“The use of broadband (in orientation and spatial frequency) stimuli facilitates learning within and between deficit scales… it has been shown that playing action video games produces improvements in monocular visual acuity and stereo acuity in amblyopic subjects. This may be due to the broadband nature of the visual images or the fact that focused attention is required during game play” – Astle et al, 2011

PL shows improvements in contrast sensitivity (Li et al., 2009), stereoacuity (Vedamurthy et al., 2016) and visual acuity (Li et al., 2011)

However, strong evidence suggests that stereopsis can be recovered or at least improved in adults with abnormal visual development using perceptual learning (Ding & Levi, 2011; Xi et al., 2014; Vedamurthy et al., 2015; Vedamurthy et al., 2016).

Recent studies have shown that adult plasticity is indeed possible (Sasaki et al., 2010; Bavelier, Levi, Li, Dan, & Hensch, 2010; Ding & Levi, 2011).

The reduction of intracortical inhibition has been implicated as the mechanism of action (Levi, Knill, & Bavelier, 2015). PL in psychophysics has been implicated as a mechanism for achieving plasticity in the adult brain (see below).

Eye patching alone is not an effective treatment for recovering visual function in adults with amblyopia (Li et al., 2011). Furthermore, there have been a number of studies suggesting that video games may be an effective treatment (CITE). However, there is a debate about whether action video games are more effective than non-action video games (CITE).

The issue with most methods applied to the recovery of stereopsis however, is that they take a long time and involve simple monotonous stimuli (Ding & Levi, 2011; Xi, Jia, Feng, Lu, & Huang, 2014; Vedamurthy, Nahum, Bavelier, & Levi, 2015; Vedamurthy, Knill, Huang, Yung, Ding, Kwon, Bavelier, & Levi, 2016), which results in low compliance and boredom.

1. Treatment techniques for stereo-anomalous/amblyopic observers
   1. Contrast balancing (Hess, Thompson & Baker, 2014; Hess, Mansouri & Thompson, 2010)
   2. Perceptual learning
      1. Improves contrast sensitivity (Li et al., 2009)
      2. Directly train stereopsis (Vedamurthy et al., 2016)
      3. Improves visual acuity (Li et al., 2011)
   3. Dichoptic training (Li et al., 2015; Li et al., 2019; Xi et al., 2014; Vedamurthy et al., 2015) shows greater levels of plasticity than monocular training alone (Li et al., 2013)

Perceptual learning

* What have we been able to improve/recover using perceptual learning?
  + Perceptual learning has also been shown to improve visual function in people with abnormal visual development (Levi & Li, 2009)
* What are the current theories on perceptual learning?
* Perceptual learning in stereo-anomalous observers

Most recently, treatment techniques for adults with amblyopia have pivoted from occlusion therapy to dichoptic training (CITE) in efforts to reduce suppression and promote binocularity.

“Findings suggests possible relationship between fine stereopsis, coarse stereopsis, and motion correspondence mechanisms” (Ho & Giaschi, 2007)

1. Anti-suppression
   1. Active
      1. Video game play
      2. PL?
   2. Passive
      1. Li et al., 2015
      2. Bossi et al., 2017
2. Occlusion therapy
   1. Patching
   2. Perceptual learning techniques show modest though significant improvements in adult amblyopes
      1. Li et al., 2005 (children)
      2. Polat et al., 2004
      3. Webb et al., 2006

While PL can improve stereoacuity in adults, it requires many trials of a monotonous psychophysical task (Ding & Levi, 2011), which leads to poor compliance and motivation. Recent studies have taken a more modern approach by using video games (Vedamurthy et al., 2015; Xi et al., 2014) and/or augmented reality (Vedamurthy et al., 2016). The goal of Aim 1 is to test whether stereopsis can be recovered/ improved using PL in an immersive 3-D VR environment.

Treatment interventions for amblyopia have traditionally focused on children since plasticity is highest during development (Movshov & Van Sluyters, 1981; Levi, Knill, Bavelier, 2015).

