An Agenda for Sensorimotor Research in Sub-Orbital Flight

Faisal Karmali, Harvard/MEEI
Mark Shelhamer, Johns Hopkins

Supported by: NSBRI, NIH, NSERC (Canada)
Special thanks: Ondrej Juhasz, Michelle Zwernemann, John Yaniec, Noel Skinner and our research subjects

How can we:

- Make sub-orbital flight more safe?
- Make sub-orbital flight more enjoyable?
- Benefit humans on Earth through sub-orbital flight experiments?

Sensorimotor disruptions

- Autonomic
  - Motion Sickness
  - Orthostatic intolerance
- Eye movements
  - Vestibulo-ocular reflex
    - Pitch
    - Roll
  - Eye alignment
    - Torsional
    - Vertical
  - Nystagmus
  - Saccade accuracy
- Postural stability
  - Gait
  - Head-body-eye coordination
- Motor coordination
  - Manual joystick control
- Orientation illusions
  - Inversion illusion

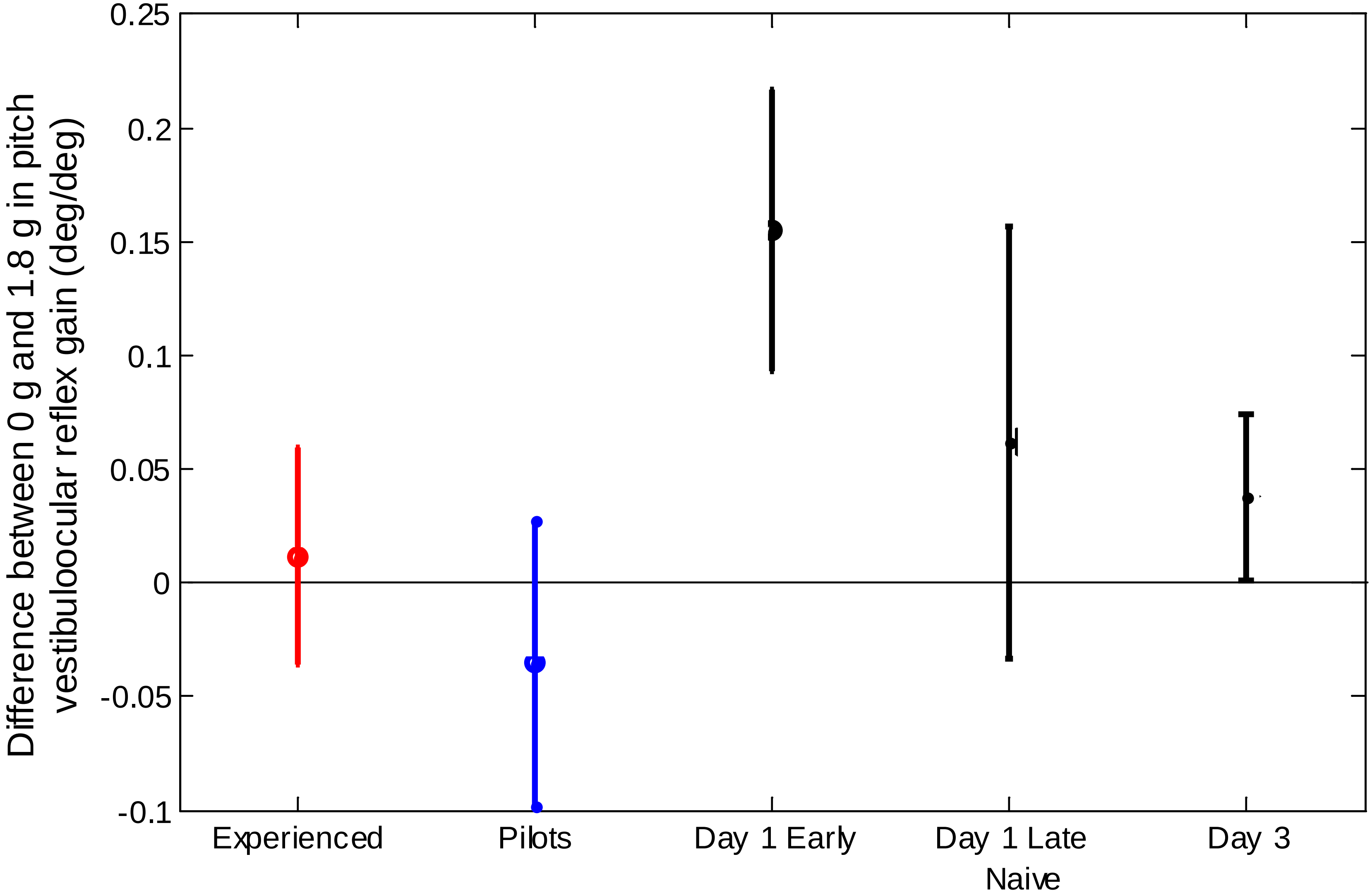
Goals

Sub-orbital passengers	Sub-orbital pilots
• Maximize enjoyment (maximize corporate revenue via customer referrals) • Accomplish research tasks	• Safely pilot the aircraft during both nominal and emergency situations Without interference from sensorimotor disruption

Overcoming sensorimotor disruptions

Strategies	Orbital flight	Sub-orbital passengers	Sub-orbital pilots
Adaptation	*****	*	*
Re-adaptation	**	*	*****
Pre-adaptation	***	*****	**
Pharmaceutical	***	***	**
Cognitive training	*****	*****	***

How quickly do we adapt?



Recommendations

Operators	Researchers
Use pre-adaptation in parabolic flight for sub-orbital passengers Emphasize recency of experience for sub-orbital pilots Develop and conduct a neurological examination for sub-orbital pilots Consider screening of passengers for latent and undiagnosed neurovestibular problems before sub-orbital flight	Study the effectiveness of parabolic flight as a tool to pre-adapt sub-orbital passengers Find sensorimotor symptoms caused by the unique sub-orbital flight trajectory, and ways to mitigate them Study the correlation between sensorimotor disruption and pilot performance and appropriate countermeasures.

