasks respectively. Green dots indicate performance of the participant on the left location, whereas purple dots indicate performance of the participant on the right location. Red stars indicate incorrect responses on trials and thresholds are represented as dashed lines perpendicular to the y axis.

Measures of Attention:

Figures 3.18 and 3.19 show the performance of the participants on the Exogenous attention and the Endogenous/ Sustained Attention (RSVP) tasks respectively. In the exogenous attention task, performance is measured as the reaction times on the congruent (valid cue) and incongruent (invalid cue) trials grouped by the location (left/ right). We observed significant effects of cue type for Participant 1 on the left location (Welch's t-test: $t(111.5) = -2.6$, $p < 0.05$) but not for the right location, whereas we did not observe any significant effect of cueing across either locations for participant 2.

103
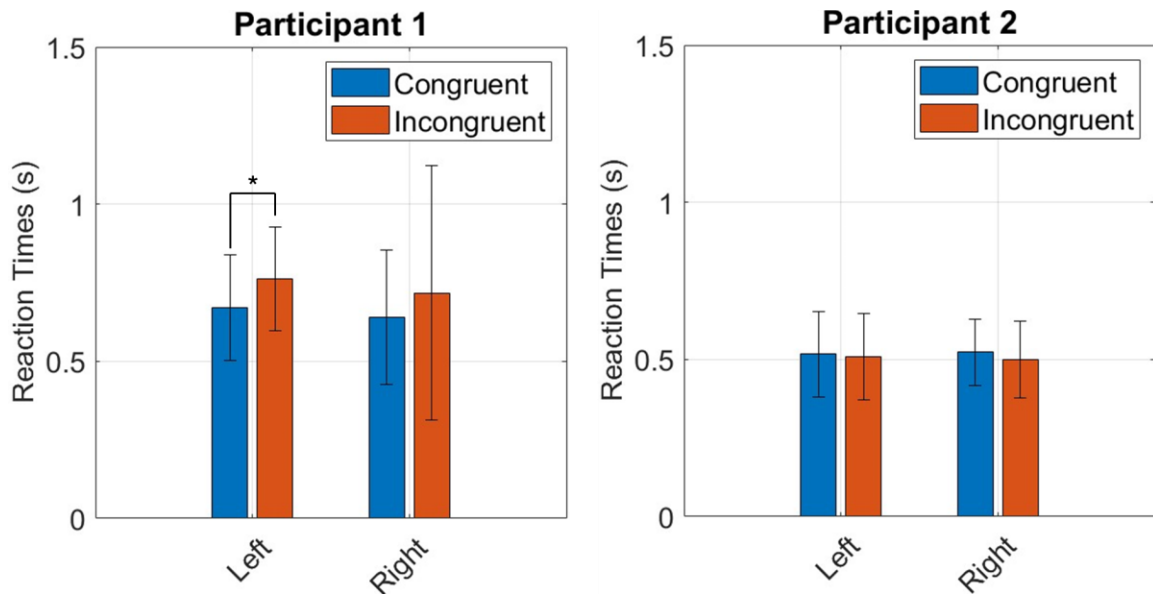
Figure 3.18. **Exogenous Attention Task Analysis:** The figure shows the reaction times (in seconds) of two participants on the task grouped by location of target presentation. The red bars indicate incongruent trials whereas the blue bars denote congruent trials. Error bars represent standard deviation.

The endogenous/ sustained attention RSVP task is represented in a different manner compared to the exogenous attention task. Particularly, here we show the reaction time differences between the congruent and incongruent trials, when the participant makes switches towards and away from their specific PRL location. Comparison of these reaction time differences between the 3 locations (PRL, untrained retinal locus (URL), and neutral location) allows us to track performance across the three locations. For example, in Figure 3.19, panel A, the participant's preferred location is indicated as PRL (on the left) whereas the other location is indicated as the URL (on the right). The bottom location is indicated as the neutral location. The arrows towards and away from each location are color coded as pink, blue and green and the values indicate the reaction time differences between the congruent and incongruent trials for each location. A negative

reaction time difference indicates that the participant was faster during congruent trials whereas a positive value indicates the converse (slower during congruent trials). It can be observed from Figure 3.19A that the participant was faster when switching from PRL to URL during congruent trials (RT diff = -0.094s) but not when switching from PRL to neutral location (RT diff = 0.044s). Additionally, this participant was faster on the congruent trials when switching from the neutral location (RT diff = -0.041s) towards the PRL as opposed to the URL (RT diff = 0.041s) and was slower when switching to both the PRL and the neutral location from the URL (RT diff towards PRL = 0.027s; RT diff towards Neutral location = 0.107s). Similarly, from Figure 3.19B it can be observed that participant 2 is (i) faster when switching from the PRL to neutral (RT diff = -0.007s) but not URL (RT diff = 0.057s); (ii) faster when switching from neutral to both PRL (RT diff = -0.031s) and URL (RT diff = -0.044s); and (iii) slower when switching from URL to PRL (RT diff = 0.011s) but faster when switching from URL to neutral location (RT diff = -0.06s).
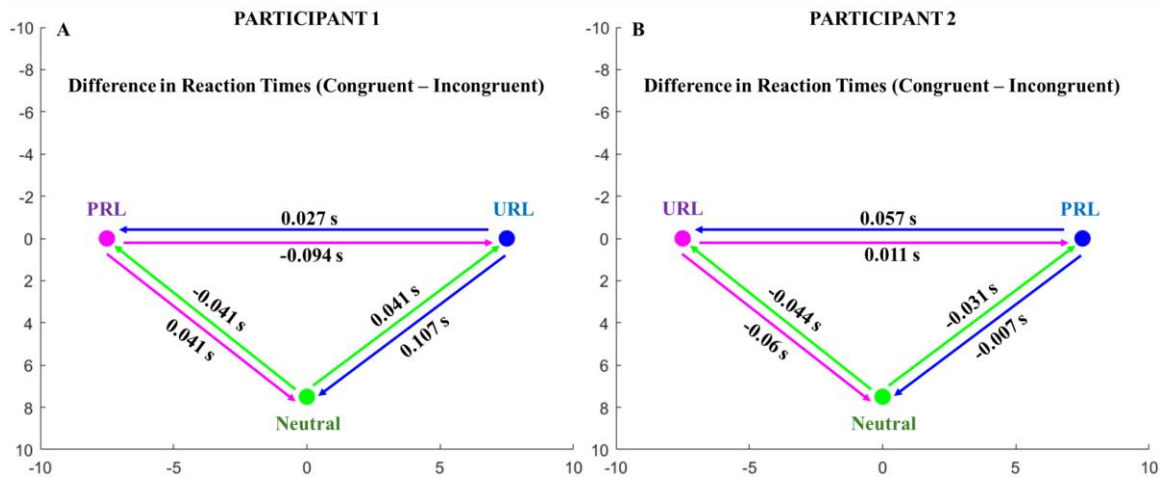
Figure 3.19. **Endogenous attention Analysis:** This figure shows the reaction time differences between the congruent and incongruent trials when switching from one location to another. A negative value indicates that participants are faster in responding to congruent trials and vice versa. The PRL for participant 1 (panel A) is on the left of the scotoma (pink) whereas the PRL for participant 2 (panel B) is on the right of the scotoma (blue). The other locations are indicated as the untrained retinal locus (URL) and neutral location.

Performance on Ecologically Valid Tasks:

Performance on MNRead task is represented as the time it takes to read the sentence without any errors. The task ends when the participant cannot read the sentence. Figure 3.20 A&B shows the performance of the two participants on the MNRead task. As expected, the time taken to complete each sentence increases as the font size decreases. From this, we can estimate reading acuity (i.e., smallest font size correctly read), maximum reading speed and the critical print size and compare these metrics within and between participants. Performance on the Trail Making Task is represented in Figure 3.20 C as the total time to completion for both Part A (connecting numbers in sequence of ascending order) and Part B (connecting alternating numbers and letters in sequential order). Although the total number of elements in both Part A and Part B are the same,

participants take longer to complete Part B, consistent with findings from previous

studies (Gaudino et al., 1995).
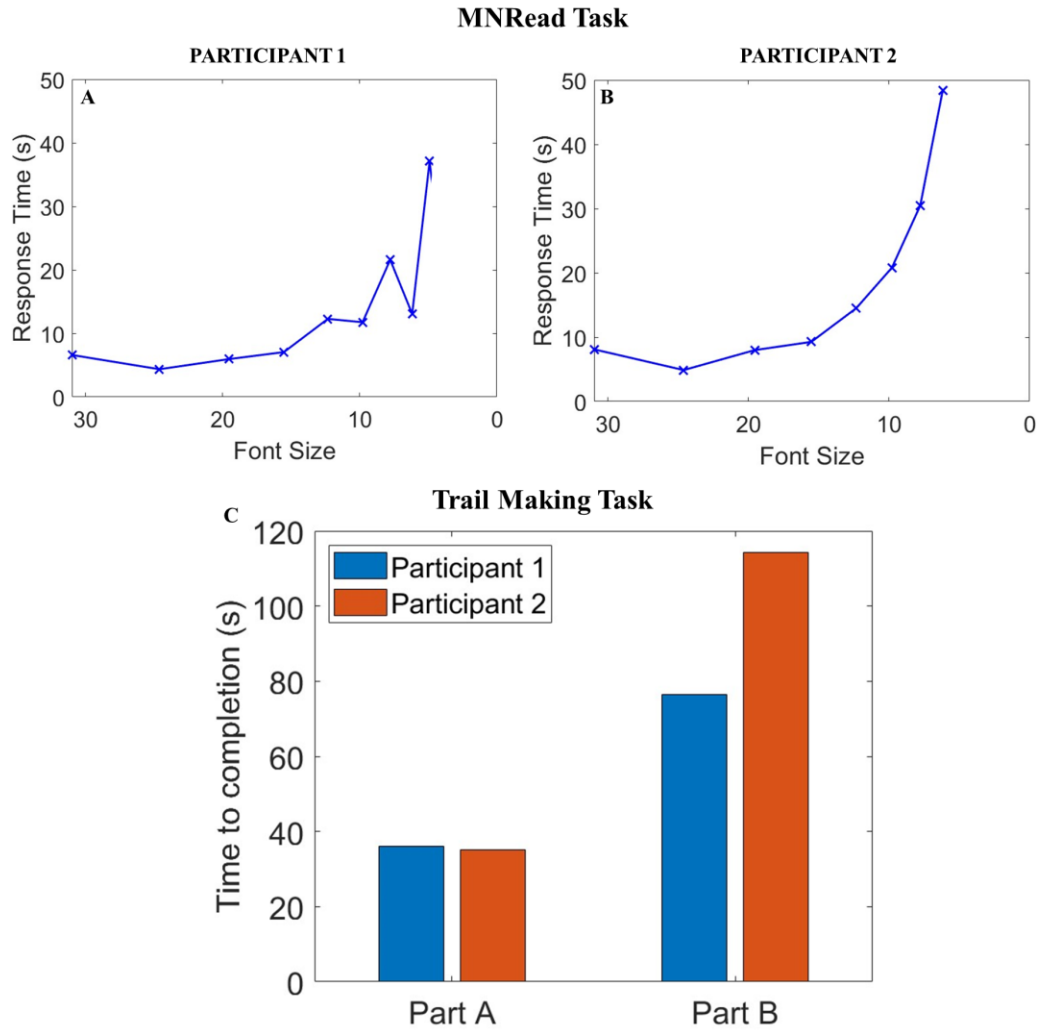
Figure 3.20. **Analyses of ecologically valid assessment tasks:** Response time (in seconds) as a function of the sentence font size for Participant 1 (panel A) and Participant 2 (panel B). Panel C shows the time to completion (in seconds) for both Part A and B of the Trail Making Task. Blue and red bars denote participant 1 and 2 respectively.

