Prediction of improved vision in the amblyopic eye after visual loss in the non-amblyopic eye

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Amblyopia arises from abnormal visual experiences in early childhood. Improved function of the amblyopic eye after visual loss in the non-amblyopic eye could be a model for residual neural plasticity. We aimed to establish the likelihood of, and predictive factors for, this improvement in function. We identified 254 individuals aged 11 years or older with unilateral amblyopia who were visually impaired after loss of vision in their non-amblyopic eye but had no other disorder affecting their amblyopic eye. 25 (10%) of 254 people had improved visual acuity in their amblyopic eye. These findings suggest there is some plasticity in the visual system of a few visually mature individuals with amblyopia, which warrants further study. Children should remain the focus of detection and treatment.

Lancet 2002; **360:** 621–22

Amblyopia is a disorder of reduced visual function in an eye, which is attributed to abnormal visual experiences during important periods of visual development in early life.[1,2] This disorder is generally considered to be unresponsive to treatment after childhood. However, there is increasing interest in improved function in the amblyopic eye after visual loss in the non-amblyopic eye, as a model for residual plasticity in the human brain.[1,2] We report the likelihood, and factors predictive of, improved vision in the amblyopic eye after loss of vision in the non-amblyopic eye.

We have described elsewhere in this issue (see this week's *Lancet* page 597) methods used to identify individuals with unilateral amblyopia, who were visually impaired after loss of vision in their non-amblyopic eye, together with details of data collection and study methodology. 1 year after initial presentation, information was obtained by questionnaire about subsequent treatment and changes in visual function. We included in the present analysis only individuals aged 11 years or older, without any other disorder affecting their amblyopic eye.

	Outcome in amblyopic eye			
	Any improvement in acuity		Improvement in acuity of ≥2 lines	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Predictive factor				
Age (*vs* ≥21 years old)	3·86 (1·12–13·2)	0·031	3·76 (0·93–15·22)	0·06
New optical treatment for amblyopic eye (*vs* untreated)	9·67 (4·69–19·99)*	<0·0001	2·59 (1·63–4·14)*	<0·0001
Acuity of 6/36 or worse in non-amblyopic eye at presentation (*vs* acuity of 6/24 or better)	2·43 (1·17–5·03)*	0·016	1·79 (1·07–3·02)*	0·027
Acuity of 6/24 or better in amblyopic eye at presentation (*vs* acuity of 6/36 worse)	1·97 (1·01–3·85)*	0·048	1·07 (0·69–1·68)*	0·750

*Adjusted for age.

Table 1: **Univariate analysis of predictive factors**

We calculated the probabilities of any, and of clinically significant, improvement in acuity in the amblyopic eye 1 year after initial presentation. We postulated a priori[1–3] that improvement in vision might be related to age; acuity of the non-amblyopic eye at presentation; previous acuity of the amblyopic eye; new treatment for the amblyopic eye; and cause(s) of, and previous treatment for, amblyopia. Since acuity was usually reported with the Snellen notation, we used this classification for analysis. We considered a gain of two lines or more of Snellen acuity to be a clinically significant improvement.

Acuity in both amblyopic and non-amblyopic eyes was treated as a binary variable, with a cutoff point of 6/24 or better versus 6/36 or worse. Age at presentation was dichotomised for univariate analysis, but was treated as a linear variable for modelling. Improvement in acuity in the amblyopic eye at 1 year was investigated as a binary outcome for univariate analysis (none *vs* any improvement, and one line or fewer versus two or more lines gained). Subsequently, to exploit its ordered structure, we treated acuity as an ordinal categorical outcome, with categories based on the number of lines gained. After preliminary univariate logistic regression analysis, we fitted cumulative odds ordinal logistic regression models, with S-Plus 2000 (MathSoft).

Of 370 people with unilateral amblyopia, with loss of vision in the non-amblyopic eye, data were available for 363 (98%) at 1 year.[2] Of these, 254 (70%) were included in the present analysis, because they were age 11 years or older (visually mature) and had no other disorder affecting their amblyopic eye. Some increase in acuity in the amblyopic eye at 1 year was reported in 48 (19%, 95% CI 14–24) people. However, an improvement in acuity of two or more lines happened in 25 (10%, 6–13). By comparison, no change in acuity in the amblyopic eye was seen in 185 (73%) people, whereas some worsening of vision was noted in 21 (8%).