Adaptation

Adaptation	Seconds - Days

Research Goals

Sub-orbital passengers	Sub-orbital pilots
• Allow passengers to fully focus on the flight experience without distraction of sensorimotor disruption • Allow passengers to complete a set of personal tasks within a short period of time, such as movement in 0 *g*, flips, looking out the window, and interacting with other passengers • Allow scientist-passengers to complete scientific tasks quickly and accurately • Consider any interactions between flight phases specific to sub-orbital flight	• Ensure that sensorimotor disruption does not interfere with the ability to pilot the aircraft during both nominal and emergency situations • Quantify re-adaptation capability by study the effect of gaps in sub-orbital exposure on functional neurological tests and actual flight performance metrics

Adaptation of otolith-ocular responses to parabolic flight

Faisal Karmali, Ondrej Juhasz,
Michelle Zwernemann, Mark Shelhamer

Presented by:
Faisal Karmali
Research Fellow
JVPL / MEEI / HMS

October 14, 2008

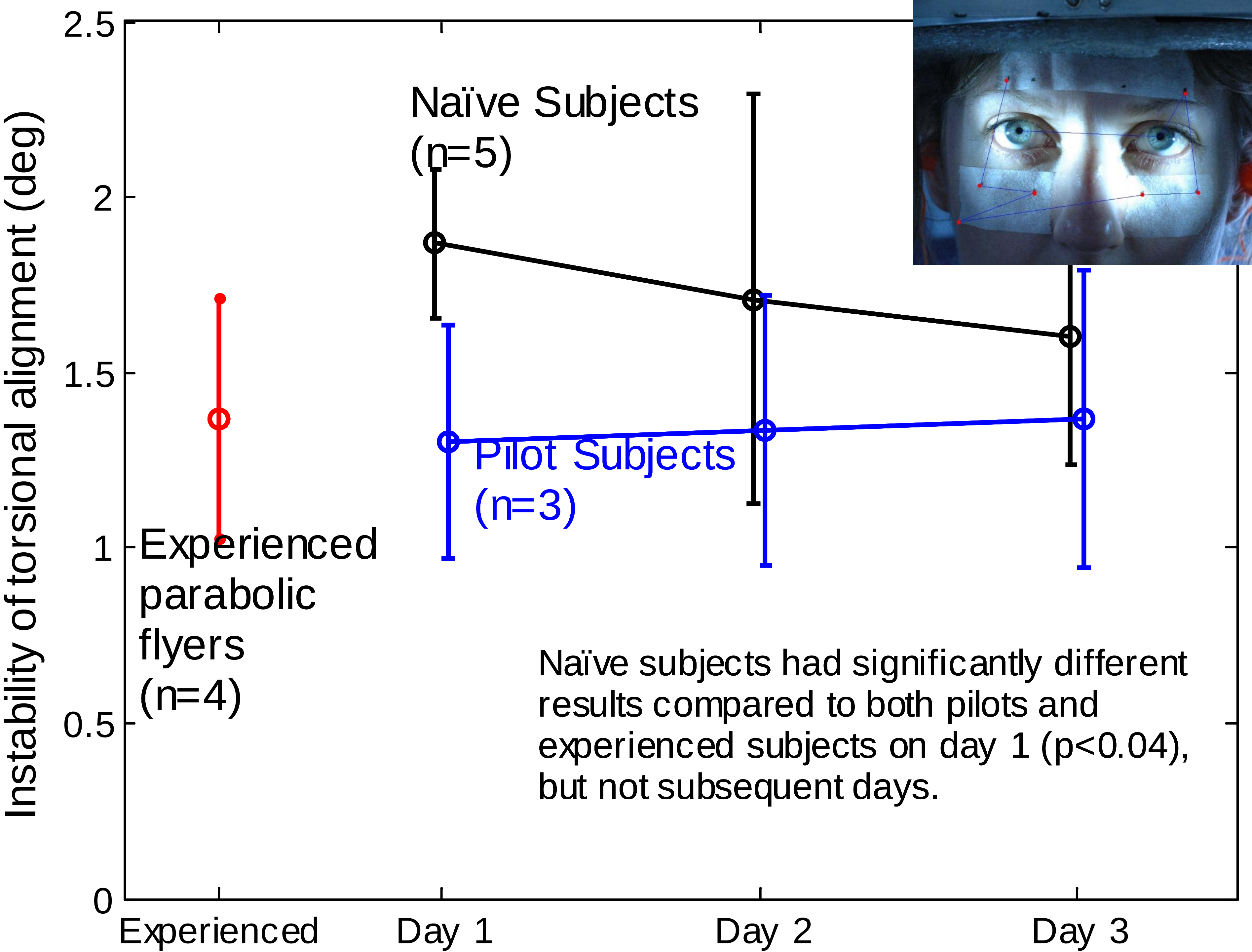
Supported by: NSBRI, NIH,
NSERC (Canada)

