NIH Public Access
Author Manuscript
J AAPOS. Author manuscript; available in PMC 2015 October 01.

Published in final edited form as:
J AAPOS. 2014 October ; 18(5): 423–426. doi:10.1016/j.jaapos.2014.05.009.

Binocular Inhibition in Strabismic Patients is Associated with Diminished Quality of Life

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Abstract

Purpose—This prospective study aims to characterize the relationship between binocular summation (BiS) and binocular inhibition (BI) on the quality of life (QoL) of adult and pediatric patients with strabismus.

Methods—A binocular summation score was measured using ETDRS and Sloan low contrast acuity (LCA) protocols at 2.5% and 1.25% contrast. Patients were categorized as having BiS (binocular visual acuity superior than better-eye visual acuity by 5 or more letters), BI (binocular visual acuity worse than better-eye visual acuity by 5 or more letters) or otherwise indeterminate (less than 5 letter difference between binocular visual acuity and monocular visual acuity of the better-eye). QoL was evaluated by the National-Eye-Institute-Visual-Functioning-Questionnaire-25 (NEI-VFQ-25), 20-item- Adult-Strabismus-Questionnaire (AS-20) and the Amblyopia-and-Strabismus-Questionnaire.

Results—There was no significant BiS or BI for high-contrast-ETDRS or 2.5% LCA tests. However, mean binocular summation score of −2.14±7.0 letters for 1.25% LCA demonstrated significant binocular inhibition (p=0.004) for this contrast level. Mean composite NEI-VFQ-25 score was significantly lower in subjects with BI on ETDRS (80±19 vs. 57±7 for subjects with BiS and BI, respectively, p=0.03), 2.5% LCA (81±14 vs. 66±16 for subjects with BiS and BI, respectively, p=0.01), and 1.25% LCA tests (91±9 vs. 72±14 for subjects with BiS and BI, respectively, p=0.005). After accounting for potential covariates, significant association persisted for BI demonstrated by 1.25% LCA (p=0.01). With BI demonstrable at 2.5%, AS-20 scores were also significantly lower (p=0.04).

Conclusion—Strabismic patients with BI had significantly lower QoL scores than those who did not, even after accounting for potential covariates, and even in the absence of diplopia.

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Financial Disclosure: Authors have no financial interest.

Introduction

Several studies have demonstrated that under certain conditions binocular visual function is superior to monocular visual function of the better eye; this finding is termed binocular summation (BiS) [1–6] This process may simply result from increased probability for improved vision as each eye operates and views independently, or it may be due to synaptic convergence and increased neural summation between the two eyes.[2,5] This phenomena is more likely to occur when visual acuity is similar between both eyes; in addition, it is more apparent in low luminance.[1,6] Conversely, in patients with wide inter-ocular visual acuity differences, the degree of BiS is reduced and may be completely reversed where binocular visual performance is inferior to monocular visual performance of the better eye. These patients see better monocularly than binocularly and this is termed binocular inhibition (BI).[1,2–6] This destructive neural interaction has been reported in subjects with amblyopia, dense monocular cataract and advanced age.[1,3,4]

It is known that strabismus can have a significant visual impact on patients' lives partially attributed to diminished depth perception and fusion abnormalities.[1,7,8] Recently it was also found that they too exhibit reduced BiS, which may largely contribute to their overall visual disability.[1]

To better study and monitor the personal impact of BiS and BI, various QoL questionnaires may be used.[6,9,10] The National Eye Institute Visual Functioning Questionnaire 25 (NEI-VFQ-25) focuses on the impact of ocular disease on patients' daily lives and overall well-being.[10] It has been used to study a variety of eye diseases including glaucoma, macular degeneration, strabismus and dry eye syndrome.[11–14] The more recently developed 20-item Adult Strabismus Questionnaire (AS-20) and the Amblyopia and Strabismus Questionnaire (ASQE) are more specific to strabismus and therefore aim to better describe the effect of strabismus on QoL.[15,16]

The objective of this study is to characterize BiS and BI in adult and pediatric strabismic patients and determine the relationship to overall QoL through the use of NEI-VFQ-25, AS-20 and ASQE questionnaires.

Methods

This single center, prospective study was approved by the Institutional Review Board at the University of California Los Angeles. Patients with strabismus were recruited from 2010–2012 from the pre-operative clinics of 4 co-authors (FGV, SJI, JLD, SLP). Trained technicians with experience in the examination of subjects for research performed all vision and survey testing. The following subtypes of strabismus were included: infantile esotropia, childhood-onset (1.5–8 years old) esotropia, acquired esotropia >8 years old, intermittent exotropia. consecutive exotropia, acquired exotropia >8 years, congenital trochlear palsy, acquired hypertropia >8 years, combined horizontal and vertical deviations > 10 PD.