Fixation Stability Analysis:

To understand peripheral viewing strategies after CVL, we focus on analyzing fixation distributions to estimate fixation stability and the location of the PRL (Crossland et al., 2004; Maniglia, Visscher, et al., 2020). Dispersion of eye positions within a trial is characterized by controlling for differing fixation locations across trials to obtain the average dispersion of eye positions within trials. This metric is a within-trial measure of the dispersion of eye positions after the first fixation of the trial, consistent with previous studies (Kwon et al., 2013; Liu & Kwon, 2016). We compute it by calculating the BCEA encompassing a given percentage of fixations (typically 68%) over a certain period (i.e., 15-30 seconds). However, in contrast to the previous studies the dispersion of fixations for each trial was normalized by trial duration and averaged across trials (Figure 3.21, column 2). This means that if the fixations are centered in different locations on different trials, this method plots all the distributions at the same location. We also used a probability density analysis that uses a KDE to visually represent clusters of high density of fixations (Figure 3.21, column 3). Of note, these analyses provide an overview of the gaze patterns of participants over time, and do not dissociate how gaze patterns differ between trials.
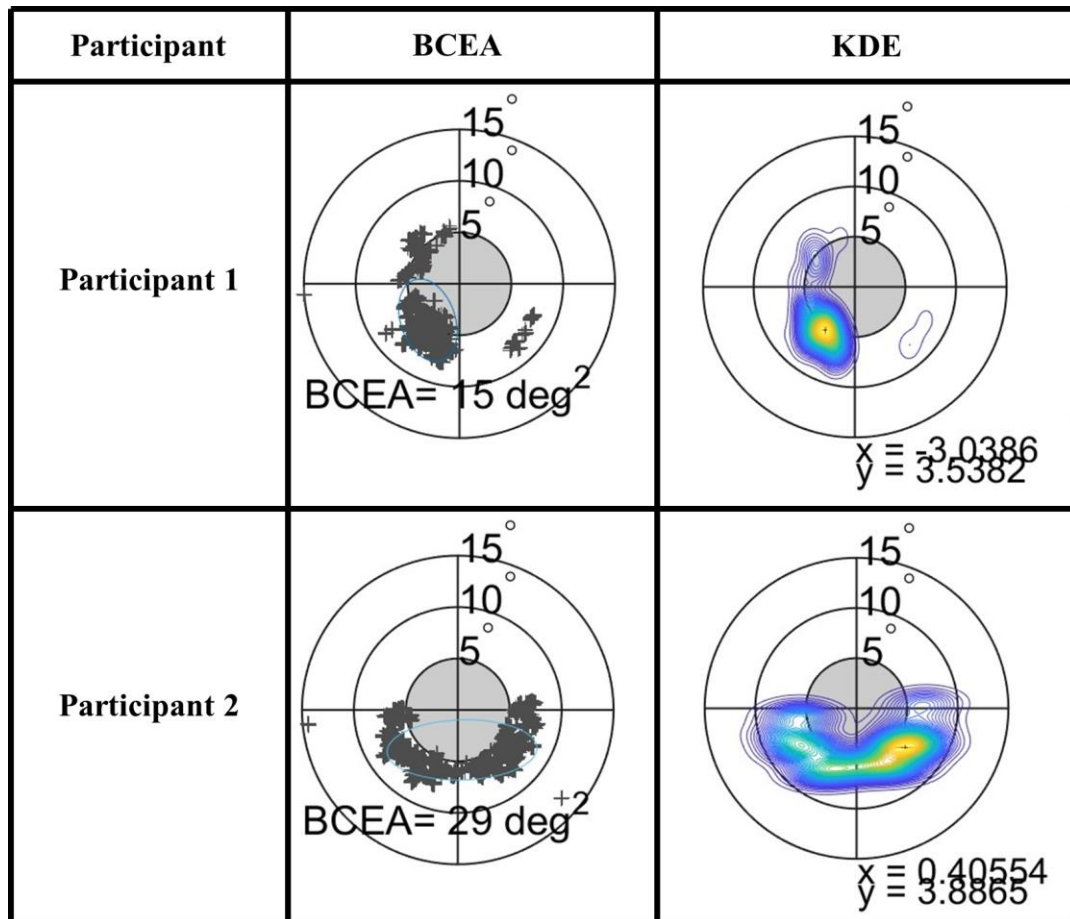
Figure 3.21. **Fixation Stability Analysis:** The figure shows the BCEA and KDE plots of fixation distributions for the two participants. The blue ellipse shown encompasses 68% of the total number of fixations in the BCEA plots. The bright yellow region in the KDE plots represent the highest density of fixations.

DISCUSSION:

In this methodological paper, we propose a gaze contingent framework for conducting

perceptual learning research in simulated central vision loss. Here, we emphasize on

several hardware, design, and methodological considerations that are required to (1)

simulate central vision loss in healthy individuals, (2) administer a wide range of

perceptual tasks, and (3) measure oculomotor and perceptual performance of participants

within this paradigm. Specifically, we first measure the combined latency of different

hardware and software systems that concur to render the perception of s-CVL. Our

findings indicate that latency significantly reduces when using a Windows OS system

compared to Mac iOS system to design tasks. Additionally, we also found small

qualitative improvements when using a VPixx eye tracker compared to the Eyelink 1000.

The current study also emphasizes the need for implementing several checks when

designing tasks (and subsequently collecting data) using gaze contingent display.

Particularly of importance, is the adaptation and familiarization of participants to the

modified viewing conditions using the scotoma by training participants to maintain stable

fixations (required for fixation dependent tasks) and jump-starting oculomotor behavior,

both of which are critical to perform perceptual tasks. We achieve this by subjecting the

participants to a fixation training and PRL induction task prior to any exposure to the

perceptual tasks. We also address experimenter bias by implementing a double-blind

assignment of participant conditions in addition to providing clear and uniform visualized

instructions (i.e., instructional task videos) to circumvent any verbal instructional biases

that may impede the participants' understanding of the tasks.

A novel aspect of our framework is its ability to support a wide range of perceptual tasks

catered to measuring performance across different levels of visual processing (low-, mid-,

and high-level). In order to effectively measure performance on these tasks, it is

important to (1) provide sufficient breaks within and between each task, and (2) design

the psychophysical demands of the tasks to estimate performance in a quick and reliable

manner that doesn't cause fatigue owing to prolonged use of visual periphery in participants with intact central vision. Thus, we use a two-stage adaptive staircase method (with some modifications in CI task) to estimate performance thresholds across different low- and mid-level visual assessments. We also ensure that the assessments are administered across two sessions such that each session is 90 minutes long including breaks implemented within each task and between tasks. Finally, we also briefly discuss the different metrics that can be analyzed to quantify oculomotor behavior representative of different peripheral looking strategies of participants.

Adapting the framework for testing in MD patients:

While this framework is designed for s-CVL in healthy individuals, it can be extended for research in MD patients. Indeed there is both prior and ongoing research in MD patients using gaze contingent displays for scotoma awareness (Fletcher et al., 2012; Fletcher & Schuchard, 1997; Frennesson et al., 1995) and we briefly discuss how our framework can be adapted for perceptual training in patients with MD. When adapting this framework for patients, it is important to keep in mind that their viewing strategies drastically differ from that of the normal sighted individuals. *Firstly,* it is well known that patients with MD tend to have unstable fixations, thus despite recent attempts at calibrating eye tracking devices used in vision research in this population (Harrar et al., 2018), this might prove challenging. To address this, we adapted the nine-point calibration/ validation for MD patients by presenting larger calibration points along with wedges and reducing the distance between the dots to appear more towards the center of the screen to avoid

viewing targets at extreme eccentricities. Furthermore, since several of the tasks designed with our framework require stable central fixation, we incorporate additional fixation aids i.e., wedges that fan out from the center of the fixation box for ease of detection. *Secondly,* simulated and pathological scotoma present a number of differences in terms of the time course of development of compensatory strategies, overall fixation stability, and might be qualitatively different (Ağaoğlu et al., 2019). It is however possible to map the shape and size of the scotoma in MD patients through Macular Integrity Assessment (MAIA) and use this to define the shape of the scotoma in our tasks (Ramírez Estudillo et al., 2017). *Thirdly,* while the metrics we have presented here might not be typical of what we might observe in patients, the possibility of breaking down eye movement behaviors and being able to characterize the development of oculomotor strategies at different stages of simulated training is a valuable tool for better understanding of the visual systems' adaptation to simulated or pathological CVL.

Using s-CVL as a model to test specificity and generalization of PL:

We are currently in the process of conducting a clinical trial study using the proposed framework to test different perceptual training strategies, using s-CVL as a model to understand specificity and generalization of PL. The motivation behind using s-CVL as a model is twofold: (1) it serves as a blank canvas to test the proposed training strategies and assess transfer of learning to other untrained tasks and location, and (2) ideal use of peripheral vision requires improvement across multiple vision domains i.e., low-, mid- and high-levels. We aim to investigate how different vision domains change together

through PL after CVL. To date, PL studies have examined a narrow range of behavioral outcomes, severely limiting our understanding of PL (Maniglia & Seitz, 2018). By measuring an array of learning outcomes, we aim to characterize profiles of learning and dissociable patterns of generalization across outcome measures. To do this, we train peripheral vision in s-CVL to determine how training different domains of vision gives rise to different distributions of behavioral changes. In addition to implementing a range of perceptual assessments that encompass all levels of visual processing, we also implement four perceptual training tasks. The training tasks designed within this framework targets early visual processing (contrast sensitivity training), mid-level visual processing (contour integration training), attention and eye movement training, and a combination training that includes all of these domains.

While not exhaustive, the proposed training strategies encompassing all three domains of visual processing, capture fundamental aspects of vision and are known to be, at least partly, separable both from visual performance and neuroscience perspectives. Here, we train participants for 20 sessions (each session lasting approximately 45 minutes) on one of the four training tasks assigned randomly. Prior to training, participant specific PRL is obtained from the PRL induction task, which is then used for training (trained retinal locus). Both baseline and post training measures of performance on the different assessment tasks are obtained to observe for transfer of learning to other tasks and untrained locations (i.e., locations other than the trained retinal locus). In addition to this we also examine pre-post changes in eye movement metrics across these tasks. Since all training conditions involve learning to perform visual tasks in the PRL, we expect both

contrast sensitivity and contour integration training tasks to show some behavioral change related to attention, albeit less than both the attention and combined training tasks. Given that the combined training condition encompasses all the other three training conditions, we expect (1) to observe behavioral changes related to all three domains of vision, (2) greatest effects in the ecologically valid tasks (MNRead and Trail Making) compared to the other three training conditions, and (3) to examine the extent to which cross-training is beneficial to each of the domains. Moreover, we also examine how PL in MD patients compares to conditions of s-CVL. Similar behavioral changes between the healthy individuals with s-CVL and MD patients would provide an important validation of the current framework, whereas finding differences between the two groups would inform which aspects of s-CVL provide a good proxy for MD patients and which aspects need further refinement. It is important to note that the clinical study conducted using this framework only examines learning and transfer of learning within two discrete locations (right or left PRLs, with the exception of the RSVP task), and does not account for participant specific PRLs and subsequently performance in other locations (top or bottom locations, although this can be examined using this framework).

Limitations:

While this framework is currently being used to train and assess performance of both healthy individuals (using simulated scotoma) and patient populations, it has a few limitations that need to be addressed. In our study we use a visible scotoma that can lead to compensatory eye movements or other strategies that may not be present in a real-

114

world scotoma that is invisible. Moreover, the use of static scotoma as opposed to dynamic scotoma that change/ grow both in shape and size (as observed in patients) doesn't allow us to study the effect of CVL longitudinally. However, it is possible to track the physical properties of the scotoma in patients (i.e., size and shape) through MAIA. Additionally, the current tasks designed using our framework do not account for visual impairments that are related to color deficiencies or face perception, but it is possible to test these aspects of vision as well. Finally, while in our study we use computer displays to simulate CVL, it is also important to study the effect of CVL in more ecological settings. While it is possible to provide a more subjective and immersive experience of s-CVL in healthy individuals using virtual reality, it is important to characterize the latency of such systems to render a smooth perception of the scotoma.

CONCLUSION:

The current paper proposes a gaze contingent display framework for conducting perceptual learning research in healthy individuals with simulated central vision loss with a specific focus on highlighting the design considerations associated with the development of such a framework. In addition to this, our novel multidimensional framework integrates multiple approaches to addressing plasticity after central vision loss, making this the first study to the best of our knowledge to explicitly evaluate the premise that effective use of the periphery after CVL jointly depends on multiple visual domains.