In univariate analysis, younger age, new optical treatment (spectacles or contact lenses), poorer acuity in the non-amblyopic eye at presentation, and better previous acuity in the amblyopic eye were all associated with increased odds of improvement in the amblyopic eye (table 1). Although new optical treatment was most strongly associated with improvement of acuity in the amblyopic eye, 12 (25%) of 48 people who had some improvement in acuity had not been treated, whereas 47 (23%) of 206 whose acuity did not improve had received treatment. We could not investigate the effect of different causes of, or previous treatments for, amblyopia due to incomplete data.

The optimum cumulative odds ordinal logistic regression model included all four main effects and two-way interactions between new optical treatment and acuity at presentation in both the amblyopic and non-amblyopic eye. The outcome categories were 0 (n=206), 1 (23), 2 (21), 3 (3), and 4 (1) lines of improvement in the amblyopic eye. We assessed the changes in the log-odds for contiguous

	Proportional odds ratio (95% CI)*	p
Predictive factor		
Age (per increasing year)	0·98 (0·96–0·99)	0·027
New optical treatment to amblyopic eye		
Untreated (n=174)	Baseline	
Treated (n=80)	70·10 (11·97–410·7)	<0·0001
Acuity of non-amblyopic eye at presentation		
6/24 or better (n=98)	Baseline	
6/36 or worse (n=156)	3·79 (0·96–15·01)	0·057
Acuity of amblyopic eye at presentation		
6/36 or worse (n=169)	Baseline	
6/24 or better (n=85)	5·38 (1·53–18·97)	0·009

*For improvement in amblyopic eye.

Table 2: **Multivariate analysis of predictive factors**

cutoff points and could not establish any significant deviations from the assumption of proportional odds. The goodness-of-fit χ^2 statistic was significant (p=0·0007). A significant interaction between optical treatment and acuity in the amblyopic eye suggested that the effect of treatment was greater in individuals with worse previous acuity in the amblyopic eye compared with those with better previous acuity. The adjusted odds ratios for each predictive factor are shown in table 2.

Our findings suggest that about one in five visually mature human beings who lose vision in their non-amblyopic eye could subsequently gain some improvement in vision in their amblyopic eye. However, only one in ten will have improvement in acuity of two or more lines. Greater severity of visual loss in the non-amblyopic eye and younger age at presentation, together with better previous acuity in the amblyopic eye and new optical treatment, are all associated with subsequent improvement in the amblyopic eye. Although most strongly associated with new optical treatment, a quarter of those who improved did so spontaneously. Our findings accord with residual plasticity outside childhood in a few people with amblyopia, which could be subject to some competitive influence from the non-amblyopic eye.

Although such plasticity in individual cases has been reported,[4] the only large-scale investigation reported is a retrospective survey of ophthalmologists, which included 144 cases.[3] The findings of that study[3] differed from ours: over a quarter of individuals had substantial improvement in acuity, arising spontaneously in most patients, and improvement in acuity was unrelated to age or depth of amblyopia. Conflicting findings have been reported for the effects of type of, and previous treatments for, amblyopia.[3,4] The importance of severity and nature of visual loss in the non-amblyopic eye has been argued, with especially good improvement reported after enucleation or central vision loss.[4] Our findings about optical treatment accord with continuing work delineating the effects of optical correction per se from those due to subsequent occlusion treatment.[5]

It cannot be established here, or from other epidemiological studies, whether the noted improvements in acuity in the amblyopic eye represent true new increase in visual function, unmasking of latent visual ability that has slipped after previous treatment, or a combination of both. Longitudinal clinical studies would be needed, using experimental approaches similar to those already used to investigate specific visual tasks in amblyopia,[2] and allowing other salient factors, such as fixation patterns, to be assessed. Continuing work on the biochemical basis of neural plasticity[1] could also help to better characterise those individuals who might have improvement in their amblyopic eye.

Further study is warranted of visually mature individuals to advance understanding of the mechanisms underlying amblyopia. Nevertheless, at a clinical level, children should remain the focus of detection and treatment strategies.

Contributors

J Rahi designed and coordinated the study. J Rahi, S Logan, and M Cortina Borja did the analysis and wrote the report. C Timms, I Russell-Eggitt, and D Taylor contributed to study design, interpretation of findings, and writing of the report.

Conflict of interest statement

None declared.

Acknowledgments

We thank all consultant ophthalmologists and their colleagues for support and contributing cases; the Steering Committee of the British Ophthalmological Surveillance Unit for the opportunity to do surveillance; and Catherine Peckham for her comments on an earlier draft of this report. This study was funded by the Research into Eye Diseases Trust, and J Rahi was supported by a grant from the Medical Research Council. The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

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