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Abstract

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Development/Plasticity/Repair

Oculomotor Instabilities in Zebrafish Mutant belladonna: A Behavioral Model for Congenital Nystagmus Caused by Axonal Misrouting

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We built a quantitative model derived from bel fwd (forward) eye behaviors. To mimic the achiasmatic condition, we reversed the sign of the retinal slip velocity in the model, thereby successfully reproducing both reversed OKR and SO. On the basis of the OKR data, and with the support of the quantitative model, we hypothesize that the reversed OKR and the SO can be completely attributed to RGC misrouting. The strong resemblance between the SO and congenital nystagmus (CN) seen in humans with defective retinotectal projections implies that CN, of so far unknown etiology, may be directly caused by a projection defect.

Key words: zebrafish; reversed optokinetic response; congenital nystagmus; oculomotor instability; achiasmatic; retinal ganglion cell axons; axonal misrouting; quantitative model; behavioral genetics

Introduction

Zebrafish mutant belladonna (bel) was originally isolated in a screen of mutations affecting retinotectal axon pathfinding. It is named for an apparent diluted pupil caused by the retinal pigment epithelium (RPE) frequently not adjoining the lens (Karlstrom et al., 1996) (see Fig. 1). In a subsequent visual behavioral screen using optokinetic response (OKR), bel mutant larvae often displayed a sign-reversed OKR (i.e., the eyes moved opposite to the optical stimulus) (Neuhauss et al., 1999). Succeeding anatomical analysis of the retinotectal projection by injecting lipophilic tracer dyes revealed that all larvae with reversed OKR were achiasmatic (Rick et al., 2000). The reliable concurrence of these two phenotypes implies a strong link between the achiasmatic condition and the reversed OKR.

Recently, bel was found to be caused by a mutation in the zebrafish Lhx2 homolog, a Lim domain homeobox transcription factor required for forebrain patterning and midline axon guidance (Seth et al., 2006). In the mid-1990s, an achiasmatic condition was first reported in humans (Apkarian et al., 1994). This rare heritable disease, termed nondecussating retinal-fugal fiber (NDRFF) syndrome, is frequently accompanied by oculomotor instabilities, with horizontal and see-saw nystagmus (Apkarian et al., 1995; Korff et al., 2003). The OKR profile in achiasmatic patients looked rather complex and appears not to be reversed (Apkarian and Bour, 2001). In addition to the reported cases in humans, an achiasmatic strain of Black Belgian sheepdogs was identified (Williams et al., 1994; Hogan and Williams, 1995). Analogous to achiasmatic humans, the absence of the optic chiasm in this canine led to congenital nystagmus (CN) (Dell’Osso and Williams, 1995; Dell’Osso et al., 1998).

Reversed OKR, on the other hand, has been described in albino humans (St John et al., 1984; Collewijn et al., 1985) and albino rabbits (Collewijn and Grootendorst, 1978). Interestingly, albinism is a condition that has been associated with altered patterns of retinal ganglion cell (RGC) decussation in the optic chiasm and deficits in eye morphogenesis (Jeffery, 1997). Moreover, reversed OKR has also been observed in normally pigmented humans where it mostly co-occurs with CN (Halmagyi et al., 1980). However, the underlying optic projection was not analyzed in these patients.

In human studies, visual dysfunctions caused by the achiasmatic defect were merely based on case reports. With the exception of the canine strain, investigators had to depend on surgically induced ipsilateral projections of RGC axons to study the achiasmatic condition in animals (Easter and Schmidt, 1977). bel provides a robust model for repeated measurements of eye movements related to the influence of the RGC misrouting. The zebrafish is a monocular vertebrate with RGCs completely pro-
jecting to the contralateral, or in the case of achiasmatic bel, to the ipsilateral side of the brain. Thus, in contrast to binocular pri-
mates and most mammals, the effects of the RGC misrouting can be
studied without the complication of a mixed projection.