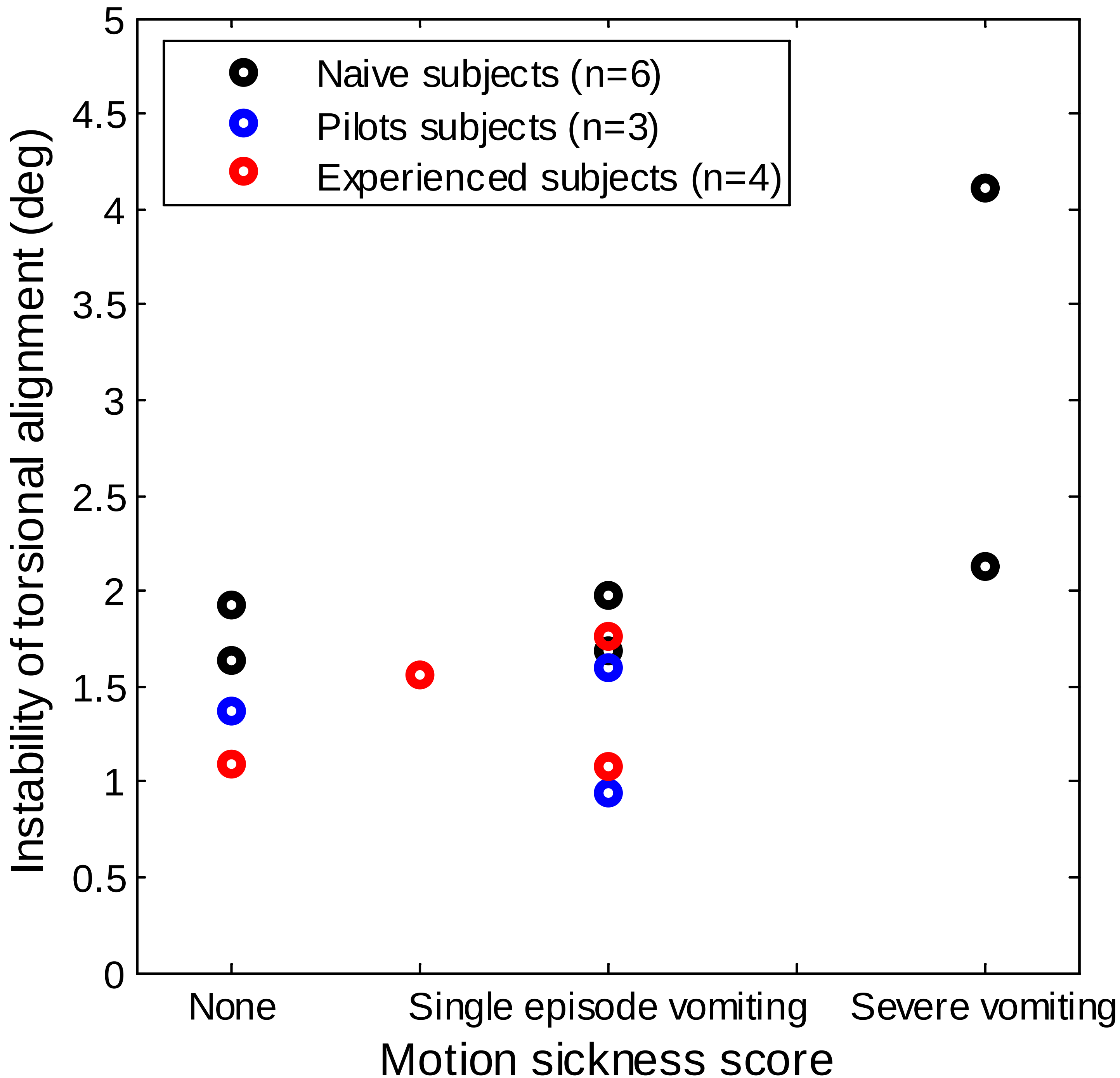
Take-home points

- In parabolic flight, certain otolith-dependent ocular responses improve over the course of 3 days of flying

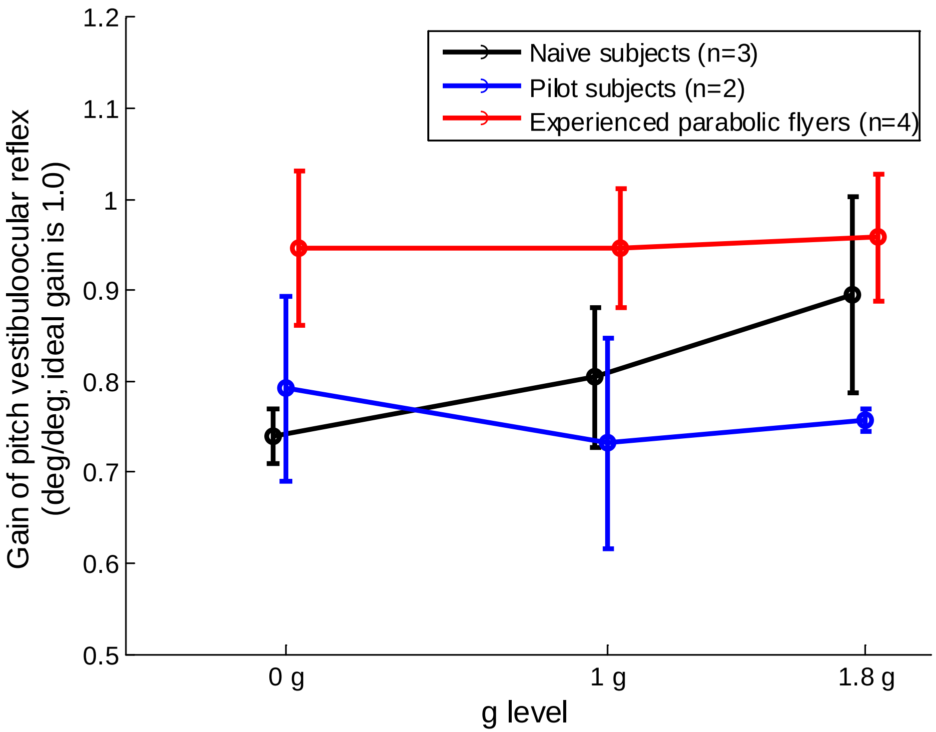
- Pilots (non-parabolic) had similar responses to experienced parabolic fliers, suggesting that certain experiences can prepare one for parabolic flight

- Adaptation of otolith-dependent pitch responses transfers to otolith-dependent translation responses