However, binocular deficits remain after occlusion therapy (Birch, 2013)

“compliance varies widely among children treated for amblyopia and visual acuity outcome is related to compliance (loudon et al., 2002, 2003; Stewart et al., 2004b, Stewart et al., 2007a,b)” from Birch, 2013

1. Why use games?
   1. Most training paradigms improve perceptual learning on a specific task (CITE)
   2. Action video game play have been shown to improve sensory, perceptual, and attentional tasks
   3. Differences between gamers and non-gamers can be seen in basic visual functions
      1. contrast sensitivity (Li, Polat et al., 2009)
   4. and higher order visual functions
      1. attention (Green & Bavelier, 2003)
   5. Playing games for a short period of time (10-50 hours) has been shown to enhance vision in normally sighted individuals improving:
      1. Contrast sensitivity (Li et al., 2009)
      2. Crowding
      3. Useful-field of view (Green & Bavelier, 2003)
      4. Attentional-blink (Green & Bavelier, 2003)
      5. Backward-masking (Green & Bavelier, 2003)
   6. Suppression is responsive to video gaming (Foss, 2017)
   7. Playing games has been shown to improve visual function in populations with abnormal visual development
   8. Cue scaffolding

Why video games?

* Most training paradigms improve learning on a specific task, but the learning does not generalize or transfer.
* Action video game play has been shown to improve sensory, perceptual, and attentional tasks.
* Differences among gamers and non-gamers can be seen in basic visual functions such as contrast sensitivity (CITE),… attention (CITE)…
* Video-game play has been shown to result in an increase in the ability to extract visual information without direct training (Li et al., 2011)
* Active and rewarding visuomotor tasks that require stereopsis
* “Playing action-packed video games enhances several aspects of vision in amblyopic adults” -VG whole enchilada
* “Training either monocularly or under dichoptic conditions results in improved visual acuity and reduced suppression in adults with amblyopia” -VG
  + “However perceptual learning and videogame play, whether monocular or dichoptic, result in limited improvement in visual acuity and stereopsis” -VG

Furthermore, there have been a number of studies suggesting that video games may be an effective treatment (CITE). However, there is a debate about whether action video games are more effective than non-action video games (CITE).

1. Why use VR?
   1. Moving from lab-based to home-based treatments, we need more engaging content and greater game variety (Gao et al., 2018)
   2. Separate images for alignment and contrast balancing
   3. Control disparity content
   4. Scaffolding
   5. Large disparities

Why VR?

While perceptual learning (PL) can improve stereopsis in adults with abnormal binocular vision, it requires many trials (Ding & Levi, 2011). Thus, attention and compliance may limit the utility of PL. Game principles can be used to tackle both challenges. Indeed, several studies have reported the benefits of using video games to treat amblyopia (CITE). Recently, the introduction of consumer Virtual Reality (VR) devices has opened the opportunity to design new PL therapies. Our aim was to test whether VR can be used to train stereo-anomalous observers to rely on disparity cues.

Moving from lab-based to home-based treatments, we need more engaging content and greater game variety (Gao et al., 2018).

Video-game play has been shown to improve uncrowded visual acuity in people with abnormal visual development (Li et al., 2011 AND OTHERS), but not in observers with typical visual development (Green & Bavelier, 2007), possibly due to the smaller room for improvement in people with typical visual development.

Video games have been shown to improve a range of visual functions (list and cite) sometimes, the visual function improved was not trained directly.