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Chapter 4: Performance on a Contour Integration task as a function of Contour shape

This study presented in this chapter discusses the implications of using a gamified vision training paradigm for promoting learning in patients with schizophrenia. While Chapters 2 and 3 propose methods and tools for PL research, this chapter takes a closer look at the advantages of designing a vision training paradigm with a translational motive. When designing perceptual training paradigms for vision rehabilitation, it is crucial that training generalizes to other tasks and domains. With this in mind, we incorporated a contour integration training paradigm that utilizes diverse stimuli, adaptive procedures and enriched feedback, components that are critical for facilitating transfer of learning, and what we attribute to being "gamified" in this case. While the study discussed here does not draw any conclusions about the generalizability of such a training paradigm, when performance on the training task was retrospectively analyzed, it revealed novel findings pertaining to the nuances of mid-level visual impairments in patients with schizophrenia. These findings are critical for the understanding of the nature and extent of visual impairments, and thereby the development of more targeted rehabilitation techniques for these patients. This study is a collaborative effort between University of California, Riverside, University of Rochester Medical Center, Nathan S. Kline Institute for Psychiatric Research, and Weill Cornell Medicine, and has been published in Vision Research.

My contributions to this work included analyzing training data, writing the manuscript for publication and submission, addressing reviewers' feedback and comments, and

proposing directives for future research informing the design of vision training paradigms

for research in patients with schizophrenia.

Title: Performance on a Contour Integration Task as a function of Contour shape in Schizophrenia and controls

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ABSTRACT:

Contour Integration (CI) is the ability to integrate elemental features into objects and is a basic visual process essential for object perception and recognition, and for functioning in visual environments. It is now well documented that people with schizophrenia (SZ), in addition to having cognitive impairments, also have several visual perceptual deficits, including in CI. Here, we retrospectively characterize the performance of both SZ and neurotypical individuals (NT) on a series of contour shapes, made up of Gabor elements, that varied in terms of closure and curvature. Participants in both groups performed a CI training task that included 7 different families of shapes (Lines, Ellipse, Blobs, Squiggles, Spiral, Circle and Letters) for up to 40 sessions. Two parameters were manipulated in the training task: Orientation Jitter (OJ, i.e., orientation deviations of individual Gabor elements from ideal for each shape) and Inducer Number (IN, i.e., number of Gabor elements defining the shape). Results show that both OJ and IN thresholds significantly differed between the groups, with higher (OJ) and lower (IN) thresholds observed in the controls. Furthermore, we found significant effects as a function of the contour shapes, with differences between groups emerging with contours that were considered more complex, e.g., due to having a higher degree of curvature (Blobs, Spiral, Letters). These data can inform future work that aims to characterize visual integration impairments in schizophrenia.

INTRODUCTION:

Schizophrenia is a psychotic disorder characterized by delusions, hallucinations, disorganized thoughts and speech, social dysfunction, and cognitive deficits (Patel et al., 2014). In addition, a range of visual perceptual problems have been reported in individuals with schizophrenia (S. M. Silverstein, 2016). These include impairments in low-level vision such as visual acuity and contrast sensitivity (Pamela D. Butler et al. 2005; Viertiö et al. 2007; Halász et al. 2013; Martínez et al. 2012; S. M. Silverstein et al. 2014; (S. M. Silverstein, 2016); mid-level vision including different aspects of perceptual organization (Chen, 2011; S. M. Silverstein & Keane, 2011; S. M. Silverstein et al., 2012; Tadin et al., 2006; Uhlhaas & Silverstein, 2005); and high-level vision such as the effect of prior knowledge on visual perception (Hahn et al., 2012; Keane et al., 2013). It has further been shown that these visual processing deficits relate to significant impairments in higher-level cognitive and social functions such as visual working memory (Dias et al., 2011; Revheim et al., 2006, 2014; Steven Silverstein et al., 2005), object recognition (S. M. Silverstein & Keane, 2011) and facial emotion decoding (P. D. Butler et al., 2009), along with poorer functional outcomes (Green et al., 2012; Rassovsky et al., 2011). According to the NIMH funded CNTRICS (Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia) initiative, two key processes have been identified as being involved in visual impairments in schizophrenia: *gain control and integration* (Pamela D. Butler et al., 2008). The aim of this study was to investigate visual integration impairments in schizophrenia by leveraging data collected in the context of a clinical trial of a visual training intervention.

Perceptual organization involves a series of visual processes responsible for integrating visual features into object representations (S. M. Silverstein & Keane, 2011). Perceptual organization is a fundamental visual process required to perform day-to-day activities such as object and face recognition and processing complex visual scenes. It is also integral for several higher-order social, functional and cognitive processes that rely on this visual information (P. D. Butler et al., 2009; Pamela D. Butler et al., 2013; Curby et al., 2013; Korjoukov et al., 2012; Sehatpour et al., 2010). It is broadly studied using a variety of tasks such as figure-ground segmentation (Roelfsema et al., 2002), shape completion (Vogels & Orban, 1987), integration of contours (Kuai & Yu, 2006; S. M. Silverstein et al., 2012), and coherent motion detection (Kurylo et al., 2017). Contour Integration (CI) refers to the ability to bind locally fragmented elements to form a perceptual shape and has been the topic of much study in efforts to understand PO. CI depends on a wide range of parameters such as (i) openness and closure of the shape of contours (Kovács & Julesz, 1993; Polat & Sagi, 1994), (ii) number of individual elements that make up the shape (Inducer number - IN), (iii) orientation offsets of the elements from the aligned orientation for that shape (Orientation jitter - OJ) (Mark W. Pettet, 1999), and (iv) curvature of the shape (Braun, 1999; Hess et al., 2003). In the current study we aim to characterize the performance of schizophrenia patients and controls over a wide range of contour shapes by manipulating OJ and IN. In the sections below, we review the processes and mechanisms governing CI in healthy individuals as well as the impairments in these processes associated with schizophrenia.

CI in patients with schizophrenia (SZ)

Numerous studies have documented mid-level visual processing impairments in SZ using a variety of behavioral, event-related potential (ERP), and functional magnetic resonance imaging (fMRI) techniques (S. M. Silverstein, 2016; S. M. Silverstein & Keane, 2011; Uhlhaas & Silverstein, 2005). For example, in a behavioral CI task that involved identifying oval shapes made up of discrete elements, patients demonstrated impaired performance in identifying shapes with high OJ compared to controls (S. M. Silverstein et al., 2012). Patients also showed abnormal performance when attempting to identify novel, ambiguous or highly fragmented forms (Beck & Palmer, 2002).

These deficits appear to have detrimental effects on higher-order functions such as perceiving degraded face stimuli (Joshua & Rossell, 2009), forming visual memory representations (Cocchi et al., 2007; Steven Silverstein et al., 2005) and decoding emotion information from faces (Turetsky et al., 2007). Such impairments are notable as they are not related to a "general deficiency" in processing information since patients perform better than controls when the task requires judgments about individual characteristics, an effect that appears to be secondary to deficits in perceptual organization (Uhlhaas & Silverstein, 2005).

fMRI investigations of CI in SZ by Silverstein and colleagues revealed reduced activity in areas of the visual cortex that have been previously observed to be crucial for CI in healthy humans and monkeys, specifically areas V2, V3, and V4 (Altmann et al., 2003; Kourtzi et al., 2003; Ostwald et al., 2008; S. Silverstein et al., 2010; S. M. Silverstein et

al., 2009). Patients exhibited elevated (possibly compensatory) activity in higher regions involved with shape processing, such as the fusiform gyrus, temporal gyri, and regions of the prefrontal cortex, coupled with overall reduced activity in frontal and parietal areas. CI deficits in SZ have also been associated with impairments in a distributed network of occipital, prefrontal, parietal and ventral temporal areas. Both ERP and fMRI studies have shown reduced activation to contours made up of Gabor elements in the extrastriate visual areas in SZ compared to neurotypical individuals (NT) (Pamela D. Butler et al., 2013; S. Silverstein et al., 2010; S. M. Silverstein et al., 2012)..

While considerable research has investigated CI in both controls and patients by manipulating individual parameters of contours one at a time, as a first step, the current study sought to examine the CI process in schizophrenia across a wide range of shapes using a modified version of a CI paradigm that the CNTRICS initiative recommended for use in treatment studies of schizophrenia (Barch et al., 2009; S. M. Silverstein et al., 2012). To this effect, we retrospectively analyzed data from a multi-site visual training study that employed a variety of contours (Circle, Ellipses, Lines, Squiggles, Blobs, Spiral and Letters) in both SZ and NT participants. We characterized CI performance of SZ and NT as the difficulty of identifying a given shape was adjusted by parametrically manipulating the orientation (OJ) and number (IN) of the Gabor elements that made the shape. The variety of shapes which differed in structure and complexity, allowed us to explore whether these features influenced CI task performance among SZ and NT participants. We note that although the stimuli used in the current study were inspired by previous investigations, the shapes were designed for the purpose of presenting a variety

of stimuli to participants during visual training – individual elements of the shapes were not systematically controlled or manipulated to adjust shape complexity per se. Consistent with previous studies, we observed decreased performance in SZ compared to NT across all shapes. However, a closer examination of the effect sizes revealed a more nuanced picture. The largest effect sizes between SZ and NT were observed for complex contours that either included abstract shapes (Blobs, Spiral) or required top-down contributions (Letters) from higher cortical areas. As discussed below, these results are consistent with prior observations regarding the nature of visual integration impairments in SZ, i.e., normal for stimuli with strong organizational cues (e.g., symmetry, familiarity, continuous contour) but impaired under conditions that place more burden on perceptual organization processes (e.g., fragmented contours, novel stimuli requiring higher demands from top-down contributions) (R. A. Knight, 1992; Raymond A. Knight & Silverstein, 2004; S. M. Silverstein et al., 1998; Steven Silverstein et al., 2005).

METHODS:

Subjects

The data used for this study were collected across three sites: Weill Cornell Medicine (WCM), Nathan S. Kline Institute for Psychiatric Research (NKI), and the University of California, Riverside (UCR). In total, 23 SZ and15 NT were recruited, specifically 13 SZ at WCM (8 males; mean age = 33.5 yrs [SD = 8.48]), 10 SZ at NKI (8 males; mean age = 45.6 yrs [SD = 9.54]), and 15 NT at UCR (5 males; mean age = 19.93 yrs [SD = 2.15]). All subjects reported normal or corrected to normal vision. Participants signed written

informed consent and were compensated for their participation ($10/hr at all sites). The study was approved by the IRB at all three sites.

General Procedure

Stimuli:

The training task was administered using a 12.9" iPad Pro (2nd generation) at all sites. The screen was placed at a distance of approximately 2ft from the participants. The screen resolution was 2732 x 2048 with the viewable screen subtending approximately 18.3° x 24.4° of visual angle. The size and orientation differences between adjacent elements in each of the contour shapes used is delineated in Table 4.1. Two parameters were manipulated using an adaptive 3 down 1 up staircase: 1) OJ which is the degree of change in orientation of the individual Gabor elements that make up the shape, relative to their optimal position, i.e., in terms of forming a smooth contour on the curve (Figure 4.2A); and 2) IN, which is the total number of elements that make up the shape (Figure 4.2B). Of note, the range of IN varied across shapes. For example, the circle shape had 16 elements whereas lines included 8 elements. The stimulus grid was made up of a total of ~440 Gabors, and the overall number of elements remained constant as both OJ and IN of the target shapes were varied. When OJ was manipulated, the elements making up the target shape were offset in orientation from the optimal orientation required for the contour. When IN was varied, the distribution of Gabor elements across the contour and distractors changed i.e., a decrease in the number of inducers was accompanied by an increase in the number of distractor elements and vice versa. This led to an increase in the

spacing between contour elements, where in all cases the elements that made up the contour were equally spaced. We note that the absolute number of inducers that can be removed before the visibility of the contours is impacted depends on the contour and the template that a participant may use to find the contour. All the Gabor elements were identical in each trial except for their positions and rotations. There were on average 2 Gabors per degree of visual angle (dva). The distribution of the distractor Gabors on the screen was held constant to minimize any density cues that would aid in identifying the shape.