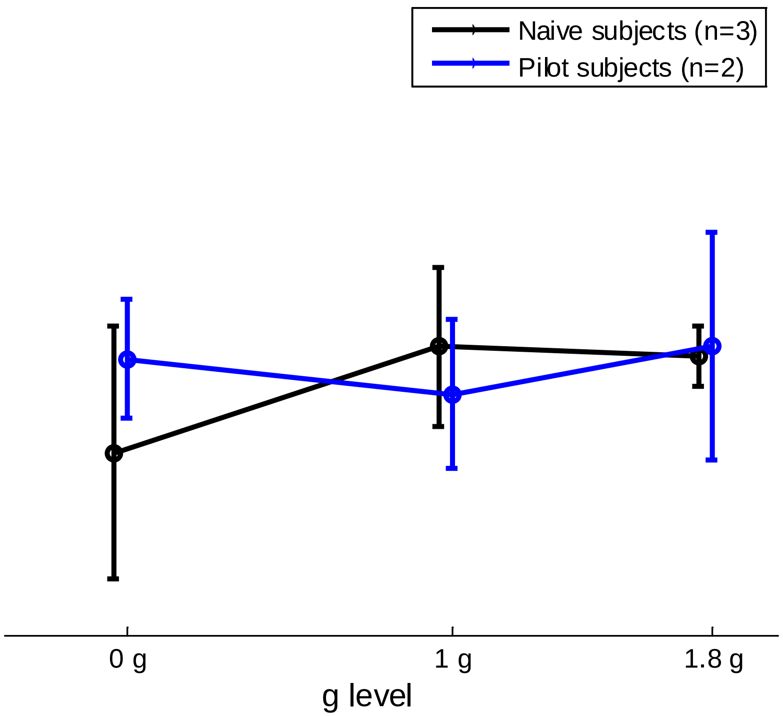

Instability of torsional alignment (deg)
2.5
2
1.5
1
0.5
0
Experienced
Day 1
Day 2
Day 3
Naïve Subjects
(n=5)
Pilot Subjects
(n=3)
Experienced
parabolic
flyers
(n=4)
Naïve subjects had significantly different results compared to both pilots and experienced subjects on day 1 (p<0.04), but not subsequent days.


Naive subjects (n=6)
Pilots subjects (n=3)
Experienced subjects (n=4)
Instability of torsional alignment (deg)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
None
Single episode vomiting
Severe vomiting
Motion sickness score

Day 1 Day 3



Naive subjects (n=3)
Pilot subjects (n=2)
Experienced parabolic flyers (n=4)
Gain of pitch vestibuloocular reflex (deg/deg; ideal gain is 1.0)
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0 g
1 g
1.8 g
g level



Naive subjects (n=3)
Pilot subjects (n=2)
0 g
1 g
1.8 g
g level

Take-home points

- In parabolic flight, certain otolith-dependent neurological responses improve over the course of 3 days of flying

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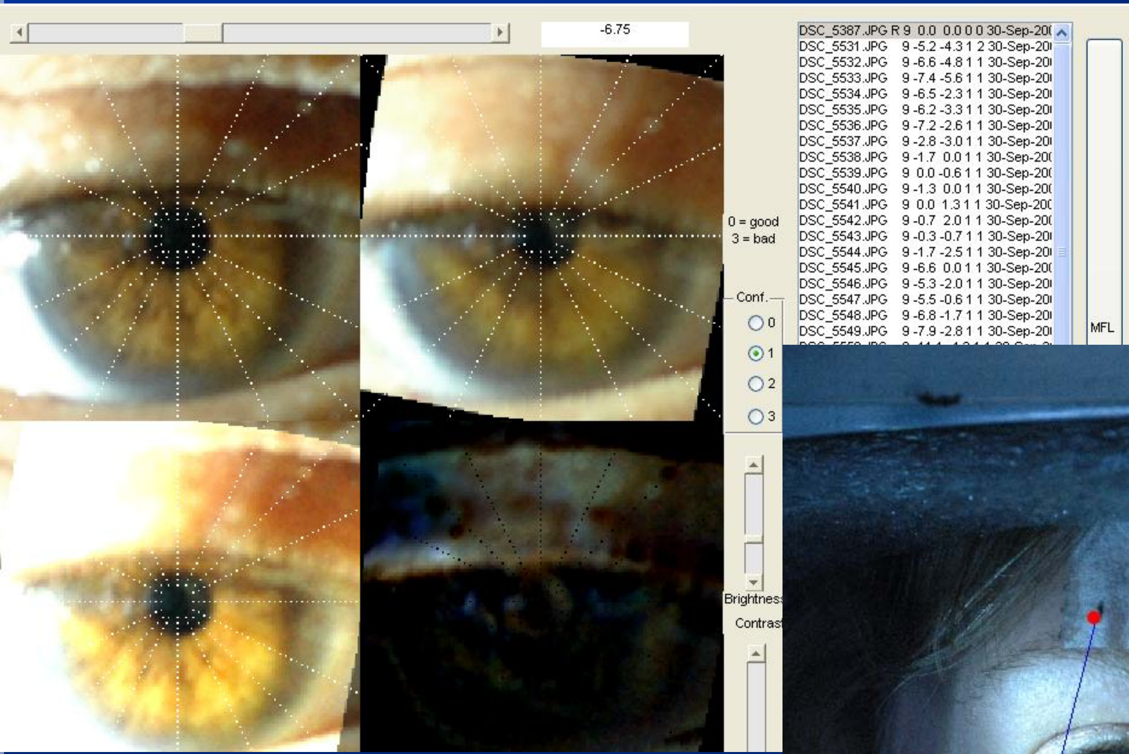
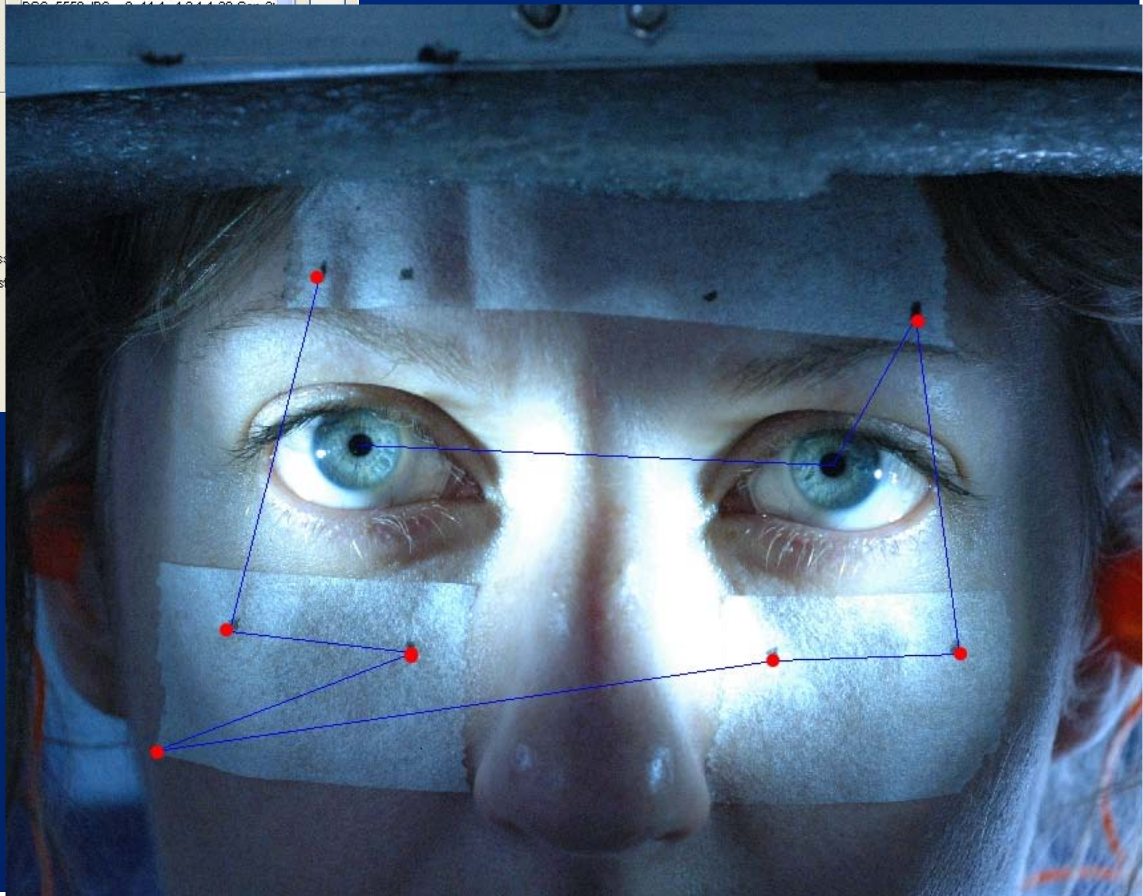
- Adaptation of otolith-dependent pitch responses transfers to otolith-dependent translation responses