In this study, we report a novel feature in achiasmatic bel
larvae: spontaneous eye oscillations (SOs) that closely resemble
CN in human patients. We describe the oculomotor abnormalities
tested and bred as described previously (Mullins et al., 1994). Outcrossed
these identification crosses as well as crosses of already identified carriers
position (dpf). Larvae at 5–7 dpf were anesthetized with 3-aminobenzoic acid
staged according to development in days postfertiliza-
Wehrheim, Germany). After polymerization at room temperature, mic-
mixture washes, and incubated in Technovit 7100 (Heraeus Kulzer,
alddehyde, dehydrated through a graded series of ethanol–water
slides (Menzel-Gläser, Braunschweig, Germany), air dried at 60°C,
stained with toluidine blue solution (0.1% in aqua dest.), overlaid with
Gaussian smoothing kernel with

Materials and Methods

Fish maintenance and breeding. The bel (bel<sup>ec2</sup>) mutant line was main-
tained and bred as described previously (Mullins et al., 1994). Outcrossed
sibling pairs were set up to identify heterozygous carriers. Clutches of
these identification crosses as well as crosses of already identified carriers
were used to assess visual behavior. Embryos were raised at 28°C in E3
medium (in mM: 5 NaCl, 0.17 KCl, 0.33 CaCl<sub>2</sub>, and 0.33 MgSO<sub>4</sub>) (Haffter
and grouped based on their OKR phenotype [wild type (wt), bel forward
and bel reverse (rev)] to calculate the respective statistics for each
group.

Experimental procedure. If not noted otherwise, the following stimu-
lation has been used. The spatial frequency of the sine-wave grating was
0.045 contrast/degree (c/deg). Contrast was varied on an interval be-
0.045 contrast/degree (c/deg). Contrast was varied on an interval be-
denotes the maximum illumination (5230 cd/m<sup>2</sup>) in one condition were treated as one data row in
which the descriptive statistics were calculated and then pulled together
and grouped based on their OKR phenotype [wild type (wt), bel forward
and bel reverse (rev)] to calculate the respective statistics for each
group.

Quantitative model. We built a quantitative model of the OKR using
MATLAB Simulink (Mathworks, Natick, MA) (see Fig. 6). The parama-
ter estimation and details on the derivation of the model are presented in
supplemental Tables 1 and 2, and the supplemental movie (available at
www.jneurosci.org as supplemental material).

The model contains fast-phase (saccade) and slow-phase circuits that
are alternately active. This corresponds to the experimentally derived data
in which the slow phase of the OKR is frequently interrupted with
saccades to reset the eye after approaching the maximum eye range. The
slow phase of the OKR is modeled with the OKR and the eye velocity-
dependent load (Ve Load block). In wt, the OKR serves the purpose of
stabilizing the visual image on the retina when the visual scene moves
relative to the retina of the fish. Accordingly, in the OKR model, the
retinal slip velocity is the error signal to minimize the retinal slip. The
retinal slip velocity is the error signal to minimize the retinal slip. The
minimum illumination in the sine-wave grating.
The maximum contrast achieved by the projector will be referred to as
100% instead of 99% to improve readability. For measuring the OKR at
different stimulus velocities, we used a back-and-forth moving sine-wave
grating with the direction changing every 5 s.

Statistical analysis. To test the main effect of stimulus contrast on the
SPV, we performed a two-way repeated-measures (RM) ANOVA for
each group (wt, mut fwd, and mut rev) with stimulus contrast and stim-
ulus velocity as within-subject factors. We then used a mixed RM-
ANOVA with group as the between-subject factor and stimulus velocity
as the within-subject factor to test whether there was a significant differ-
ce in contrast sensitivity between groups. Fish with unrealistically
high-contrast sensitivities of >100 were not included in the analysis.
same statistical method was used to test whether the three groups differed on saccade peak velocity. Because mixed RM-ANOVA cannot handle missing data, some fish had to be excluded from the analysis.

**Results**

The zebrafish mutant bel is a recessive mutation named after its “enlarged” pupils caused by an RPE defect (Fig. 1A, B) (Wilhelm et al., 1991; Karlstrom et al., 1996; Feinsod, 2000). This prominent feature is a consequence of the RPE failing to adjoin the lens, thereby leaving a visible gap (Fig. 1D, E, asterisk). Approximately 40% of bel display a reversed OKR (bel rev), which is when a clockwise moving stimulus elicits counterclockwise eye movements while the remaining larvae have a normal sign OKR (bel fwd). This behavioral abnormality correlates perfectly with noncrossing optic fibers at the midline. Hence all bel rev are achiasmatic (Rick et al., 2000). Despite an equivalent pigmenta
defect in bel rev and bel fwd, the optic nerves of the latter cross normally at the midline and form an optic chiasm. bel rev, in contrast, have an achiasmatic phenotype with the optic fibers projecting into the ipsilateral brain hemisphere (Fig. 1C–E, arrows). Figure 1F–H shows the OKR traces typically generated by the three phenotypes. Frequently interrupted through fast resets (saccades), the eyes of wt move in the same direction and approximately at the same velocity as the stimulus (Fig. 1F). The OKR geometry of bel fwd looks very similar to that of wt as the eyes of bel fwd move parallel to the stimulus during the slow phase, although the overall velocity and the number of saccades per time unit are reduced (Fig. 1G).