Contour Shape	Size (in dva)	Range of Orientation differences between adjacent inducer elements (in deg°)
Circle	6.1	0 – 30
Vertical Line	8.38	0
Horizontal Line	8.38	0
Vertical Ellipse	6.1	0 – 30
Horizontal Ellipse	6.1	0 – 30
Rotated Ellipse	6.1	0 – 30
Spiral	5.24	0 – 30
Blob 1	6.86	0 – 30
Blob 2	6.86	0 – 30
Blob 3	6.86	0 – 30
Vertical Squiggle	10.75	0 – 30
Horizontal Squiggle	10.75	0 – 30
Letter p	7.62	0 – 90
Letter b	7.62	0 – 90
Letter d	7.62	0 – 90

Table 4.1. **Size and range of orientations differences** between adjacent elements for each of the contour shapes used in the study.
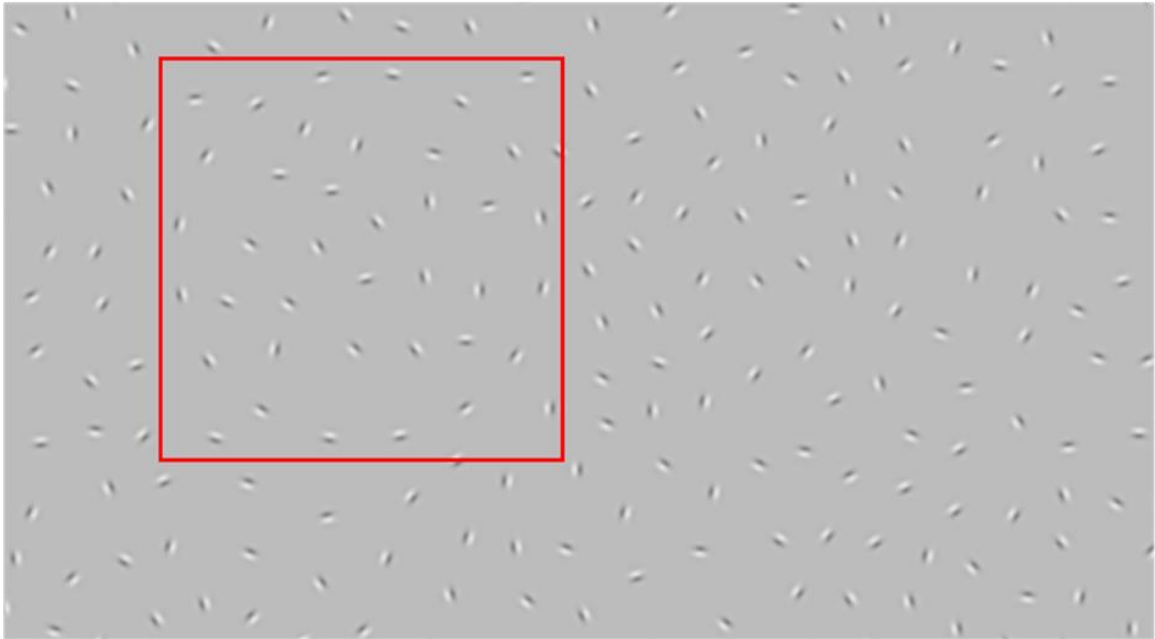
Figure 4.1. **Sample image of the Circle contour shape** on the screen as presented to the participants at 0° orientation jitter and 16 inducer Gabor elements (easy condition).
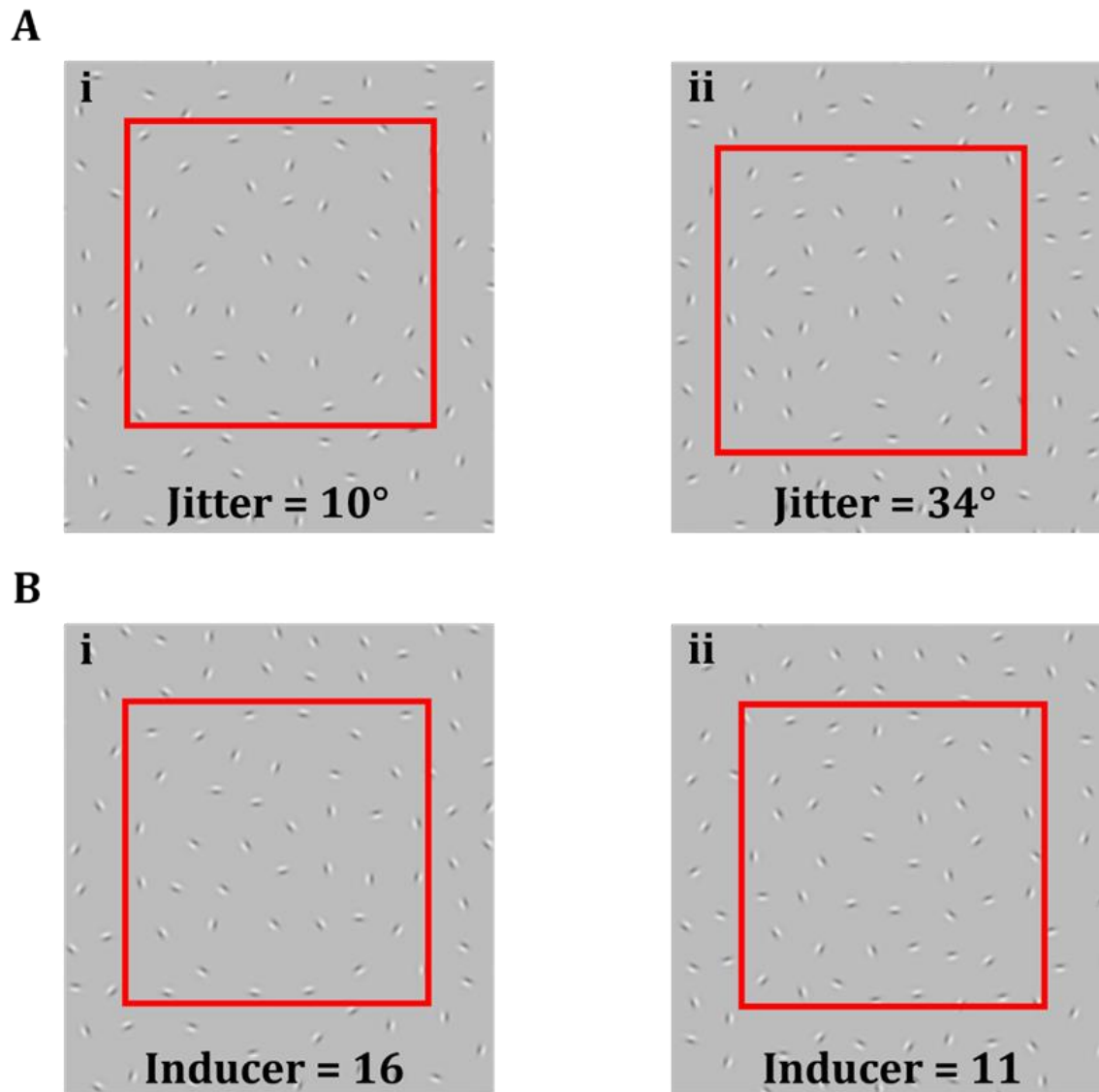
Figure 4.2. A) **Different levels of jitter difficulty** was used during the course of training. (i) Jitter of 10° (moderate difficulty), and (ii) Jitter of 34° (high difficulty). B) Varying numbers of inducers were also used; the lower the number of inducers, the harder the task, (i) A Circle shape made up of 16 elements (low difficulty), and (ii) of 11 elements (high difficulty). The contour shape is highlighted within the red box and is surrounded by distractor Gabors of random orientations.

Experimental Procedure:

Subjects participated in 40 visual training sessions (S. M. Silverstein et al., 2020), which

included performing the CI training task that is the focus of this study. In each session

participants completed multiple blocks of CI training for approximately 30 minutes per

session, during which they were presented with a subset of different contours of varying

shapes (Figure 4.3) on an iPad screen with background distractors (Figure 4.1). The

Circle shape was presented as the first stimulus for every training session, whereas the

other contour shapes (lines, ellipses, spiral, blobs, squiggles and letters) were only

presented for a subset of the training sessions. As noted above, the study was designed to

introduce stimulus variety during training and not to specifically test differences in

processing across contour shapes; thus, individual contour shape frequency was unevenly

distributed across sessions. The two contour salience manipulations, OJ and IN, were

varied in alternating blocks for each shape (Figure 4.2A and 4.2B). On each trial, a

single stimulus of one of the contour shapes was presented within a field of distractor

elements. Participants were required to tap (using a stylus tool) anywhere on or within the

border of the contour shape for their response to be recorded as correct. Trials were

presented in 2-min blocks. Each trial lasted up to 10 s (depending on the participant's

reaction time) during which the stimulus would appear on the screen and remain so until

a response was made, or the participant was timed out of the trial. Thus, the number of

trials per block, and total number of blocks per session, depended on the speed of the

participant's responses to targets. The NT group completed on average a total of

approximately 9 ± 0.62 blocks per session and about 37 ± 5.67 trials within each block.

Similarly, the SZ group completed a total of about 9 ± 0.96 blocks per session with each block comprising approximately 36 ± 5.55 trials. Participants received trial by trial visual and auditory feedback, specifically a smiley face for correct and a red cross for incorrect responses and increasing tones over an octave for correct and an unpleasant beep for incorrect responses, respectively. Visual feedback for correct responses comprised 3 levels: a yellow smiley face denoted a quick response (< 3 s), a white smiley face denoted a slightly delayed response (> 3 s but < 6 s) and an orange smiley face denoted a very delayed response (> 6 s). Participants were presented with their overall performance scores (i.e., total number of correct and incorrect responses) at the end of each block (Figure 4.4). The SZ group underwent training on the contour shapes for up to 40 sessions (3-5 sessions a week). NT performed the 40 training sessions in 20 days i.e., two sessions per day. The order of the contour shapes presented to both the groups was fixed throughout the study.
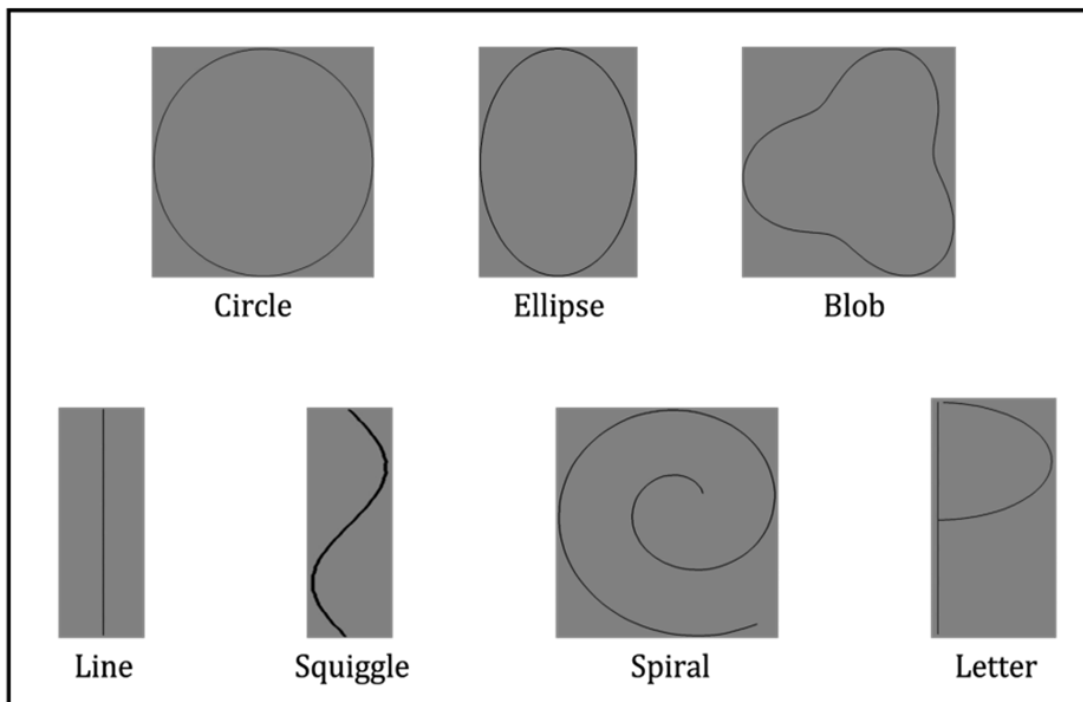
Figure 4.3. **Examples of the contour shapes** by stimulus category presented to the participants during the CI training. For the full set of contour shapes used, refer to Supplementary Figure 1.