Measuring static eye position



- **OCR**
- **Torsional alignment**
- **Vertical alignment**



- **Nikon D70 digital camera**
- **Subjects’ head upright/ tilted**

Measuring pitch VOR gain

- Active sine-like head movements
  - 0.3-1.6 Hz. Results based on 0.6-1.3 Hz
  - 20-30º
  - 40-90º/sec
- Fixating stationary point in the light.
- Eye movements were recorded using a head-mounted video system (Chronos).
- Gain computed by least-squares fitting of eye velocity to head velocity, for each cycle of motion.

Adventures in weightlessness:

Adaptation of otolith-dependent ocular responses to parabolic flight

Faisal Karmali, Ondrej Juhasz,
Michelle Zwernemann, Mark Shelhamer

Presented by:
Faisal Karmali
Research Fellow
JVPL / MEEI / HMS

MEEI Vestibular Seminar
March 24, 2008


HARVARD

The bottom line…

1. Parabolic flight consists of specific flight trajectories that provide periods of 0 g and 1.8 g.

2. Subjects experience sensorimotor disruption when initially exposed to parabolic flight, specifically in the pitch vestibuloocular reflex and torsional alignment.

3. Over the course of three days in parabolic flight, responses became appropriate in 0 g, 1 g and 1.8 g.

4. Responses in 1 g were not affected by adaptation in 0 g and 1.8 g, suggesting context-specific adaptation (rather than generalized sensory rearrangement)