Finally, the waveform of the reversed OKR is presented in Figure 1H. Aside from the reduced overall velocity, the most characteristic feature of the OKR of bel rev is the antiparallel eye movement to the stimulus.

**Stimulus contrast (cₛ) sensitivity**

The OKR gain (eye velocity/stimulus velocity) linearly correlates with the logarithm of the stimulus pattern contrast regardless of spatial frequency in zebrafish larvae (Rinner et al., 2005). Because Rick et al. (2000) showed that the number of saccadic eye movements per time interval were unaffected by stimulus velocity changes in bel rev, it is conceivable that the eye movements are equally unaffected by cₛ manipulation. Such a result would be consistent with the notion that the reversed OKR is driven by a stimulus-independent internal pacemaker mechanism. Therefore, we investigated the effect of varying cₛ on the OKR of bel rev larvae. Figure 2A–C shows that the SPV of bel rev (F₁₀,₃₂ = 18.513; p = 0.000) exhibited a positive linear relationship with the logarithm cₛ, analogous to bel fwd (F₁₀,₃₂ = 36.737; p = 0.000) and wt (F₁₀,₃₂ = 82.103; p = 0.000). When plotting against the normalized SPV, it is even more evident that the gain of the OKR is affected much in the same way in all three types of fish (Fig. 2D–F). Then we calculated the threshold contrast by intersecting the regression line for each fish and

**Figure 1.** Phenotypes of bel larvae at 5 dpf. A, B, A gap between the lens and the pigmented epithelium of the eye gives the appearance of enlarged pupils in bel larvae (B). C–E, Transverse sections of the retina and brain. The ipsilateral projection of the eye on saccade peak velocity. Because mixed RM-ANOVA cannot handle
group with the horizontal line at SPV = 1.5°/s (noise floor of the SPV data). The temporal contrast sensitivity (reciprocal of threshold contrast) (supplemental Table 2, available at www.jneurosci.org as supplemental material) is similar in all groups along different SPV (F(2,18) = 0.036; p = 0.965). Hence, the reversed OKR is influenced in contrast and not independent on visual input.

Stimulus velocity challenge
Figure 2, A and B, shows that, given the same contrast, both wt and bel fwd eye velocities raise with increasing stimulus velocity until they reach their peak at 32°/s. These results extend the previous finding of Rick et al. (2000), who reported independence of gain and stimulus velocity. Our results confirm this abnormal relationship between input velocity and eye velocity. However, with more precise measurements, we observed a slight dependence on stimulus velocity in bel rev at low velocities of 4–16°/s. The same effect is still present at reduced contrast (Fig. 3C). To verify this observation, we tested the OKR on an extensive range of stimulus velocities. Figure 3A shows that the SPV of both wt and bel fwd correlated positively with low stimulus velocities (i.e., <32°/s), decreasing steadily thereafter. In bel rev, however, the SPV started at a much higher value and reached its maximum two steps earlier than wt and bel fwd, and it already began to decline at a stimulus velocity of 24°/s. The peak SPV was comparably lower in bel rev and bel fwd. Thus, the OKR of bel rev had significantly reduced stimulus velocity dependence with the SPG exceeding one when the stimulus velocity was <16°/s (Fig. 3B). This is in contrast to wt and bel fwd that only displayed gain values ≤1 (Fig. 3B).

We also compared the saccade peak velocity among the three groups to exclude the possibility that the optokinetic profile seen in bel rev and bel fwd is a result of a motor deficiency. The peak velocity reached during the saccades was similar in all three groups across stimulus velocities (Fig. 3C). Hence, the saccade system and the motor performance appears to be unaffected by the bel mutation. Additionally, to understand the cross-feed between the two brain hemispheres, we computed the velocity of the unstimulated eye as the fold change of the stimulated eye velocity. This value was, on average, 1.27 in bel rev, whereas in wt and bel fwd, it was 0.76 and 0.82, respectively. The higher amplitude of the unstimulated eye in bel rev indicates that the major signal was fed into the ipsilateral hemisphere.

