Comparative AAPOS Validation of the Birefringent Amblyopia Screener with Isolated Small-Angle Strabismus

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Video abstract

Background: The Rebion blinq binocular birefringent ocular alignment screener was recently commercially released, but it did not yet have validation by American Association for Pediatric Ophthalmology and Strabismus (AAPOS) uniform guidelines.

Methods: Children and adults from a high-risk eye practice had screening by blinq with validation by AAPOS 2003 guidelines. Then, the blinq was compared to the Adaptica 2WIN with CR corneal reflex strabismus estimation by AAPOS 2003 guidelines plus additional efforts to identify patients with diminished binocularity.

Results: Blinq in 100 patients compared to 2003 AAPOS amblyopia risk factors (ARF) had sensitivity 67%, specificity 75% and PPV of 82%. Both blinq and 2WIN were completed by 87 patients median age 6.5 years. Sensitivity, specificity and positive predictive value (PPV) for blinq were 75%, 68% and 81% whereas 2WIN had 91%, 68% and 84%. The blinq referred two young patients with isolated, small-angle strabismic amblyopia that 2WIN refractive function passed.

Conclusion: Despite its non-refractive design to identify binocular foveation, blinq performed well with refractive and strabismic uniform risk factors and a PPV greater than 80%.

Clinical Trials Registry: NCT04195711.

Keywords: birefringent, photoscreening, amblyopia, fixation instability, amblyopia risk factor, strabismus

Introduction

Binocular objective portable retinal birefringent screening became commercially available late in 2019. Conceived and developed by Drs. David Hunter and David Guyton since 1991,1,2 this device recently called “blinq” (Rebion, Boston, MA) seeks to determine whether a patient can consistently align both visual axes on a small target or not.3

Instrument-based amblyopia screening has been available for more than two decades. Some devices employ near-coaxial flash to produce analyzable, refraction-related pupillary crescents. One such infrared, on-site interpreted photoscreener is the 2WIN (Adaptica, Padova, Italy). Adaptica also developed an infrared transmitting occluder for the measurement of intermittent and constant strabismus by Hirschberg analysis4 so the 2WIN with CR function provides appropriate comparison with blinq since they both screen for issues related to ocular misalignment.

The vision screening committee of the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) developed and published uniform guidelines for the detection of refractive and strabismic amblyopia risk factors (ARFs). The 2013
update to AAPOS uniform guidelines rendered infant and toddler ARFs more specific in an attempt to reduce false-positive referrals while the older triad in 2013 guidelines closely resembles the non-age dependent 2003 guidelines. Some older patients capable of giving a reliable assessment of stereopsis and ocular suppression were compared to blinq binocular foveation and therefore the non-age-dependent 2003 guidelines were selected. The Rebion blinq had not yet been critically analyzed based on the uniform AAPOS standards. For strabismus, blinq was compared to 2WIN with the CR corneal reflex function with uniform ARFs and additional efforts to select patients without binocular fusion.

Methods

This prospective evaluation of clinical tests (NCT04195711) had an institutional review by Providence Hospital and complied with HIPAA and the Declaration of Helsinki. Responsible parents/adults provided signed informed consent and youth younger than 18 years, and those older than 7 years gave written assent for participation in the study. Parental written consent was obtained for linked videos used for educational purposes. Access to de-identified raw data will be maintained at https://www.abcd-vision.org/recipes/blinq%202WIN%20de-ID%20ABCD.pdf

As a part of a new or follow-up comprehensive eye examinations, patients were screened with two novel objective devices according to AAPOS Uniform guidelines.\(^5\),\(^6\) The primary outcome was blinq compared to age-independent 2003 AAPOS guidelines. Following the dry refraction, alignment (cover test) and sensory testing, cycloplegic refraction was performed 30 or more minutes after cyclopentolate 1% drops. In cooperative patients, sensory tests including Worth 4-dot, Stereo Fly and PDI Check were performed to characterize binocularity. For younger patients, binocular function was estimated by Bruckner Test and 4-base out prism cover.

Each patient was screened with a recently commercially released blinq screener according to the manufacturer’s recommendations. The blinq can yield initial interpretation of “pass” or “refer” but also “timed out” or “inconclusive” which, according to manufacturer instructions should be evaluated as if a “refer.” An example of blinq birefringent screening is shown in this video: https://vimeo.com/robertarnold/blinq2wincr.

Patients were screened with the binocular infrared autorefractor 2WIN (software version V5.0 171018 without Kaleidos protective housing) according to manufacturer guidelines. For ocular alignment confirmation, the CR corneal reflex component of 2WIN photoscreener (Adapta, Padova Italy) was used.\(^4\) Refractive referral criteria were not age-stratified and are anisometropia ≥1.50D, cylinder ≥ 1.75 D, hyperopia ≥2.25 D and myopia ≥4.5D. Strabismus referral from the 2WIN CR function was ≥ 5 PD tropia. A video demonstrating the infrared occluder on the 2WIN is shown in this video: https://vimeo.com/robertarnold/cr2win.