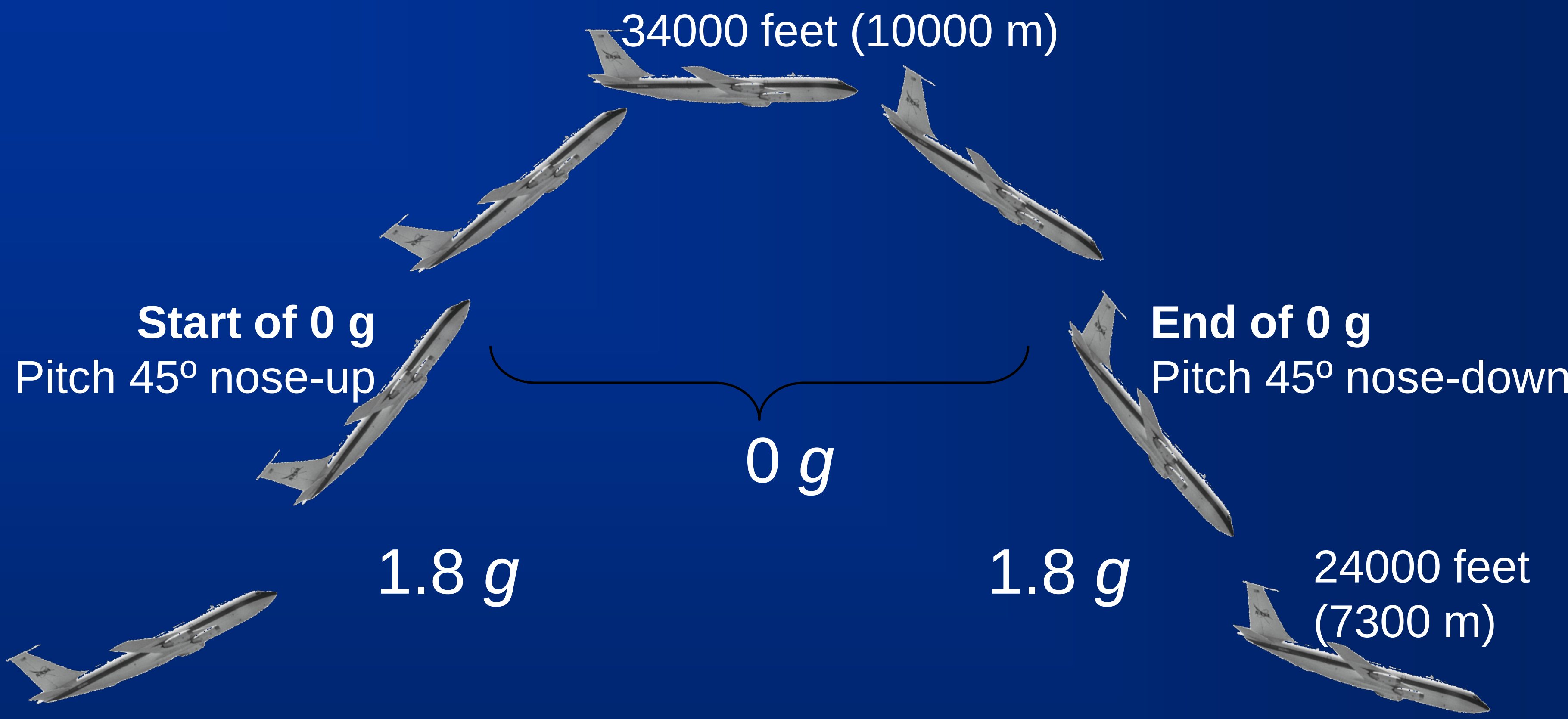
Outline

- Background: Parabolic flight
- Background: Science
- Methods: Recording eye position
- Results
- Conclusions

Background
Parabolic Flight

Mercury astronauts training aboard a C-131B (1959)

- Play movie: C:\Faisal\kc-135\Skew\KC135_March2002_Day3_MarkFaisal.avi
- Play movie: C:\Faisal\kc-135\Pictures\Aug2006\walkingupsidedown.mov



g = *gia* = gravitoinertial acceleration ⇒ the occupants' <u>perceptions</u> of gravity

- Play movie: c:\Faisal\kc-135\Pictures\Apr2006\HPIM2161.MPG

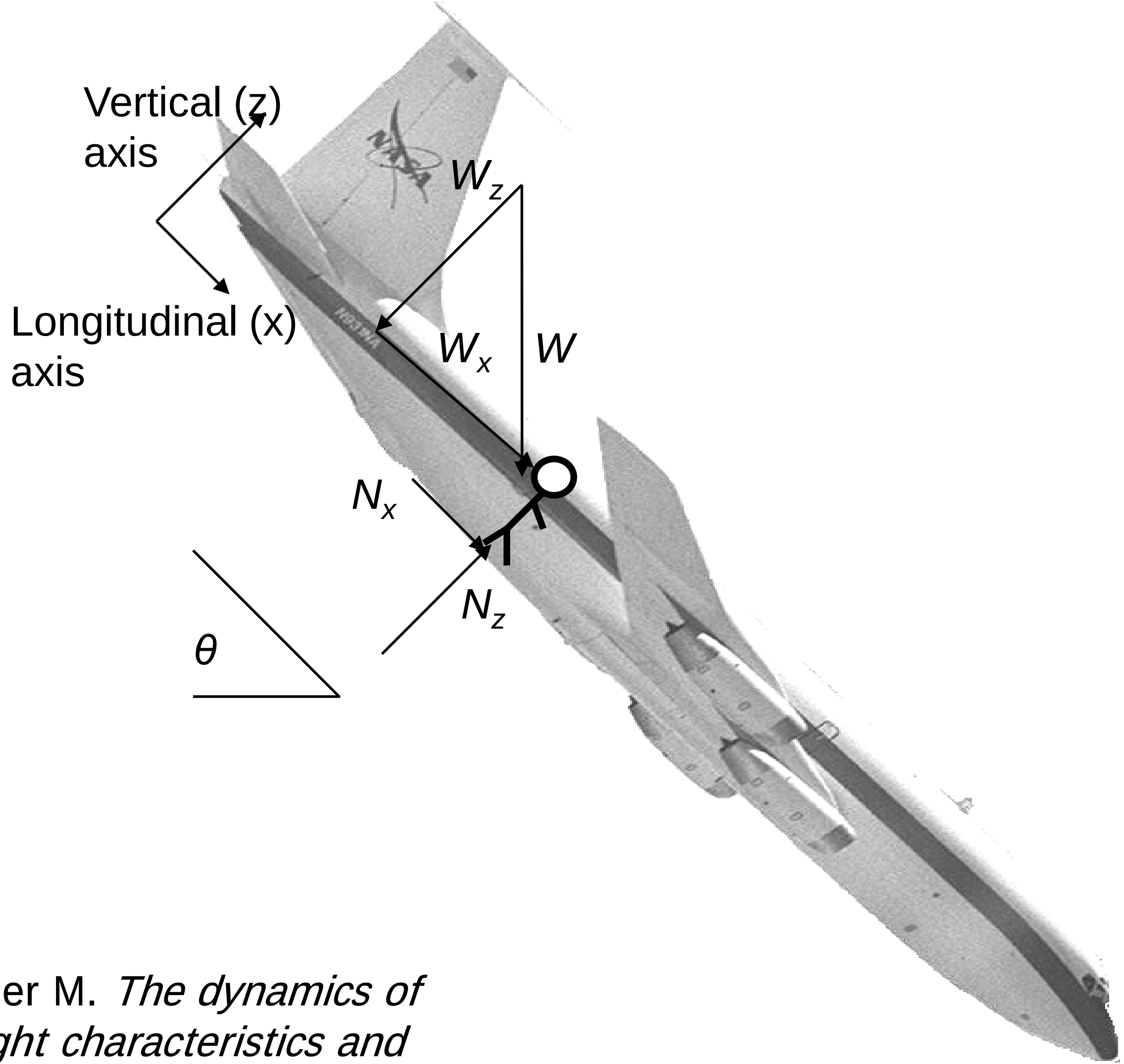
It is not zero gravity!