We operationalized performance on the CI training task using OJ and IN thresholds. For each contour shape, participants started at the easiest level (0° jitter and the largest number of elements for each corresponding shape) during each block. The parameters were adapted in 2 stages. The first stage used a "streaking" staircase in which the difficulty level was increased on every trial until an error was made. Once an error was made, the second stage was initiated, which used a conventional 3 down 1 up staircase procedure. For each contour shape, thresholds for OJ and IN were calculated by taking the average of the reversals on the staircase over all blocks and over all training sessions for that shape. We calculated the within subject standard error of mean for each shape

and group using methods described by (Loftus & Masson, 1994). This involves subtracting the grand mean across all conditions for each participant prior to estimating standard deviation and then dividing by the square root of the number of participants.
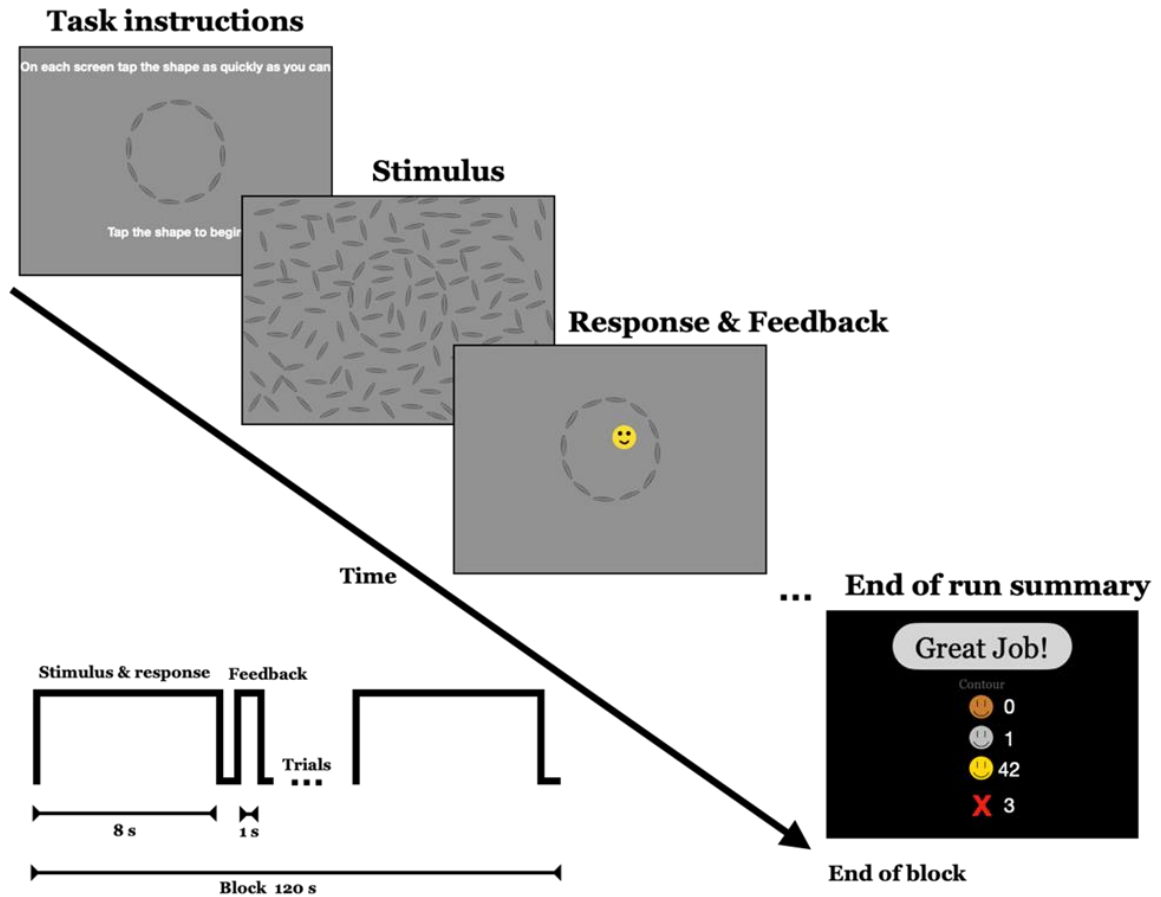
Figure 4.4. **Task structure in each trial and block.** Each session consisted of multiple blocks, with a single type of contour shape presented in each block, with shape type varying across blocks. Each block started with presenting the shape to be detected, followed by the stimulus screen, which was presented for approximately 8 seconds or until the participant responded. Feedback was provided, specifically a smiley face for correct responses paired with a pleasant tone and a red cross paired with an unpleasant beep for incorrect responses. Each block was made of multiple such trials and lasted for a total of 120 seconds. A summary screen of the participant's performance was provided at the end of each block.

RESULTS:

CI Performance: Orientation Jitter Manipulation: Figure 4.5 presents the average jitter

thresholds of NT and SZ on 7 contour shapes averaged across all training sessions. We

performed a 2 (groups) x 7 (shapes) Mixed Methods ANOVA (MM- ANOVA) on the

average orientation jitter thresholds across all participants for each shape. Since the

Mauchly's test of sphericity was significant $\chi^2(20) = 42.889$, p = 0.002, the Greenhouse-

Geisser corrected results are reported ($\varepsilon = 0.735$). The MM-ANOVA revealed main

effects of contour shapes (F (4.412,149.998) = 83.282, p < 0.001, $\eta_p^2 = 0.710$,

Greenhouse-Geisser $\varepsilon = 0.735$) and, group (F (1,34) = 7.706, p < 0.01, $\eta_p^2 = 0.185$) and a

significant shape x group interaction (F (4.412, 149.998) = 4.492, p = 0.001, $\eta_p^2 = 0.117$,

Greenhouse-Geisser $\varepsilon = 0.735$). These results indicate that thresholds differed both as a

function of contour shape and group (NT vs SZ). Qualitatively, NT outperformed SZ in

identifying contours of all types, with the exception of Blobs (Figure 4.5). Cohen's d

effect sizes were calculated to observe the magnitude of these group differences for each

contour shape. Large effect sizes for shapes that significantly differed between the two

groups on the OJ parameter were observed (Spiral t (37) = 3.616, Bonferroni corrected p

< 0.001, Cohen's d = 1.1130; Letter t (37) = 3.575, Bonferroni corrected p < 0.01,

Cohen's d = 1.0912).
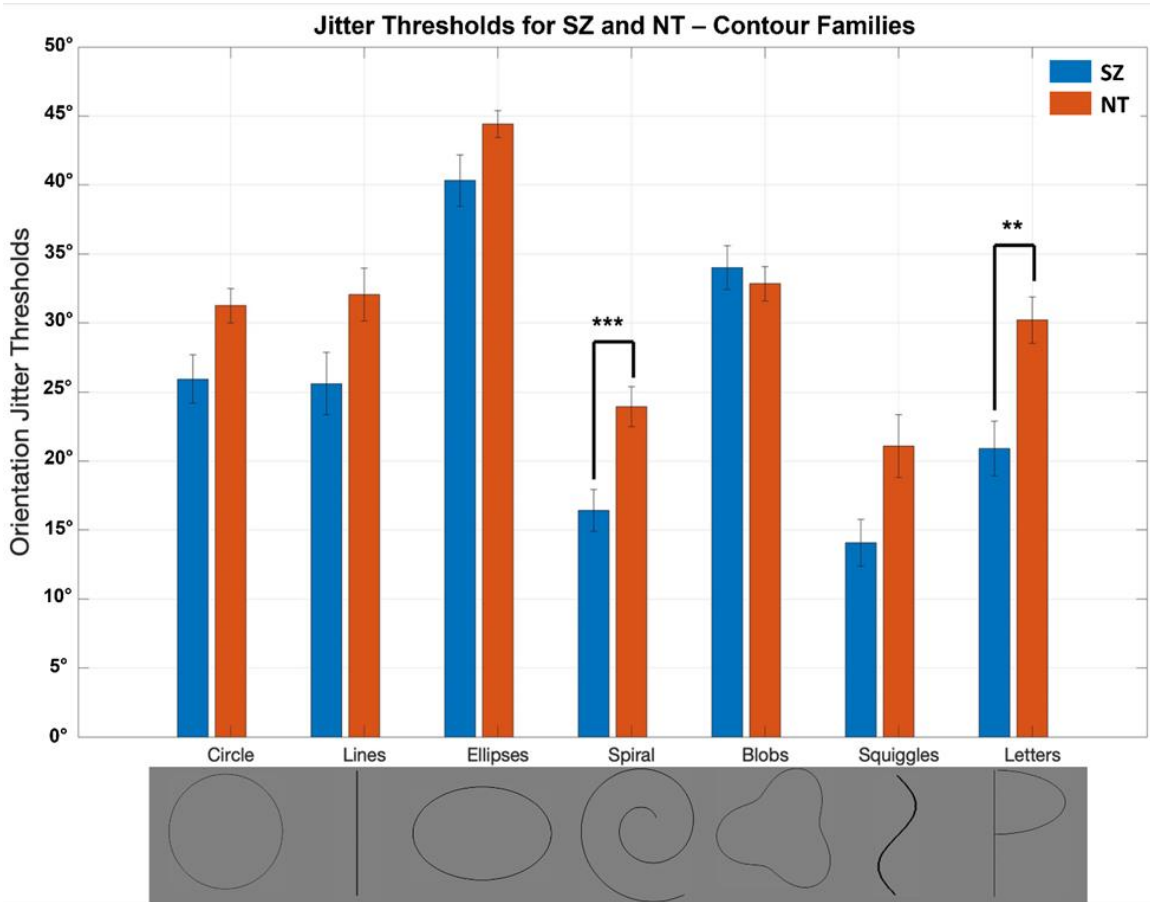
Figure 4.5. **Jitter thresholds for SZ and NT by Contour Type:** Average Orientation Jitter thresholds of SZ and NT groups on families of different contour shapes. Here red bars denote the performance of NT, and blue bars the performance of SZ. Error bars denote within subject standard error (Loftus & Masson, 1994). The y axis denotes the average jitter thresholds (with higher thresholds indicating better performance), and the x-axis represents the family of contour shapes used. ** → p < 0.01; *** → p < 0.001

CI Performance: Inducer number Manipulation: Figure 4.6 shows performance of SZ

and NT groups as inducer numbers were manipulated. We conducted a Greenhouse -

Geisser corrected (Mauchly's test $\chi^2(20) = 51.710$, p < 0.0001, ε = 0.694) 2x7 MM-

ANOVA using the average inducer thresholds calculated from the blocks in which the

inducer numbers were manipulated and observed a similar pattern of results as reported

for jitter. The ANOVA indicated significant main effect of shapes (F $(4.163, 141.547)$ = 704.824, $p < 0.001$, $\eta_p^2 = 0.954$) and group (F $(1,34)$ = 17.094, $p < 0.001$, $\eta_p^2 = 0.335$) and a significant interaction for shapes x group (F $(4.163, 141.547)$ = 12.618, $p < 0.001$, $\eta_p^2 = 0.271$). Large effects of shape and a moderate effect of group x shape interaction was also observed as indicated by the η_p^2 values. Thus, as observed for the jitter thresholds, the inducer thresholds differed both as a function of the contour shape and group (NT v, SZ). Of note, lower inducer thresholds indicate better performance on a contour shape. This can be conceptualized as requiring fewer elements to detect a contour embedded in a noisy background. Posthoc tests on this parameter were conducted using Bonferroni corrected p values and Cohen's d effect sizes. Results indicated large effect sizes and significant differences between some of the shapes as shown in the Figure 6 (Blobs t (37) = 8.259, $p < 0.001$, d = 2.2391; Squiggles t (37) = 3.819, $p < 0.001$, d = 1.1102; Letters t (37) = 4.001, $p < 0.001$, d = 1.2223). As displayed in Figure 4.6, qualitatively, NT outperformed SZ for all contour shapes. The largest group differences were observed for the Blob contours.