Vision Screening

After informed consent, all subjects underwent a detailed vision exam with their current refractive correction. High contrast distance visual acuity was tested at 3 meters using the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol. Vision was measured in the right eye, left eye and binocularly and this sequence was randomly assigned prior to testing for each subject. The score for high contrast visual acuity was the number of correct letters identified (maximum possible score is 70, Snellen equivalent 20/12.5).

Sloan acuity was tested at low contrast levels of 2.5% followed by 1.25% in a dimly lit room at 3 meters. Similarly, the low contrast vision score was the number of letters correctly recognized (maximum score 70).

Self-Reported Quality of Life

Vision related QoL was assessed using three standardized questionnaires. Patients completed the NEI-VFQ-25 and in addition to the composite score, 5 relevant sub-categories were chosen a priori and calculated to further explore their association with binocular summation. These categories were: general vision, near activities, distance activities, driving and dependency. The dependency sub-category refers to reliance on others due to diminished vision and was chosen as several participants did not drive or were too young to drive. In adjunct to the NEI-VFQ-25, subjects also completed either the AS20 if they were 18 years or older or the ASQE if they were less than 18 years of age.

Statistical Analysis

Demographic features of the subjects were summarized using descriptive statistics. To calculate the binocular summation score, the subjects' better-eye monocular score was subtracted from their binocular score. Patients were then categorized as having either BiS (binocular visual acuity better than better-eye visual acuity by 5 or more letters), BI (binocular visual acuity worse than better-eye visual acuity by 5 or more letters), or indeterminate (less than 5 letter difference between binocular visual acuity and better-eye visual acuity). The mean binocular summation score for each test (ETDRS, 2.5% LCA, and 1.25% LCA) was compared to a value of zero using a one-sample t-test to determine a significant difference from zero (ie. whether BiS or BI was significant for the overall group), with 0.05 considered statistically significant. Analysis of variance was used to investigate patient subgroups for binocular summation, inhibition, and indeterminate scores. Finally, linear regression analysis was performed to evaluate additional co-variates and their effect on QoL and its relationship with BiS scores. The co-variates included were gender, age, diplopia status, binocular summation score, and visual acuity.

Results

Demographic Data

One hundred and eight strabismic patients were enrolled in this study. Fifty-one percent of subjects were male. Forty-five (49%) patients noted subjective diplopia. Strabismus sub-types included: infantile esotropia (15%), childhood-onset (1.5–8 years old) esotropia (10%), acquired esotropia >8 years old (13%), intermittent exotropia (20%), consecutive

exotropia (15%), acquired exotropia >8 years (2%), congenital trochlear palsy (10%), acquired hypertropia >8 years (10%), combined horizontal and vertical deviations > 10 PD (3%).

Binocular Summation

The mean binocular summation score for high contrast ETDRS vision and 2.5% LCA was 0.45±4.12 letters and 0.41±6.26 letters, respectively. Neither of these scores was significantly different than zero (p=0.3 and 0.5 respectively), indicating a lack of significant binocular summation or inhibition for the overall group. For the lowest contrast level tested (1.25% LCA), the mean score was −2.14±7.00 letters, which was significantly less than zero (p=0.004), signifying overall binocular inhibition for this metric.

Overall for ETDRS acuity, 5% of subjects demonstrated binocular summation and 5% demonstrated binocular inhibition, while the majority were indeterminate with scores between −5 and +5 letters. As the contrast level was reduced, the incidence of BiS and BI increased. At 2.5% LCA, 13% of subjects exhibited BiS, while 10% had BI. In comparison in 1.25% LCA group, 12% of subjects demonstrated binocular summation, while 23% demonstrated binocular inhibition (Table 1).

Vision related quality of life

In general, our patients with binocular inhibition demonstrated significantly lower overall composite scores on the NEI-VFQ-25 questionnaire compared to subjects with binocular summation. For ETDRS acuity, subjects with BiS had an average composite score of 80±19 compared to 57±7 in patients with BI, p=0.03. Subjects with BiS in 2.5% LCA had a mean composite score of 81±14; patients with BI had an average score of 67±15, p=0.01. Lastly, subjects' with BiS in 1.25% LCA average composite score was 91±9 and was 71±14 for patients with BI, p=0.004 (Table 2).