- In parabolic flight, the plane accelerates downwards to match gravity, so the net force is zero.
- Even in orbit, there is still gravity (~9.37 m/s^2 at 300 km)

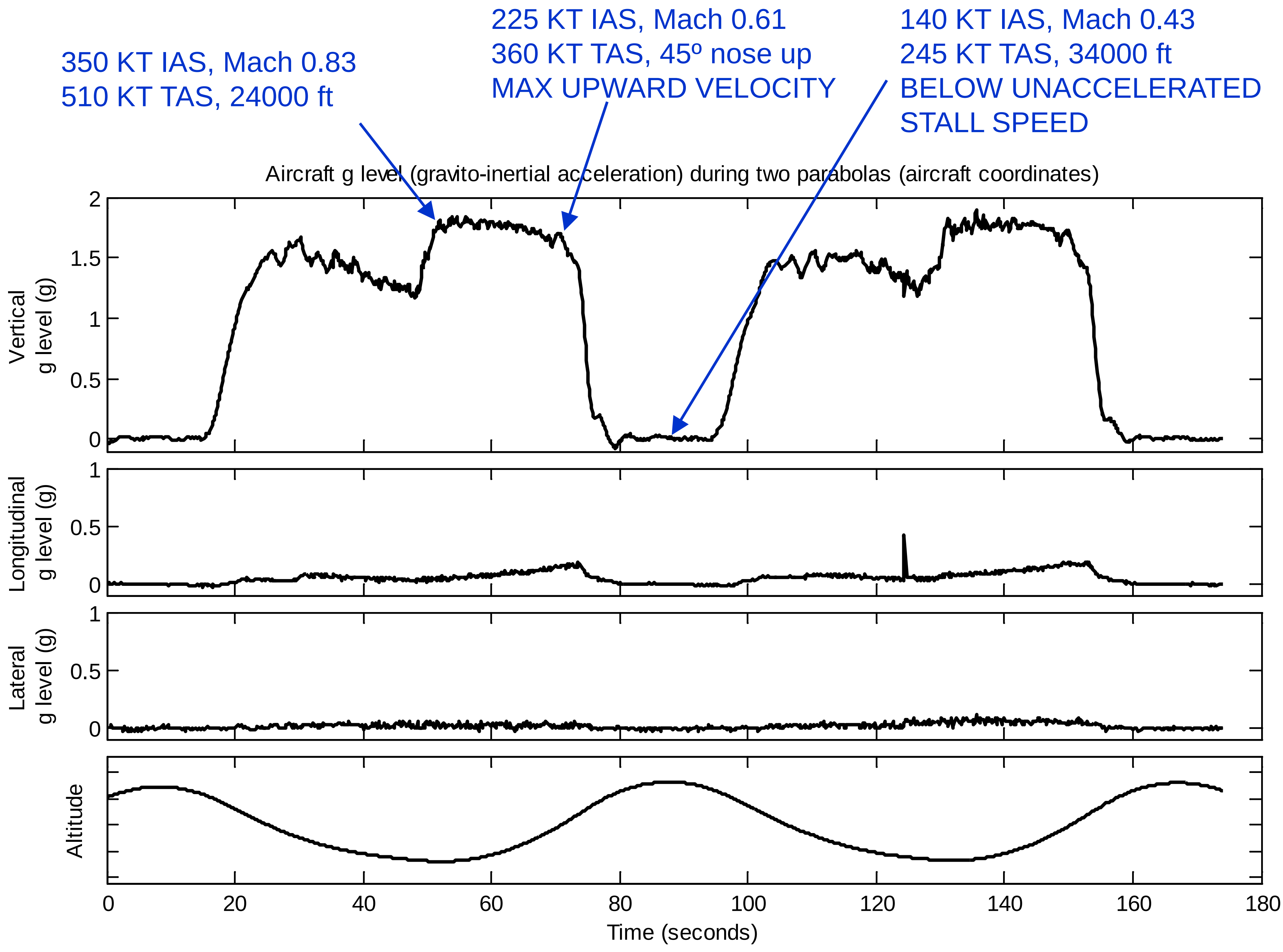
Preferred terms ⟷ *Less correct*

freefall weightlessness microgravity zero gravity
zero g
gravitoinertial acceleration (gia)

Why doesn't everybody fall to the front of the plane?



Karmali F, Shelhamer M. *The dynamics of parabolic flight: flight characteristics and passenger percepts.* Acta Astronautica (In press)


350 KT IAS, Mach 0.83
510 KT TAS, 24000 ft
225 KT IAS, Mach 0.61
360 KT TAS, 45º nose up
MAX UPWARD VELOCITY
140 KT IAS, Mach 0.43
245 KT TAS, 34000 ft
BELOW UNACCELERATED
STALL SPEED
Aircraft g level (gravito-inertial acceleration) during two parabolas (aircraft coordinates)
Vertical g level (g)
Longitudinal g level (g)
Lateral g level (g)
Altitude
0
0.5
1
1.5
2
0
20
40
60
80
100
120
140
160
180
Time (seconds)

Rotational dynamics

- The aircraft is rotating through 90º every 30 seconds

Angular velocity of 3 º/s	➔	Centripetal acceleration of 0.006 g
Angular acceleration of 2 $º/s^2$ during transitions between 0 g and 1.8 g	➔	Tangential acceleration of 0.07 g

- Our paper claims these are “barely at the threshold of detection” of the semicircular canals!