Performance on CI task as a proportion of inducer reduction: We also analyzed the performance on the CI task as a function of the proportion of inducer reduction that can be tolerated (Figure 4.7). Each shape had different starting inducer values (refer to Supplementary Table T1). Thus, in order to directly compare performance across shapes, we calculated the percentage of inducer elements that, when deleted from the original starting number of elements, impacts the performance of participants in the NT and SZ groups. To do this we divided the absolute threshold (i.e., difference between the starting

inducer value and the threshold of the participants during each training session) by the starting inducer value for each shape (original number of elements that make up the contour shape). This was then averaged across all training sessions and participants for each shape and multiplied by 100 to obtain the percentage of tolerance of inducer reduction. A higher positive value on the y axis in Figure 4.7 indicates better tolerance for inducer deletion. We then conducted a Greenhouse – Geisser corrected (Mauchly's test $\chi^2(20) = 72.076$, $p < 0.001$, $\varepsilon = 0.547$) 2x 7 MM-ANOVA on these values and observed significant main effects of shape (F $(3.28,111.516) = 57.008$, $p < 0.001$, $\eta_p^2 = 0.626$) and, group (F $(1,34) = 15.916$, $p < 0.001$, $\eta_p^2 = 0.319$) and a significant interaction for shape x group (F $(3.28,111.516) = 5.594$, $p < 0.001$, $\eta_p^2 = 0.141$). Moderate to large effects for group x shape interaction and shapes were observed as indicated by the respective η_p^2 values. Post-hoc tests revealed large effect sizes between the two groups on different contour shapes as well as significant differences between the groups on all shapes with the exception of lines and ellipses (Figure 4.7). Consistent with previous studies, NT group has better tolerance for inducer deletion across all contour shapes compared to the SZ group.

Evaluating Effect Sizes for each Contour Shape: Effect sizes are an efficient and reliable method to compute the magnitude of an experimental effect, independent of sample size (Cohen, 1992; Ferguson, 2009). For the purpose of this study, we computed the Cohen's d effect sizes of the group differences for each shape by parameter manipulation, i.e., OJ and IN after controlling for multiple comparisons (Table 4.2). Large effect sizes (d > 1) were observed for complex contour shapes i.e., Spiral, Blobs and Letters, for both the OJ

144

and IN manipulations (highlighted in dark red). These results indicate that the

performance of the SZ and NT groups were strikingly different when these contour

shapes were presented. We observed notable similarities between the effect sizes for the

OJ and IN manipulations overall (although see results for the Blobs, Table 4.2). The most

interesting finding was the large effect sizes between the two groups (SZ and NT) for

contours such as Blobs, Spiral and Letters, all of which are complex shapes that require

integrations over multiple regions of the contour for identification.
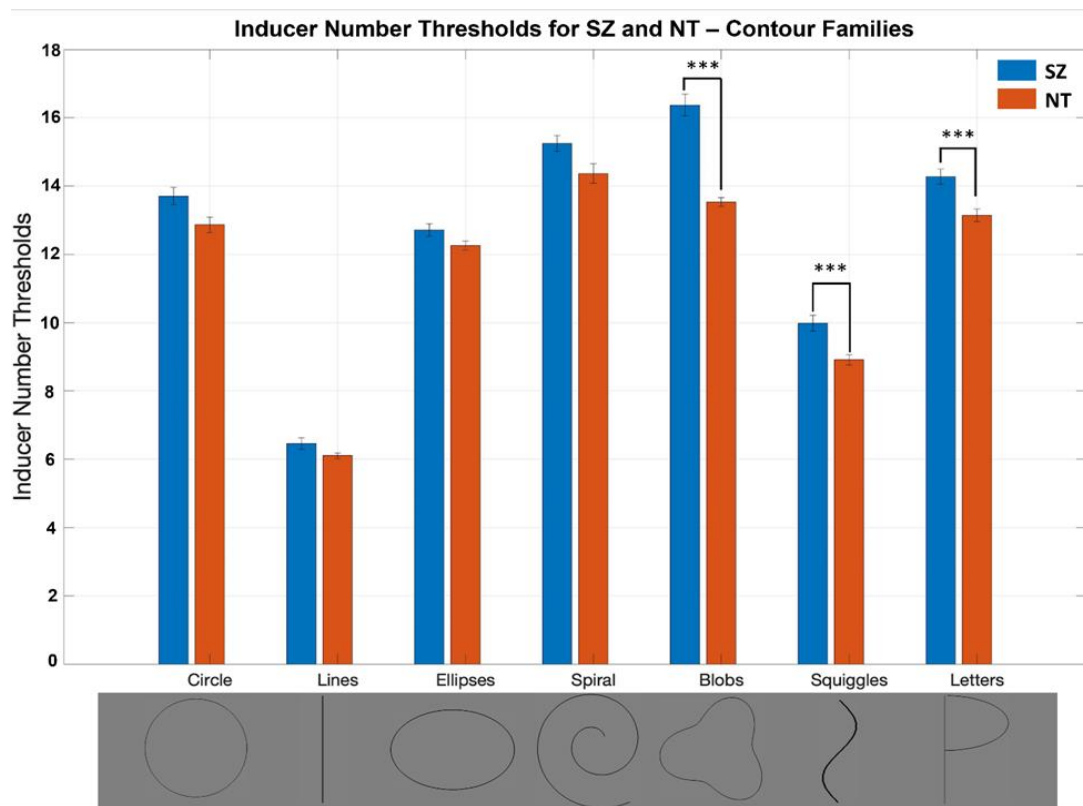
Figure 4.6. **Inducer thresholds for SZ and NT by Contour Type:** Average Inducer thresholds
of SZ and NT groups for families of different contour shapes. Red bars denote the performance of
NT, and blue bars the performance of SZ. Error bars denote within subject standard error (Loftus
& Masson, 1994). The y axis denotes the inducer number thresholds, and the x-axis represents the
family of contour shapes used. The lower the inducer thresholds, the better performance. $* \rightarrow p <$
$0.05; *** \rightarrow p < 0.001$
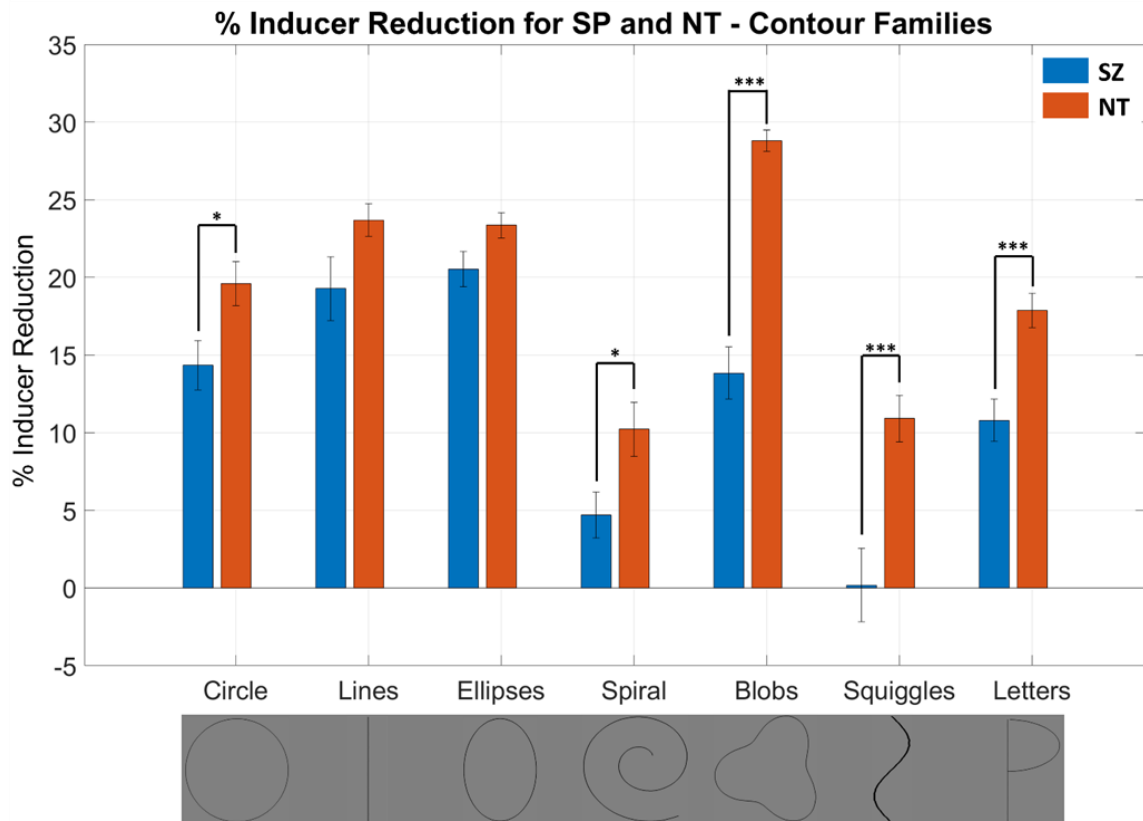
Figure 4.7. **Inducer thresholds expressed as a proportion of original contour length for SZ and NT by Contour Type:** The proportion was calculated as the reduction of inducer number at threshold relative to the inducer number in the original contour for families of contour shapes and expressed as a percentage. Red bars denote the performance of NT, and blue bars the performance of SZ. Error bars denote within subject standard error (Loftus & Masson, 1994). The y axis denotes the % reduction of inducer number, and the x-axis represents the family of contour shapes used. Higher values on the y axis indicate better tolerance to deletion of elements. * → p < 0.05; *** → p < 0.001

DISCUSSION:

The current study examined performance of NT and SZ on a range of contour shapes

differing in their degrees of curvature and closure. Specifically, we implemented a CI

task using 15 different shapes that can be classified into 7 families as seen in figure 4.3

(also refer to supplementary figure S1), in the context of a visual training study. These

shapes inherently vary in terms of curvature and closure while the orientation and the number of elements making up the shape were manipulated during each training session.

Consistent with prior findings, we observed that contour integration was impaired in SZ when compared to NT. While this points to an overall impairment in the ability to integrate disconnected collinear fragments for numerous types of shapes, a novel finding from this study is that the degree of impairment appears to vary as a function of the type of shape.

Contour Shapes	OJ	IN
Circle	0.72	0.75
Line	0.67	0.53
Ellipse	0.54	0.58
Spiral	1.11	0.78
Blob	-0.17	2.24
Squiggle	0.84	1.11
Letter	1.09	1.22

Large

Small

Table 4.2. Cohen's d effect sizes of group differences (NT vs SZ) for each contour shape in a color-coded fashion, with dark red indicative of the largest effects and the light pink indicating the smallest.

Several previous studies controlled for curvature of the contours, and open contours were often constructed by introducing "turning points" which is done by cutting and flipping a

part of a closed contour thereby changing the angle between two adjacent elements at least once (Braun, 1999; M. W. Pettet et al., 1998; Poom, 2002; Tversky et al., 2004). Open contours can also be conceptualized as contours that are discontinuous around the shape. Multiple studies have observed that increasing the number of turning points negatively impacts the performance on a contour shape (Kovács & Julesz, 1993; Mathes et al., 2006; M. W. Pettet et al., 1998; Mark W. Pettet, 1999). However, these studies have only focused on simple shapes that involved, for example using circles and/or connecting two halves of a circle to form an 'S' shape. Our aim here was to characterize CI in SZ using a wide variety of 2D representations of simple and complex shapes that resembled shapes that may be familiar to participants. These contained varying degrees of curvatures ranging from having equal (circle) or no turning points (lines), to having a large number of turning points (spiral/ blobs/ letters). Our results appear to be in accordance with previous observations for shapes with high curvatures i.e., poorer performance on these shapes in both groups. However, to the best of our knowledge, there have been no prior studies that examined the performance of NT and SZ on highly complex shapes akin to the spiral, letters and blobs used in this study.