SOs
At the cessation of the moving grating, we made the intriguing observation of SOs in 20–80% (different for all clutches) of bel rev (supplemental movie, available at www.jneurosci.org as supplemental material). Those fish exhibiting the SOs do so for most of the time as soon as they are able to perceive the pattern (Shallo-Hoffmann et al., 1999). As presented in Figure 4A, in addition to sporadic saccades, the eyes of wt stopped moving with the cessation of motion in the surround. Yet, the eyes of bel rev continued to be moving, displaying alternating waveforms of very different character compared with the reversed OKR (Fig. 4B). To investigate the properties of the SO, we tested bel rev at different stimulus conditions. In contrast to wt, the eyes of bel rev keep oscillating when presented with a still grating (Fig. 4A, B). In complete darkness, the eyes of both wt and bel rev cease moving (Figs. 4C,D). As a result, the oculomotor instability seen in bel rev cannot be attributed to a motor system instability (efferent) but must be caused by a sensory deficiency. Under illumination without grating, eye movements of bel rev discontinued (Fig. 4E). In addition, Figure 4E also shows that the SOs occur at the sole pres-
alternated with a still grating (filtered when the eye velocity exceeded 18°/s. The SPV was derived by calculating the mean of the absolute eye velocity per condition. Conditions with a contrast of 100% and a v_s of 8°/s were alternated with a still grating (v_s = 0°) at differing contrasts (100-40-10-40-100%). Light gray bars, wt (n = 8); dark gray bars, bel rev (n = 7).

Because we have demonstrated a positive correlation between the reversed OKR and c_s, we wanted to elucidate the relationship between the SO and c_s. Thus far, we know that the eyes of bel rev oscillate at 100% contrast and remain stationary at 0% contrast. We presented gratings to bel rev and wt at varying c_s in a moving and in a still version with each condition preceded by a moving grating. Figure 5 shows that the SOs are modulated by the c_s similarly to the reversed OKR of bel rev and the normal OKR in wt larvae. Therefore, SOs are dependent on visual input but not on motion in the surround.

Quantitative model
To further prove that the reversed OKR and SOs are caused by the ipsilateral projection of the RGC in bel rev, we built a model to replicate the normal OKR with the transfer functions estimated based on bel fwd data presented in Figure 3 (n = 18) and used for the parameter estimation of the OKR and Ve Load transfer function (Fig. 6B) (supplemental Table 1, available at www.jneurosci.org as supplemental material) (R² = 0.9722). The resulting transfer function of the OKR element is presented in Figure 6C. The initial eye position, the initial eye velocity, and the saccade parameters such as the maximum eye range were estimated based on the corresponding empirical data set displayed in Figure 7, A, C, and E, because these parameters show remarkable between-subject variability. The normal OKR generated by the model is shown in Figure 7B. To replicate the projection defect in the OKR model, we changed the value of the gain element between the retinal slip velocity and the OKR element input to −1. Through this modification, we were able to successfully replicate the reversed OKR (Fig. 7D) and the SO (Fig. 7F).

Discussion
bel rev display OKR and SO. Both of these behaviors are visual-input dependent and correlate with contrast. The unique SO closely resembles the involuntary eye movements in human patients affected with CN. bel encodes a Lim domain homeobox protein Lhx2, and the loss of its function specifically leads to disruptions in three major axon pathways in the forebrain, which are as follows: the anterior commissure, the post-optic commissure, and the optic chiasm at the midline (Seth et al., 2006). In bel homozygous mutants (bel fwd and rev), a variable fraction of RGC axons aberrantly project into the ipsilateral brain hemisphere that has been associated with a reversed OKR (Rick et al., 2000). To understand the causal chain between the optic misprojection and these abnormal oculomotor behaviors, we undertook an in-depth analysis of visual performance in achiasmatic bel larvae based on an optokinetic stimulation paradigm.