Possible mechanisms for broad transfer in video game players

* Probabilistic inference (Green, Pougetm & Bavelier, 2010)

For neural correlates of amblyopia, see Kiorpes & Daw 2018

* “Stereopsis is the most common deficit associated with amblyopia under ordinary binocular viewing conditions (Webber & Wood, 2005)”
* Recovery of stereoacuity may require more active treatment in strabismic than in anisometropia amblyopia
* Since deficits in visual acuity seem to develop after the onset of fixation preference, some studies suggest that stereoscopic pathways are present and potentially fully functional in some people with binocular and spatial deficits (Birch & Stager, 1985).
* Furthermore, coarse stereopsis, which is defined as the ability to decipher depth from large disparities and double vision, seems to be spared in some infants with amblyopia and/or strabismus (Giaschi, Lo, Narasimhan, Lyons, & Wilcox, 2013). These results suggest that people with amblyopia may indeed have the ability to experience depth from binocular disparity.
* Normal binocular summation in people with amblyopia after contrast adjustment between the two eyes
* Recent studies suggest that treatment for amblyopia should be aimed at eliminating suppression (Hess et al., 2010; Li et al., 2011; Li et al., 2013; Hess et al., 2014)
* Suppression may be the gating mechanism in the amblyopic brain (Li et al., 2013)
* Stronger suppression is correlated with worse stereoacuity and visual acuity in the amblyopic eye. Thus, there is a correlation between monocular and binocular deficits in amblyopia (from Thompson, 2019)
* “Patients with amblyopia also have impaired binocular vision. In particular, the fellow eye often suppresses the amblyopic eye when both eyes are open (Birch, 2013), and stereopsis is impaired or absent and stronger interocular suppression has been associated with poorer stereopsis and visual acuity .”
* and a new classification system that takes into consideration the complex interaction between refractive error, spatial visual performance, and eye alignment may be required (Maurer & McKee, 2016).
* In addition to reduced visual acuity (Holmes & Clarke, 2006), adults with amblyopia show deficits in: Contrast sensitivity (Hess & Howell, 1977), crowding (Levi & Klein, 1985; Levi, 2008), motion perception (Ho & Giaschi, 2007; Simmers et al., 2003), contour integration (Levi et al., 2007)
* Furthermore, although binocular Binocular deficits that arise from a binocular system that is difficult to balance (Ding & Levi, 2014) include: Suppression (Tavers, 1938; Birch, 2013) and poor stereoacuity (CITE). Since suppression seems to be the bottleneck of stereopsis, and stronger suppression is correlated with worse stereoacuity and visual acuity in the amblyopic eye (Thompson, 2019 BUT CITE OTHERS!), our focus is to train stereopsis directly. WHO HAS ALREADY TRAINED STEREOPSIS DIRECTLY, CITE!
* Most often, the amblyopic eye exhibits reduced visual acuity and poor contrast sensitivity, especially at higher spatial frequencies (Levi, 1991). This loss of spatial sensitivity is not due to optical factors, but rather is a result of neural loss in foveal function (Levi, 1991).

REFS:

1. Awan, M., F.A. Proudlock, D. Grosvenor, I. Choudhuri, N. Sarvanananthan and I. Gottlob (2010). An audit of the outcome of amblyopia treatment: a retrospective analysis of 322 children. Br J Ophthalmol **94**(8): 1007-1011.
2. Howard & Rogers, 2012
3. Held, Birch, & Gwiazda, 1980
4. Petrig, Julesz, Kropfl, Baumgartner, & Anliker, 1981
5. Held, 1991
6. Birch & Petrig, 1996
7. Banks, Aslin, & Letson, 1975
8. Hess, R.F., Li, X., Lu, G., Thompson, B., & Hansen, B.C. The contrast dependence of the cortical fMRI deficit in amblyopia; a selective loss at higher contrasts. *Hum. Brain Mapp.* **31**, 1233-1248, doi:10.1002/hbm.20931 (2010).
9. Li, X., Dumoulin, S.O, Mansouri, B., & Hess, R.F Cortical deficits in human amblyopia: their regional distribution and their relationship to the contrast detection deficit. *Invest. Ophthalmol. Vis. Sci.* **48**, 1575-1591, doi:10.1167/iovs.06-1021 (2007).
10. Webber AL, Wood J, Gole GA, Brown B. Effect of amblyopia on self-esteem in children. Optometry and Vision Science. 2008b;85:1074–1081.