We note that the current study failed to find significant differences between the groups on squiggles and lines, which has been observed in previous studies (Robol et al., 2013; Schallmo et al., 2013). This could be attributed in large to the methodological differences adopted in the current study. Firstly, while both studies focused on peripheral contour detection, the present study was a foveal visual search task where the stimulus stayed on the screen for a long duration (8 s) allowing the participants to search the grid for the

target. Secondly, we had designed the squiggles to be relatively easy to find, including having more inducers, and so the stimuli are not directly comparable as well. Further, the number of elements in the squiggle shape was at the cusp of the inducer threshold that could have also potentially contributed to the task itself being harder, leading to the lack of significant differences observed. Again, we note that our study was designed for contour training and thus our contours were not systematically controlled in the same manner as some previous studies in literature.

It is also possible that the large effect sizes for group differences for complex contours could be explained by the RBC (Recognition – By – Components) theory as put forth by Biederman (Biederman, 1987). According to this theory, geons (generalized cone components) can be derived from five detectable properties in a 2D image: curvature, collinearity, symmetry, parallelism and cotermination, and when two or three geons can be recovered from the input, objects can be quickly recognized even when they are degraded. RBC also posits that if contours were deleted at regions of high saliency (i.e., points along the contour that would be easy to bridge by extensions of collinearity or curvilinearity), then recognition would be impossible. For example, when IN is manipulated, these may possibly be degrading the regions of concavity in complex contours, which would explain the strikingly large effect sizes (table 4.2) for Blobs when IN is changed. This would also lead to potential tradeoffs between the two parameters that were manipulated (OJ and IN).

We note that further research will be necessary to better understand mechanisms, and likely individual differences in how SZ leads to decreased performance on CI. In the case of the specific deficit in identifying complex contours could be due to the impaired top-down feedback found in previous studies of schizophrenia (Pamela D. Butler et al., 2013; S. Silverstein et al., 2010; S. M. Silverstein et al., 2012). However, an alternative explanation could be the weakened long-range horizontal connections in both striate and extrastriate visual areas (Pamela D. Butler et al., 2008; Keane et al., 2012; Kéri et al., 2005). While this study cannot address these mechanistic questions, our findings highlight that CI is a dynamic process in which changes in several parameters (e.g., curvature, contour smoothness, contour element density) can lead to changes in perception.

Limitations

While there are several interesting insights from the current study regarding perceptual organization, and specifically about how contour integration is affected in individuals with schizophrenia relative to neurotypical individuals especially for complex contours, there are several limitations of the current study that must be kept in mind when considering these findings: *Firstly*, we note that this study was a retrospective analysis of the data obtained from a training study, and thus contours were not specifically chosen to parametrically determine the specific features of the contours that influenced the performance. Further, we averaged thresholds across multiple sessions of the training period and did not explicitly address training effects (although each contour was

distributed across training, and both NTs and SZs were presented with the same sequence of contours). In addition, while we examined performance on a wide range of shapes, the shapes were initially designed with the purpose of achieving variety during training, and differences between shapes, such as complexity and curvature, were not systematically manipulated. *Secondly*, the sample size is small, and so there may not have been sufficient power to detect some group differences. Specifically, we did not observe significant aging effects between the two groups despite previous studies observing such differences (E. Roudaia et al., 2012; Eugenie Roudaia et al., 2008, 2013). While on average SZ were older than the NT group, lack of these effects could be due to the small sample size in our study. Nevertheless, even with the current sample size, the study was able to show effective qualitative and quantitative differences in the performance between the two groups. *Thirdly*, dissimilar training structure might also be another cause for a lack of marked differences for certain shapes. SZ underwent training for 40 sessions with 3-5 sessions per week (with a maximum of one session per day), whereas the NT completed the same 40 sessions over 20 days, with two sessions per day. This may have contributed to differential training effects across groups and could have resulted in fatigue in the control group which might have also affected their performance. *Fourthly*, in addition to the contour shapes being different, insufficient/ unequal sessions per contour shape presentation could have affected the results. For example, participants were presented with the Circle contour for all 40 training sessions while the Spiral contour was presented for 9 sessions. The total number of sessions for the rest of the contours (including different subsets of each family of contour shape) are denoted in

151

parentheses as follows: Lines (3), Ellipse (5), Blobs (6), Squiggles (2) and Letters (6).

This could have contributed to better performance on shapes that were presented more

frequently than others. We did, however, examine potential differences between

perceptual and learning thresholds for the circle contour, as explained in the

Supplementary material (Appendix 1).

Additionally, NT and SZ participants in the study were recruited from different sites

leading to uncontrolled differences between these research sites impacting the

performance. While we ensured that the experimental setup across all sites were identical

(i.e., viewing conditions, display devices, and tasks) further studies are needed that

recruit participants for both groups at the same site to eliminate the likelihood of any

differences in performance.

Lastly, the task was particularly challenging for high curvature contours when IN was

manipulated, most likely because the baseline number of elements was not sufficient to

capture the shape of the contour when embedded in a noisy background. This might have

put the participants in a difficult condition at the beginning of the trial, which could have

affected their performance as well.

Future Directions

The current study represents an exploratory investigation of CI in schizophrenia using

several commonly studied shapes. A more thorough and balanced study that

systematically assesses the parameters should be conducted to further advance our

understanding of how CI impairment in schizophrenia varied as a function of shape type. It would also be beneficial to systematically vary the curvature of the closed and open shapes independently with an equal number of trials between participants to arrive at a more accurate and reasonable threshold for each shape.

We also note that prior studies in healthy older adults using the CI task indicate age-related deterioration in performance, specifically when varying parameters of orientation jitter and closure of the shape (Casco et al., 2011; Hipp et al., 2014; E. Roudaia et al., 2012; Eugenie Roudaia et al., 2008, 2013). While our sample was likely too small, and not sufficiently varied to address age-effects in contour integration, it will be important for future studies to use age-matched controls to offer more clarity regarding schizophrenia-related deficits.

SUMMARY:

The current study extends past work on perceptual organization in schizophrenia by examining performance under different shape conditions, and with multiple grouping manipulations (contour smoothness, contour density, and contour closure). Consistent with several prior studies we observed a general pattern of reduced performance in SZ compared to controls on all the shapes. Upon close observation, the shapes in which we observed the largest group differences were the more complex shapes, as judged intuitively i.e., shapes with curvatures that require integration over multiple regions of the contour. However, further studies, with larger samples, that control the manipulation of parameters like curvature and additional stimulus types, are needed to confirm these

results. Nevertheless, the current study reinforces that in addition to a pattern of generally poor perceptual organization in schizophrenia, there are certain conditions and stimulus parameters that are more likely to reveal impairments in patients. In particular, stimuli of moderate complexity, for which rapid top-down effects normally help achieve contour integration and perceptual closure, are the most demanding for patients relative to controls, suggesting a schizophrenia-related breakdown in modulating perception based on top-down feedback involving stored shape information. Future studies centered on visual rehabilitation for patients with schizophrenia should focus more on strategies that could improve performance on these key factors.

Funding information

SUPPLEMENTARY MATERIAL:
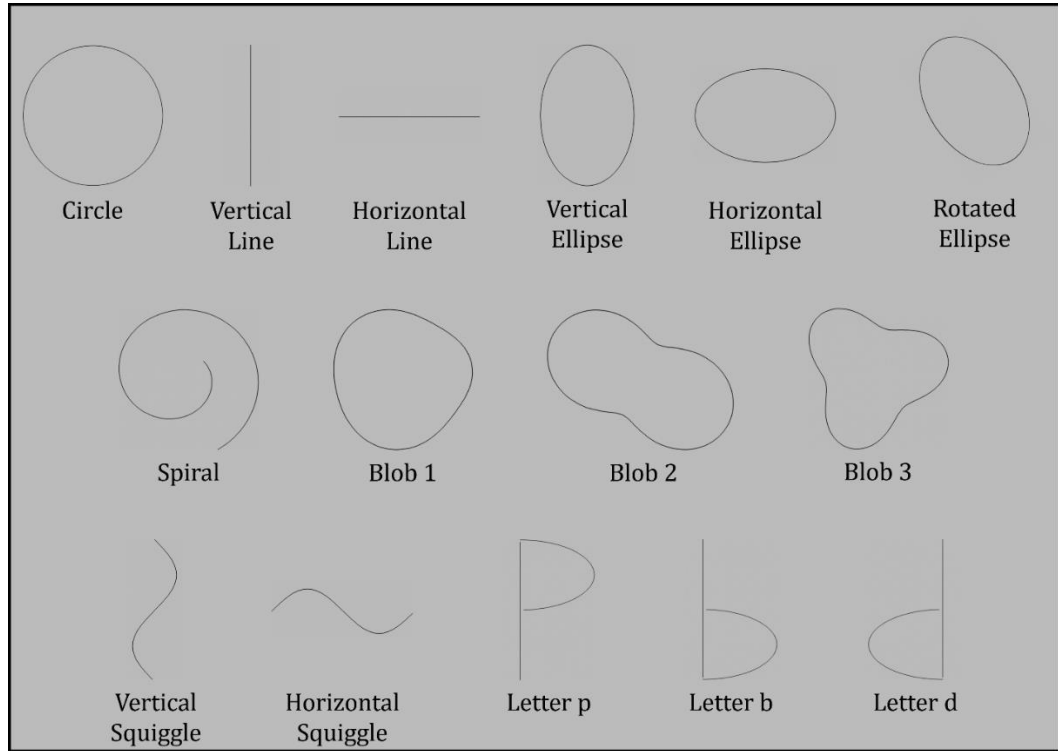
Figure S1: Outline of all the contour shapes used in the study
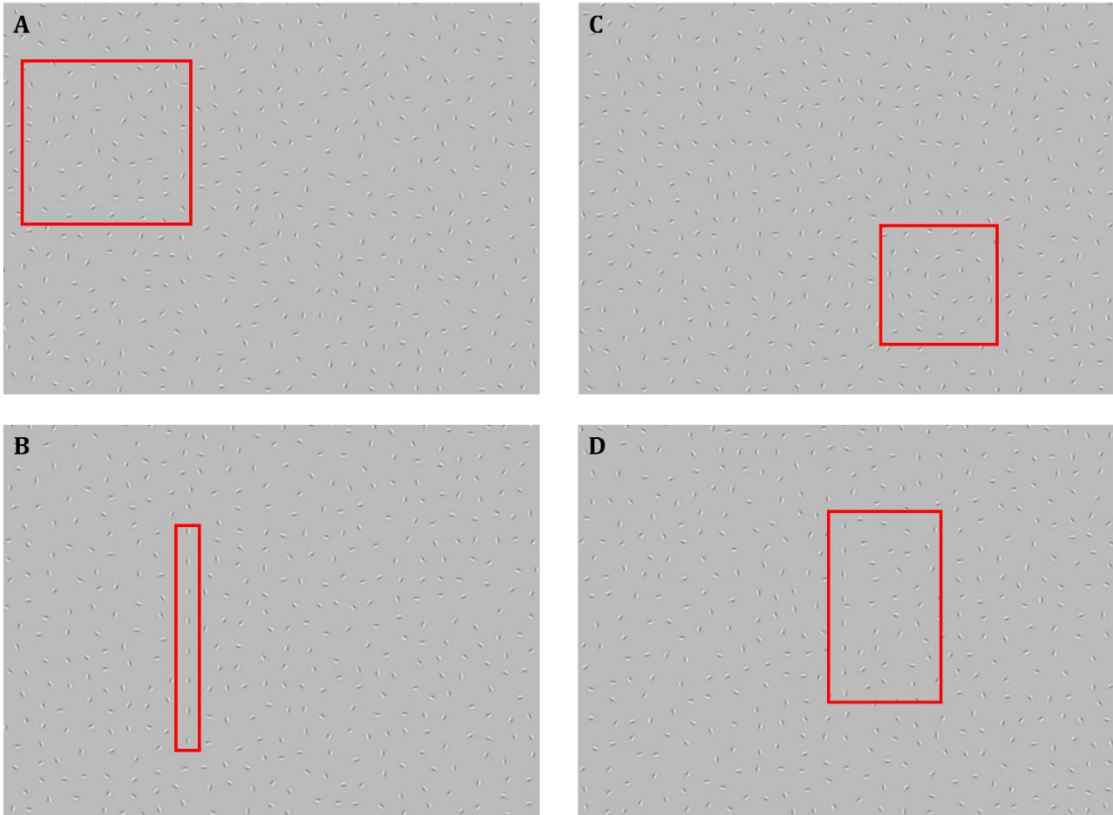
Figure S2: Subset of contour shapes A) Blob3, B) Vertical Line, C) Spiral, D) Letter P along with distractors used in the study. The shapes are highlighted within the red box.

