**INTRODUCTION.**

**Why is stereopsis important?**

Stereopsis, defined as depth perception from binocular disparity, is a perceptual experience that gives rise to a rich 3-D environment from two 2-D retinal images (Howard & Rogers, 2012). However, abnormal visual experience during the “sensitive period” of development may result in reduced or absent stereopsis (Held et al., 1980; Petrig et al., 1981; Held, 1991; Birch & Petrig, 1996; Banks et al., 1975). Stereopsis has been implicated as a major factor in everyday visuomotor tasks (Meltmoth & Grant, 2006; Melmoth et at., 2009) and is often impaired in people with abnormal visual development (Webber & Wood, 2005; Meltmoth et al., 2015; Levi, Knill, & Bavelier, 2015). Indeed, people who are stereo-blind or -anomalous exhibit deficits in precision grasping (Grant, Melmoth, Morgan, Finlay, 2007; Melmoth, Finlay, Morgan, & Grant, 2009), particularly in the kinematic aspects that rely on visual feedback and online corrections (Meltmoth & Grant, 2006; Melmoth et at., 2009). Furthermore, while binocular mechanisms seem to be intact in people with amblyopia (Birch & Stager, 1985; Baker et al., 2007; Ding & Levi, 2014; Hess et al., 2014; Giaschi, Lo, Narasimhan, Lyons, & Wilcox, 2013), they are functionally suppressed when viewing binocularly (Tavers, 1938; Birch, 2013). Thus, for the overall well-being of people with amblyopia, stereopsis may be an important function to strengthen.

**Background on amblyopia**

Amblyopia, the leading cause of visual loss in children, is a neuro-developmental disorder (Hess, Li, Lu, Thompson & Hansen, 2010; Li, Dumoulin, Mansouri, & Hess, 2007) that arises from an imbalance between the ocular inputs to the visual pathway. It is characterized as reduced visual acuity in an otherwise normal eye despite best optical correction (Holmes & Clarke, 2006) and is typically secondary to misalignment of the visual axis (strabismus) and/or unequal refractive error (anisometropia). However, categorization of amblyopia based on etiology may be too restrictive (Maurer & McKee, 2016) since amblyopic deficit interactions are complex. Indeed, people with amblyopia experience sensory deficits, such as reduced visual acuity (Holmes & Clarke, 2006), contrast sensitivity (Hess & Howell, 1977; Levi & Harwerth, 1977; Levi, 1991) and positional acuity (CITE). In addition, they also experience higher-level deficits, such as crowding (Levi & Klein, 1985; Levi, 2008), motion perception (Ho & Giaschi, 2007; Simmers et al., 2003; Mier et al., 2016), contour integration (Levi et al., 2007), visual decision making (Farzin & Norcia, 2011), visual attention (Hou et al., 2016) and stereopsis (Webber & Wood, 2005). The combined sensory, higher-level deficits and interactions make amblyopia a difficult condition to treat.

**Treatment techniques for children and adults with amblyopia**

Current treatment options following full optical correction for children with amblyopia are: Patching, atropine, or bangerter filters, with patching being the most common (Holmes & Levi, 2018), although not always effective (Awan et al., 2010). Treatment compliance remains a major obstacle in treating children with amblyopia (Steward et al., 2004; Steward et al., 2007) and treatment response after the age of seven is reduced (Steward et al., 2003). Although there are no established treatments for adults with amblyopia, evidence suggests that adults retain a level of plasticity (Levi & Polat, 1996; Bavelier et al., 2010; Levi, 2012; Tsirlin et al., 2015) that can be leveraged to recover visual function after the sensitive period of visual development (Ding & Levi, 2011; Xi et al., 2014; Vedamurthy et al., 2015; Vedamurthy et al., 2016). However, patching alone does not seem to be an effective treatment in the adult population (Li et al., 2011). Recently, researchers have suggested perceptual learning (PL) as a treatment option and reported modest but significant improvements in visual function (Levi & Polat, 1996; Polat et al., 2004; Ding & Levi, 2011 and others). However, learning effects can be limited to the trained stimulus and eye (Jinping et al., 2010), which is problematic since amblyopia encompasses a wide range of deficits. Furthermore, laboratory-based PL techniques usually involve simple stimuli and a monotonous response (Ding & Levi, 2011; Xi, Jia, Feng, Lu, & Huang, 2014), which presents a problem with compliance and boredom. Recent incorporation of dichoptic training (Li et al., 2015; Li et al., 2019; Xi et al., 2014; Vedamurthy et al., 2015) with PL has shown greater levels of plasticity than monocular training alone (Li et al., 2003). However, as we transition from laboratory- to home-based treatments, the need for more engaging content remains.

**Why use video games?**

Most laboratory-based training paradigms are monotonous and show improvement on a specific task. However, amblyopia is a complex visual condition exhibiting low-level sensory as well as thigh-level processing deficits. Action video games have been implicated as a viable option for increasing performance on a wide range of visual functions in a more engaging manner. Indeed, action video game players show enhanced low-level visual functions (Li, Polat et al., 2009) as well as higher-level attentional processing (Green & Bavelier, 2003) compared to non-gamers and non-action video-gamers alike. Furthermore, playing an action video game for a short period time (10-50 hours) has been shown to improve contrast sensitivity (Li et al., 2009), visual acuity (Li et al., 2011), useful-field of view (Green & Bavelier, 2003), attentional-blink (Green & Bavelier, 2003) and backward masking (Green & Bavelier, 2003) in non-gamers, suggesting that playing action video games can improve a wide range of functions without specific training. In addition, several studies, including clinical trials (Gao et al., 20018), have reported benefits of using video games to treat amblyopia (Li et al., 2009; Li et al., 2011; Vedamurthy et al., 2015a; Vedamurthy et al., 2015b; Portela-Camino et al., 2018). Importantly, suppression, a hindrance to binocular function in amblyopia (Hess et al., 2010; Hess et al., 2014), seems to be responsive to video game play (Foss, 2017). The complex nature of amblyopia requires a more heroic effort to recover the many visual functions that are affected. Video game play provides an enriched and complex environment where successful players learn to exploit task-relevant information while suppressing task irrelevant information (Bavelier et al., 2012), which may be a good platform for bringing together current semi-successful treatments.

**Why VR?**

Recent commercialization of Virtual Reality head-mounted displays (VR-HMDs) have opened the opportunity to design therapies that incorporate gaming techniques and build upon successful laboratory-based techniques such as PL and dichoptic content. VR-HMDs provide researchers and clinicians with the ability to present separate images to each eye, which aids in alignment and contrast balancing; Both of which are important for successful improvement of visual function in people with amblyopia. In addition, large disparities, which are seen as a possible draw-back of the current state of VR-HMDs, can actually be beneficial in training stereopsis in people with abnormal visual development since the amblyopic brain has been shown to respond to large disparities (CITE). Furthermore, VR-HMDs provide the ability for researchers to control disparity content, which can be used for depth cue scaffolding. Moving from lab- to home-based treatments, the combination of dichoptic PL and depth cue scaffolding in an enriched VR environment provides a platform for creating therapies that build upon the many years of laboratory and clinical research. Our aim was to test whether depth cue scaffolding in VR can be used to train stereo-anomalous observers to rely on disparity cues in effort to encourage the use of depth cue scaffolding in dichoptic PL techniques for people with amblyopia.