The Rebion blinq is a unique screening method and therefore we sought to provide appropriate uniform and unique validation. In addition to non-age stratified AAPOS 2003 Uniform guidelines, we collected all cases characterized by constant or persistent strabismus whether large- or small angle employing cover test, 4 base out test, Bruckner Test and 2WIN CR function. Binocular function was tested with Stereo Fly, Worth-Dot (Stereo Optical, Chicago) and also with the autostereoscopic stereo test on PDI Check (PDI Check, Anchorage) as well as monocular near visual acuity and suppression.\(^7\) Methods of retinal videographic analysis of fixation instability were not available for this study.\(^8\),\(^9\)

Results

One hundred patients aged 9±10 years, median 6.5 years were screened by blinq before confirmatory exam. The prescreening probability of 2003 AAPOS amblyopia risk factors was 66%. Consistent with manufacturer guidelines, the 12 “timed out” and 1 inconclusive results were counted as “refer” yielding a sensitivity of 67%, a specificity of 75% and a positive predictive value of 82% for amblyopia risk factors (Table 1 top half). Of 51 patients diagnosed with refractive amblyopia, blinq timed out in 7, referred 26, passed 17 and defined one as “inconclusive.” Of 31 patients with strabismic amblyopia, blinq timed out on 5, referred 22, passed 3 and declared “inconclusive” in one.

Eighty-seven patients were screened by both blinq and 2WIN. Sixteen were referred from photoscreen and 14 had developmental delays (autism, Downs, fetal alcohol). By 2003 AAPOS uniform guidelines, 28 had refractive amblyopia risk factors and 15 had strabismus while 13 had both refractive plus strabismic risk factors. The prescreening prevalence of risk factors in these pediatric eye and strabismus patients was 64%.

The second half of Table 1 gives validation statistics for both devices. The blinq had 13 screenings for which the interpretation “timed out” and one as inconclusive. The average age for “timed out” blinq interpretations was 3.4 years with range 0.7–8 years. The 2WIN had three screenings for which no interpretation reading was obtained. As per blinq manufacturer
By 2003 guidelines, Blinq had sensitivity 75%, specificity 68% and positive predictive value 81% compared to 2WIN with corneal reflex: sensitivity 91%, specificity 68% and PPV 84%. Adding cases with presumed limited binocularity, Blinq had sensitivity 64%, specificity 71% and PPV of 85% while 2WIN with CR function had sensitivity 87%, specificity 82% and PPV 93%.

Two patients were particularly instructive. The first was an 11-year-old girl with amblyopia recently detected by her local optometrist. She had no history of strabismus surgery and no eye exam or spectacle wear before age nine. Her visual acuity with +0.75 +0.25 x 99 right and +1.25 +0.25 x 80 left eye was 20/20+ and 20/320- with 10 PD constant esotropia. She had 800 s of arc Stereo Fly and suppressed Worth 4-dot distance. Cover test showed 10 PD.

Table 1 Validation Statistics Comparing Rebion Blinq “Blinq” To AAPOS 2003 Uniform Guidelines (Top) and Then Compared To Adaptica 2WIN with CR Strabismus Estimation “CR2”

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Notes: ‘i’ indicates inconclusive interpretations. Sensitivity is “sens,” specificity “spec” and positive predictive value “PPV”. “Prev” is the prescreening probability. In addition to exam criteria from the American Association of Pediatric Ophthalmology and Strabismus (AAPOS) refractive and strabismic risk factors “2003” additional cases were included with sensory, optical or motor evidence of diminished binocularity “strab +.” X+ and X- are true or false confirmatory exam findings while sc+, sc- and sci are screening refer, screening pass and screening inconclusive. The final comparison (“Ambly”) is with all cases defined as either strabismic and/or refractive amblyopia 20/40 or worse or two inter-eye line difference.
that should be included as an option for in-device reporting. The referral rate and PPV from routine, community preschool screening needs to be clarified.

Disclosure

Dr. Arnold is a board member and President of PDI Check that developed a vision screening game for the Nintendo 3DS and Glacier Medical Software that markets ROP Check cloud-based NICU monitoring software. Dr. Arnold coordinates the Alaska Blind Child Discovery which has received discounted instruments from several vendors. Dr. Arnold is an investigator and protocol developer for the Pediatric Eye Disease Investigator Group. Dr Arnold has a patent PDI Check pending to Robert Arnold and Alex Damajian. The author reports no other conflicts of interest in this work.

References