Contrast sensitivity remains unchanged, and stimulus velocity dependence is reduced in reversed OKR
The OKR has been used as a behavioral measure to examine the contrast sensitivity in both cats (Donaghy, 1980) and humans (Lecuire et al., 1991; Harris and Smith, 2000). We have shown that the eye SPV in bel rev maintains a logarithmically linear function of stimulus contrast (c_s) just as in wild-type larvae (Rinner et al., 2005) despite the sign reversal (Fig. 2A–D). Moreover, the similar slopes of the normalized SPV versus the logarithmic c_s across the three phenotypes (wt, bel fwd, and bel rev) indicate that contrast sensitivity stays unaffected by the bel mutation (Fig. 2D–F). Statistical analysis of contrast sensitivity based on linear regression has confirmed this. Thus, the optokineti- n. Hence, the reversed sign of the retinal slip detection may account for the much higher SPG and the reduced stimulus velocity dependence at low stimulus velocities. In bel rev, the regenerative feedback
loop of the OKR receives a sign-reversed error signal, causing the retinal slip to increase gradually.

At stimulus velocities beyond the SPV peak, all three groups showed a gradual decrease in SPV with increasing stimulus velocity. It is reasonable to explain the SPV and the SPG drop as a consequence of motion blurring caused by the failure of the OKR mechanism to compensate for the retinal slip, thus allowing for high retinal slip velocities to occur. Assuming that the sensory detection has a fixed-frame rate, motion blurring can be understood as a temporal integration of the stimulus in the retina, leading to reduced perceived \( c_v \). Thus, the SPV decay can be explained in terms of a reduced perceived \( c_v \). Because, in both bel fwd and bel rev, the maximum velocity reached during saccades is the same as in wt, the lower peak SPV in bel fwd and bel rev implies a sensory deficiency and/or a reduced efficiency of the OKR circuitry rather than a motor defect. At very high stimulus velocities, the eye stops following the moving grating as a consequence of motion blurring with the SPV converging to a theoretical asymptote at \( \sim 1.5°/s \) (noise floor of the SPV data). Finally, it is worth mentioning that, after both bel fwd and bel rev have reached their peak SPV, their curves essentially overlap (also the OKR gain curves), which well supports the idea that these two groups show a very similar OKR decay regardless of the reversed sign in bel rev. The weaker OKR of bel fwd and bel rev might be attributed to observed subtle retinal defects, particularly affecting amacrine cells of the retina (Seth et al., 2006).

Because we used a monocular stimulation paradigm in our OKR experiments, we were also interested in the behavior of the unstimulated eye, which may help us extend our knowledge about the cross talk between the left and right brain areas involved in the OKR. It turned out that, in bel rev, the unstimulated eye performed at a higher rate than the stimulated eye. In wt and bel fwd, on the other hand, the unstimulated eye showed a comparably weaker response. Interestingly, the multiplicative inverse of the left/right-eye gain in wt is comparable to the left/right-eye gain in bel rev. This may be because of a gain between the contralateral optic tectum and the ipsilateral motor neurons that increases the drive on the stimulated eye in wt. In bel rev, in contrast, that gain is missing in the stimulated eye but drives the unstimulated eye, leading to the reciprocal of the left/right-eye gain. This provides additional proof to the hypothesis that the optokinetic phenotype of bel rev is caused by the underlying RGC projection defect (data not shown).

**Both SOs and reversed OKR are caused by the achiasmatic projection**

The SOs have been only observed in bel rev. We have shown that this intriguing behavior requires visual input with a pattern presented and is contrast sensitive. All of these properties indicate that SOs have the same underlying cause as the reversed OKR.

Thus, the neural projection error in the brain is the main reason of both abnormal oculomotor behaviors.

The main function of the OKR is to stabilize the visual image on the retina. In this simple sensorimotor feedback system, the visual motion sensor detects the motion of the visual environment relative to the retina as an input signal that then elicits compensatory eye movements, the output response, to reduce the slip velocity of the retinal image. Thus, the retinal slip serves as the error signal in this closed feedback loop, and the eye adjusts its velocity according to the perceived pattern velocity. The aim of this controlling negative feedback loop is to reduce the slip velocity ideally to zero. Based on this principle, we have built a quantitative model to simulate the neural circuit of OKR in larval zebrafish. In the achiasmatic condition (bel rev), the signal from the eye always feeds into the wrong hemisphere, leading to a nasal-temporal reversed perception. The attempt to compensate the retinal slip takes the wrong direction, thereby actually increasing the retinal slip. The resulting positive feedback loop is incapable of stabilizing the visual system, causing the observed, unstable oculomotor behaviors in bel rev. This idea is supported by the successful replication of the reversed OKR and the SO by reversing the sign of the error signal (retinal slip) in the model. Analogous to the model in which the initial eye velocity has to differ from zero, spontaneous eye movements such as a saccade are necessary to initiate SOs in bel rev.