When analyzing the 5 sub-categories of the NEI-VFQ-25 questionnaire, all subjects with binocular inhibition exhibited lower average scores than those with binocular summation; this trend was noted for all three chart-types (ETDRS, 2.5% and 1.25% Sloan LCA) and was statistically significant for the 1.25% LCA. For this test (Table 3), patients with BI had significantly lower mean scores for general vision (p=0.008), near activities (p=0.03) and dependency (p=0.04). A statistically significant difference was also found for subjects with BI for ETDRS acuity in the dependency category (p=0.02).

In order to account for known covariates that affect both QoL and BiS, a linear regression analysis was performed. The analysis evaluated composite NEI-VFQ-25 scores and the following co-variates: BiS score, age, sex, presence of diplopia, and visual acuity. The results of the linear regression analysis (Table 4) revealed a statistically significant association between lower BiS scores for the 1.25% LCA level and lower QoL scores (p=0.02) after accounting for the aforementioned potential covariates.

A secondary analysis of strabismus-specific QoL metrics was performed. Subjects aged <18 years answered the ASQE questionnaire while adult subjects answered the AS-20 questionnaire. QoL scores on the AS-20 were significantly lower in subjects with BI for

ETDRS visual acuity (p=0.04) and 2.5% LCA (p=0.04, Table 2). For the ASQE questionnaire, subjects with BI for 1.25% LCA had a lower overall QoL score, however this difference was not statistically significant (p=0.13; Table 2).

Discussion

Our study analyzes the relationship between binocular summation and QoL in strabismus patients through the use of the NEI-VFQ-25, ASQE and AS20 questionnaires. The NEI-VFQ-25 is a 25-item general questionnaire that is sensitive to disease progression.[11–14] In the present study, patients with binocular inhibition had lower overall composite scores on the NEI-VFQ-25. When compared to subjects with binocular summation, this difference was statistically significant for all contrast levels. Furthermore, the presence of BI at 1.25% LCA was significantly associated with diminished QoL even after accounting for potential confounders, including age, gender, and the presence of diplopia.

In addition we analyzed 5 sub-categories of the NEI-VFQ-25 (general vision, dependency, driving, near vision activities and distance vision activities) and found that subjects with BI demonstrated lower overall scores in each subscale. In subjects with BI for the 1.25% LCA test, this difference was statistically significant for general vision (p=0.008), near vision activities (p=0.03) and dependency (p=0.04). Subjects with BI in high contrast acuity, also showed reduced dependency sub-scores when compared to patients with BiS (p=0.02).

Although the majority of patients in our study did not report diplopia, a significant number demonstrated BI and reduced QoL. This illustrates that the functional impact of strabismus on QoL is not solely related to double vision; rather patients without diplopia can have reduced binocular acuity and report diminished QoL.

The NEI-VFQ-25 is a general health related questionnaire that is applied to a broad range of ophthalmic conditions.[11–14] The AS20 and ASQE are both patient-derived surveys that are specific to strabismus.[15,16] When comparing the AS20 to NEI-VFQ-25 questionnaire, Hatt *et al* found more patients had sub-normal composite scores on the AS20 than NEI-VFQ-25, and this was true for patients with and without diplopia.[14] In our study, patients with binocular inhibition had significantly lower overall scores on AS20 when compared to subjects with binocular summation (Table 2). Patients less than 18 years of age completed the ASQE questionnaire, and those with BI in 1.25% LCA had decreased composite scores; though this difference was not statistically significant. Of note, this trend was not present in subjects with BI in 2.5% LCA, and in subjects with BI in high contrast ETDRS acuity, zero subjects were less than 18 years of age. Thus our findings for these two vision groups, may simply reflect the smaller number of subjects less than 18 years of age that were eligible to complete this questionnaire.

Overall our data shows increased BI as contrast level is reduced. With high contrast ETDRS letters, BI was found in only 5% of subjects, while 23% of strabismic subjects exhibited BI for 1.25% LCA. This finding agrees with previous studies of normal subjects tested with Sloan LCA charts – as contrast is decreased, the prevalence of BI increases.[1,9] It has also previously been shown in multiple sclerosis and in strabismus.[1,9] Increased BI for 1.25%

LCA is important, since low contrast acuity may actually represent a patient's day-to-day environment and can explain vague ocular symptoms often reported by patients with strabismus that cannot be demonstrated on physical exam.[1,4]