Contour Shape	Starting # of inducers
Circle	16
Vertical Line	8
Horizontal Line	8
Vertical Ellipse	16
Horizontal Ellipse	16
Rotated Ellipse	16
Spiral	16
Blob 1	19
Blob 2	19
Blob 3	19
Vertical Squiggle	10
Horizontal Squiggle	10
Letter p	16
Letter b	16
Letter d	16

Table T1: Starting number of inducers for each contour shape

Appendix 1:

Here we look at potential differences between patients with schizophrenia and neurotypical individuals on the circle contour shape keeping in mind any effects of learning that might have affected the thresholds. We specifically focus on the circle contour because it is the only shape that was presented across all 40 training sessions in

the current study. We group the performance of the participants into two: Perceptual

Threshold which is the average performance on the first 10 sessions (leaving out session

1 as we assume that any performance during the first session is related to learning the

task cognitively) and Learning Threshold which is the average performance on the last 10

sessions. Figure S3 below shows these thresholds for both groups.
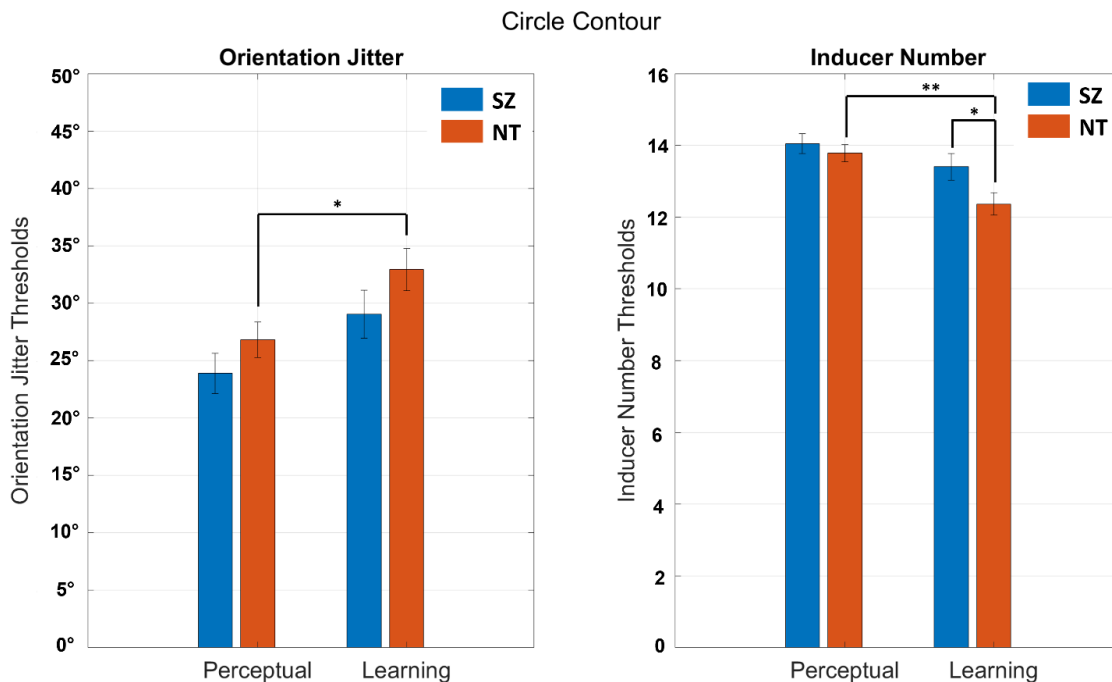
Figure S3: Figure shows the orientation jitter (left) and inducer number (right) thresholds for the circle contour shape. Perceptual thresholds are calculated by averaging the performance of participants during sessions 2-11 and learning thresholds are calculated by averaging performance during sessions 31-40. Red and blue bars denote NT and SZ participants respectively. Error bars denote 2 SE. * → $p < 0.05$, ** → $p < 0.01$

It can be observed from the figure that SZ group showed no statistically significant

difference between the perceptual and learning thresholds when both OJ and IN were

manipulated. On the other hand, significant differences were found between the

perceptual and learning thresholds for the NT group when both OJ (t (27.19) = -2.56, p <

0.05) and IN (t (26.35) = 3.61, p < 0.001) were manipulated indicating that NT showed larger degrees of improvement as a result of training on the circle contour shape. We also found significant differences between the learning thresholds in SZ and NT groups when IN was manipulated (t (33) = -2.15, p < 0.05).

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Chapter 5: Discussion and Conclusion

As a first step towards addressing the limitations and gaps that exist in the field of PL, we discuss the design and development of methods and tools that can potentially achieve robust and unbiased results, as well as even aid and inform future studies aiming to understand mechanisms that facilitate specificity and generalizability of PL strategies. Moreover, current work discussing novel findings regarding mid-level visual impairment in patients with schizophrenia, emphasizes the implications of designing a "gamified" vision rehabilitation paradigm with a translational motive, stressing the need for the development of informed and targeted methods with strong foundations in the field of PL. While this work has merely opened avenues for further studies, it holds significance in the advancement of PL research.

Applications in basic PL research:

The field of PL has had a plethora of findings that contributed to understanding theories surrounding the specificity and generalizability of several paradigms. However, given that most of these results stemmed from small N studies and suffered from replicability issues, there is not yet well defined and robust results suggesting which PL paradigms lead to specificity and which ones lead to transfer of learning, and even more so the extent to which each of the established paradigms can transfer. While theories and mechanisms of PL provide key insights and answers to some of these questions, it is important to conduct large scale studies across multiple sites, with heterogeneous and diverse samples to test these different paradigms (Seitz et al., 2023).

On one hand, the PLFest platform described in Chapter 2 is designed to serve this exact purpose. Firstly, this platform is capable of functioning on both tablets and computers with the ability to support a wide range of perceptual and cognitive tasks. This allows researchers to design PL paradigms to explore different theories of perceptual learning. Rightfully so, currently, this platform is being used to implement existing paradigms that have previously shown specificity and transfer of learning to identify the mediators (different PL paradigms) and moderators (participants and individual differences) of PL. At present, PLFest supports PL of spatial vision and approaches that include training of not only standard perceptual paradigms (like orientation discrimination tasks), but also training with flanking stimuli (Polat et al., 2012; Yu et al., 2004), use of noise (DeLoss et al., 2015), training with diverse stimuli (Deveau, Jaeggi, et al., 2014; Deveau, Lovcik, et al., 2014), attentional training (Donovan et al., 2015; Szpiro & Carrasco, 2015), and even allows for testing multisensory facilitation (Seitz et al., 2006; Shams & Seitz, 2008). Given that this platform is able to reliably measure performance in selective yet fundamental visual tasks, it allows for achieving robust and unbiased results targeted at answering these long-standing questions in the field. Potential applications of this platform is virtually limitless: (1) it can be coupled with EEG and eye tracking tools to examine the oculomotor and neural underpinnings of training, (2) it holds potential for testing and/or training participants in remote conditions providing access to research in underserved communities, (3) is flexible and adaptable for designing new PL paradigms, and (4) is open source and free of cost thereby removing barriers to access publicly available datasets and promote transparency in research.

On the other hand, the gaze contingent framework highlighted in Chapter 3 aims to inform basic PL research by utilizing s-CVL as a model to test specificity and generalizability of selective PL paradigms. While not exhaustive, this model allows for a more comprehensive understanding of training related benefits of PL particularly due to the fact that it taps into the blank slate of the visual periphery thereby allowing for the ability to identify locus of plasticity across different brain regions. This framework is a useful tool for advancing basic perceptual learning research because it allows researchers to: (1) investigate the role of oculomotor behavior in PL by tracking eye movement during perceptual training helping researchers gain insights into how eye movements can contribute to learning and how can it be optimized to improve training outcome, (2) design training paradigms that can improve both perceptual and oculomotor function by providing a controlled environment in which to manipulate visual stimuli and corresponding oculomotor behavior facilitating the development of training paradigms that either target both the combined perceptual and oculomotor systems, or each of these systems individually, and (3) study the effects of PL on oculomotor behavior by measuring several metrics across a wide range of tasks both before and after training. A notable selling point of the proposed framework is that, to the best of our knowledge, there is no existing body of work that meticulously factors into several design related aspects, such as the concurrence of hardware and software components, priming crucial oculomotor behavior for efficient use of visual periphery, and carefully considering the psychophysical and visual demands for conducting PL research using this model.

Applications in visual rehabilitation:

There exists a large body of research in VPL that has demonstrated brain plasticity and improvements in perceptual performance inspiring researchers to apply PL strategies in clinical settings for patients with visual impairments (Cavanaugh et al., 2015, 2019; Levi, 2020; Maniglia et al., 2021; Polat et al., 2012; Sabesan et al., 2017). However several challenges remain (Levi, 2020; Lu et al., 2016) due to specificity of PL paradigms limiting the benefits of training to the trained stimuli and tasks negatively impacting the translational merit of these paradigms. However, a few studies have overcome this specificity of training by implementing a combined approach to training including diverse and naturalistic stimuli, rich feedback and gamified paradigms (Deveau et al., 2013; Deveau, Lovcik, et al., 2014; Deveau & Seitz, 2014) and observed transfer of learning in clinical populations.

While the studies highlighted in chapters 2 and 3 mainly focus on research in healthy individuals, these methods and tools can be adapted to test and/or train patients with a wide range of visual impairments. Firstly, the PLFest platform, although currently not validated in clinical populations, holds great promise in supporting research and development of PL paradigms that are of translational importance. Specifically, the simplicity of this platform to support established PL strategies that have previously shown generalization of learning is encouraging for research in clinical populations. Secondly, while the gaze contingent framework described in chapter 3 shows representative results from healthy individuals with s-CVL, it can be easily adapted for conducting PL research in patients with age-related macular degeneration. The ability of

this framework to support a more holistic intervention approach, encompassing eye movement planning, cognitive control mechanisms and visual perceptual learning holds great promise in identifying key strategies that could lead to generalizability of learning in these patients. Prior research conducted in our lab with a modified version of this framework has shown improvements in visual acuity at the preferred retinal locus in these patients (Maniglia et al., 2021).

The study emphasized in Chapter 4 is proof of concept that such diverse training could in theory allow for the development of targeted visual rehabilitation in clinical populations. While findings from this study do not answer questions regarding the generalizability of training, it does provide valuable insights into the nature and extent of visual impairments in patients with schizophrenia. Taken together, the result from this study underscores the importance of developing rehabilitation that is more focused towards exploiting the findings of this study, thereby alleviating in part this mid-level visual impairment in patients.

Limitations and Future directions:

The current work emphasized in my thesis holds great potential for PL research, however, it is also important to note that there are few limitations to its practical applications. Firstly, one of the primary limitations of my thesis is that the collective body of work is best suited for studies conducted in controlled laboratory settings and therefore, cannot be, at the moment, substantiated to real world practical changes and must be met with skepticism. Secondly, although the proposed tools and methods open exciting possibilities of research for PL of spatial vision, it does not account for studies

and research centered around using moving visual stimuli and thereby cannot provide insights into the specificity and generalizability of PL trained using these tasks. Thirdly, the novel findings from chapter 4 need to be validated with more controlled manipulations and task design before integrating into visual rehabilitation paradigms. Finally, it is important that these methods and tools are validated in clinical populations prior to conducting PL studies in patients.

Final Remarks:

This collection of studies investigates different facets of PL, with a focus on developing rigorous and accessible methods to advance PL research. While each chapter in this thesis addresses this need in distinctive ways, collectively these studies emphasize the need for achieving unbiased and robust findings in PL research, introduce novel tools and approaches to address limitations in the field, and provide insights into the nuances of visual processing deficits in clinical populations, thus paving the way for future research in this field.

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