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**Figure 6.** A detailed model used for the computer simulation of the reversed OKR and the SO observed in bel rev. A. Diagram of the OKR model in which neural and physical variables have not been distinguished to increase readability. B. The steady-state error (steady-state retinal slip) versus the SPV curve based on which parameters of the OKR transfer function and the Ve Load transfer function have been estimated. The gray curve is the estimated function used for the model. Error bars indicate SEM. C. The shape of the OKR transfer function based on the estimated parameters. \( \nu_e \), Stimulus velocity; \( \nu_s \), retinal slip velocity (error); \( \nu_{OKR} \), eye acceleration output of the OKR-transfer-function element; \( \text{Ve Load} \), eye velocity load element (reducing the eye acceleration). \( \nu_{SPV} \), eye acceleration output of the Ve Load element; \( \nu_{DFP} \), slow-phase eye acceleration; \( \nu_{DSP} \), eye acceleration generated by the Saccade System (fast phase); \( \nu_{DSP} \), eye acceleration of the OKR circuitry (slow and fast phase); \( \nu_e \), eye velocity; \( \nu_s \), eye position; SPV, steady-state eye velocity; SSE, steady-state error (residual retinal slip velocity when the SPV has been reached). The variables and formulas used in the model blocks are discussed in supplemental Tables 1 and 2 and the supplemental material (available at www.jneurosci.org as supplemental material).
SOs closely resemble the CN in humans

In belladonna, we have shown that the SO phenotype is most likely correlated with the underlying anatomical defect. Human patients affected with similar RGC projection defects also often suffer from an involuntary rhythmic eye movement, CN (Apkarian et al., 1994, 1995), which closely resembles the SO. It has been shown that a specific form of infantile nystagmus that is involuntary and conjugate, involving regular epochs of “active” and “quiet” phase (congenital periodic alternating nystagmus), is prevalent in CN associated with albinism (Abadi and Pascal, 1994). In some bel rev with a long recording time of SOs, we have observed analogous transitions in waveform characteristics. Our model is capable of replicating these waveforms and even a sudden stop of the SO: equal signs of the pre- and post-saccadic (\(v_{pre},v_{post}\)) eye velocity produce a beating nystagmus (jerk nystagmus), whereas different signs cause a pendular nystagmus. Random variation of the post-saccadic eye velocity leads to a periodic alternating nystagmus. Finally, the SOs cease when the post-saccadic eye velocity equals zero (data not shown).

Another abnormality we have observed in bel rev is frequently occurring spinning swimming behavior. This moving instability could well be related to failure of the eye to lock on an object in the visual field. In patients with vestibular neuritis, for instance, voluntary suppression of nystagmus reduces postural sway and increases balance (Jahn et al., 2002; Glasauer et al., 2005). Also, here nystagmus is associated with postural instability, further supporting the link between CN in humans and the SO in bel rev.

In contrast to achiasmatic mammals with binocular vision, bel rev provides a relatively clean model for studying visual behaviors in relation to optic nerve projection defects. The conflict between correct and erroneous information in binocularity is one explanation why, in patients with NDRFF and albinism, the OKR profile is complex, and reversed OKR has not been observed. In NDRFF syndrome patients, misprojections are mixed with remaining correct ones, and as also the case in healthy humans, some RGCs project ipsilaterally. Similarly, in albinism patients, about half of the axons correctly project to the contralateral hemisphere, whereas those destined for the ipsilateral hemisphere project contralaterally as well. Because fish have monocular vision, all of the optic fibers cross the midline forming the optic chiasm and project to the contralateral hemisphere. The half brain of the achiasmatic fish therefore receives only visual information from the “wrong” eye. This gives us a unique chance to study the visual defect caused by retinotectal axon pathfinding errors directly.

We have linked the reversed OKR and CN to the same underlying neural circuit defect, using the mutant belladonna as a behavioral tool. In this study, we used the mutant as a behavioral model of oculomotor instabilities such as nystagmus. The underlying molecular nature of the mutation is not informative in this context. Indeed, we drew comparison to the human condition that is, in all likelihood, not molecularly but behaviorally comparable to bel.

References