The results of this study should be understood within the context of its limitations. Since this was a clinic-based study, we included all subjects with strabismus who were eligible to enroll – therefore, many different strabismus sub-types were included; specific types of strabismus may have a higher prevalence of binocular summation or inhibition or be associated with lower QoL. In addition, our setting as a tertiary-care institution may induce some selection bias for particular types of strabismus. Finally, given the multitude of potential confounders for studies on QoL, it is possible that we did not account for a covariate in our linear regression that may have impacted the results. However, in spite of these limitations, we believe that these data reveal that the presence of BI for low contrast tasks in patients with strabismus correlates with QoL. Due to this association, we recommend measuring binocular and monocular visual acuity in strabismus patients, as the presence of binocular inhibition may provide useful information to patients and clinicians regarding the functional effects of strabismus.

Acknowledgments

Grant Support (SLP): NIH/NEI K23EY021762

Knights Templar Eye Foundation

Oppenheimer Family Foundation

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Table 1

Percentage of Strabismic Subjects with Binocular Summation and Inhibition

Test	Binocular Summation (BiS score >5 letters)	Indeterminate (−5 letters< BiS score <+5 letters)	Binocular Inhibition (BiS score < −5 letters)
ETDRS	5%	89%	5%
2.5% LCA	13%	76%	10%
1.25% LCA	12%	65%	23%

BI: binocular inhibition; BiS: binocular summation; ETDRS: early treatment diabetic retinopathy study (high contrast visual acuity); LCA: low contrast acuity

Table 2

Mean QoL Scores of Strabismic Subjects

	ETDRS	**2.5% LCA**	**1.25% LCA**
	NEI-VFQ-25 Composite Score		
BiS	80±19	81±14	91±9
Indeterminate BiS	77±15	77±15	75±16
BI	57±7	67±15	71±14
P Value (Anova)	**0.03**	**0.01**	**0.004****
	AS-20 QoL Composite Score		
BiS	22.50	34.88	40.17
Indeterminate BiS	32.94	32.91	29.71
BI	11.25	16.38	30.76
P value (Anova)	**0.04**	**0.04**	0.40
	ASQE QoL Composite Score		
BiS	20.00	19.75	20.50
Indeterminate BiS	12.96	11.81	12.44
BI		24.00	11.50
P value (Anova)	0.21	0.06	0.13

** Remains statistically significant after Bonferroni correction

BiS: Binocular summation Score; BI: Binocular inhibition

Binocular summation score calculated as the difference between the binocular letter score and the better eye letter score for the ETDRS, 2.5% Sloan, and 1.25% Sloan letter charts.

ETDRS: early treatment diabetic retinopathy study (high contrast visual acuity); LCA: low contrast acuity; ANOVA: analysis of variance

Table 3

Mean QoL Sub-category Score of Strabismic Subjects With Binocular Summation and Binocular Inhibition of 1.25% Low Contrast Acuity

	Binocular Summation (BiS score >5 letters)	**Indeterminate (−5 letters< BiS score <+5 letters)**	**Binocular Inhibition (BiS score < −5 letters)**	**p-value (ANOVA)***
NEI-VFQ-25 Composite	91±9	75±16	71±14	**0.004**
General Vision Subscale	86±13	69±20	63±19	**0.008**
Near Activities Subscale	92±11	77±2	70±23	**0.03**
Distance Activities Subscale	88±13	75±20	73±23	0.1
Dependency Subscale	97±6	86±19	78±26	**0.04**
Driving Subscale	88±11	69±24	75±19	0.1

*ANOVA comparing QoL scores between subjects with binocular summation, indeterminate scores, and binocular inhibition for 1.25% LCA.

BI: binocular inhibition; BiS: binocular summation; ETDRS: early treatment diabetic retinopathy study (high contrast visual acuity); LCA: low contrast acuity

Table 4

Effects of Co-variates on National Eye Institute Visual Functioning Questionnaire-25

Co-Variate	p-value	Co-Variate	p-value	Co-Variate	p-value
ETDRS Chart		**2.5% LCA**		**1.25% LCA**	
Sex	0.9	Sex	0.4	Sex	0.3
Age	0.04	Age	0.1	Age	0.2
Diplopia	0.3	Diplopia	0.3	Diplopia	0.2
BiS Score	0.4	BiS Score	0.3	BiS Score	**0.02**
	0.01	Visual Acuity	0.07	Visual Acuity	0.4
R^2	0.26	R^2	0.22	R^2	0.25

BiS: binocular summation; LCA: low contrast acuity

J AAPOS. Author manuscript; available in PMC 2015 October 01.