Karmali F, Shelhamer M. *The dynamics of parabolic flight: flight characteristics and passenger percepts.* Acta Astronautica (In press)

Otolith stimulation

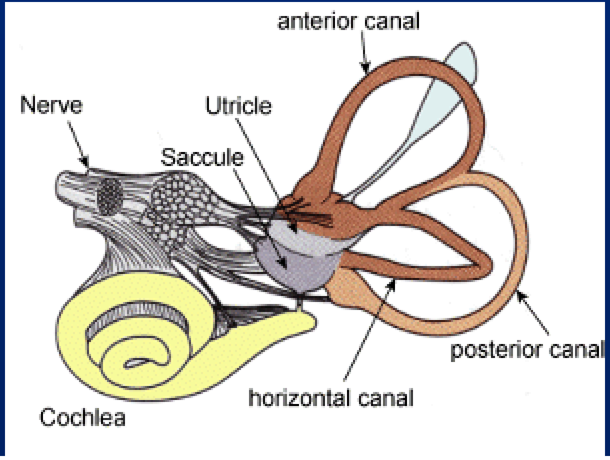
Why they call it the “Vomit Comet”

- Approximately 40-60% of participants get sick on their first flight. The next day, <u>most are fine</u>.
- A sensorimotor rearrangement has occurred. This learning is retained for months.
- We want to improve our understanding of these adaptive processes.
- Studied a range of sensorimotor responses at different neural levels: brainstem through to perceptual
  - based on design MVL Spacelab experiments

Background

Vestibular-Ocular Reflexes

- **Otolith organs** measure linear acceleration and gravity (contains **utricle** and **saccule)**
- **Semicircular canals (SCC)** measure angular velocity



- Eye movements opposite of head movements
- **Conjugate:** eyes move together
- **Disconjugate**: difference between left and right eyes

VOR gain=Eye velocity / head velocity

Eye movements and otolith organs

- Eye misalignments occur in parabolic flight and whole-body pitch rotation – otolith implicated (Markham, Diamond, Karmali)
- Ocular counterroll is reduced after space flight (Clarke 2000, Moore 2003, Vogel 1986).
- Pitch VOR still exists when canals deactivated (Angelaki)
- Otolith-dependent misalignments can be adapted with static head positioning using a visual-vestibular mismatch (Schor)

Hypotheses

1. **Context-specific adaptation**: learning a set of specific responses that is calibrated for each g level.
   - Example: initially inappropriate otolith-driven responses, which eventually become appropriate (correctly calibrated) in each g level.

2. **Generalized adaptation**: learning a set of general responses, each of which is simultaneously appropriate for multiple g levels.
   - Example: gradual decrease in otolith-driven responses, reflecting overall lack of reliability of otolith information as g level varies.

Methods

Experimental design

- Three consecutive days of flying per subject
- Responses tested:
  - Pre-parabolas
  - Early
  - Late
  - Post-parabolas
- 14 subjects: 5 experienced, 6 naïve, 3 pilots
- Measurements:
  - torsional alignment
  - ocular counterroll
  - vertical alignment
  - pitch VOR gain – active & passive
  - Also tried linear VOR, SVV, SPV
- No medication for motion sickness

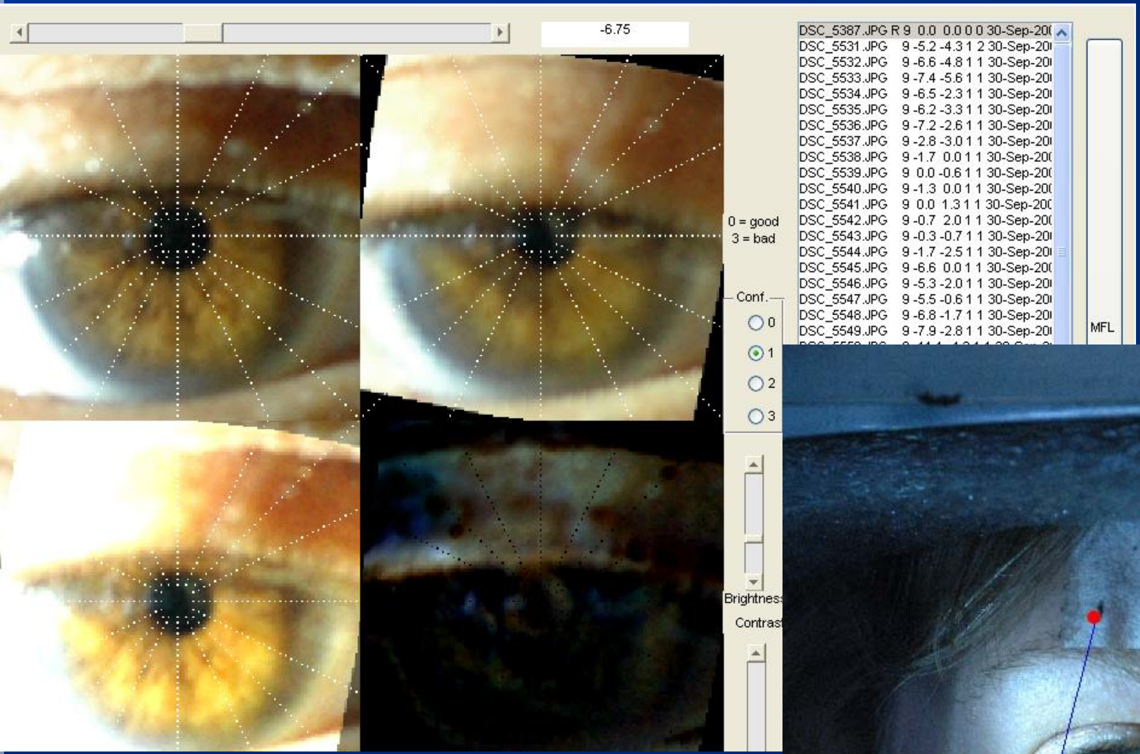
Experimental design

Day 1	Day 2	Day 3
Pre-parabolas	Pre-parabolas	Pre-parabolas
Early (first 10 parabolas)	Early (first 10 parabolas)	Early (first 10 parabolas)
Late (last 10 parabolas)	Late (last 10 parabolas)	Late (last 10 parabolas)
Post-parabolas	Post-parabolas	Post-parabolas

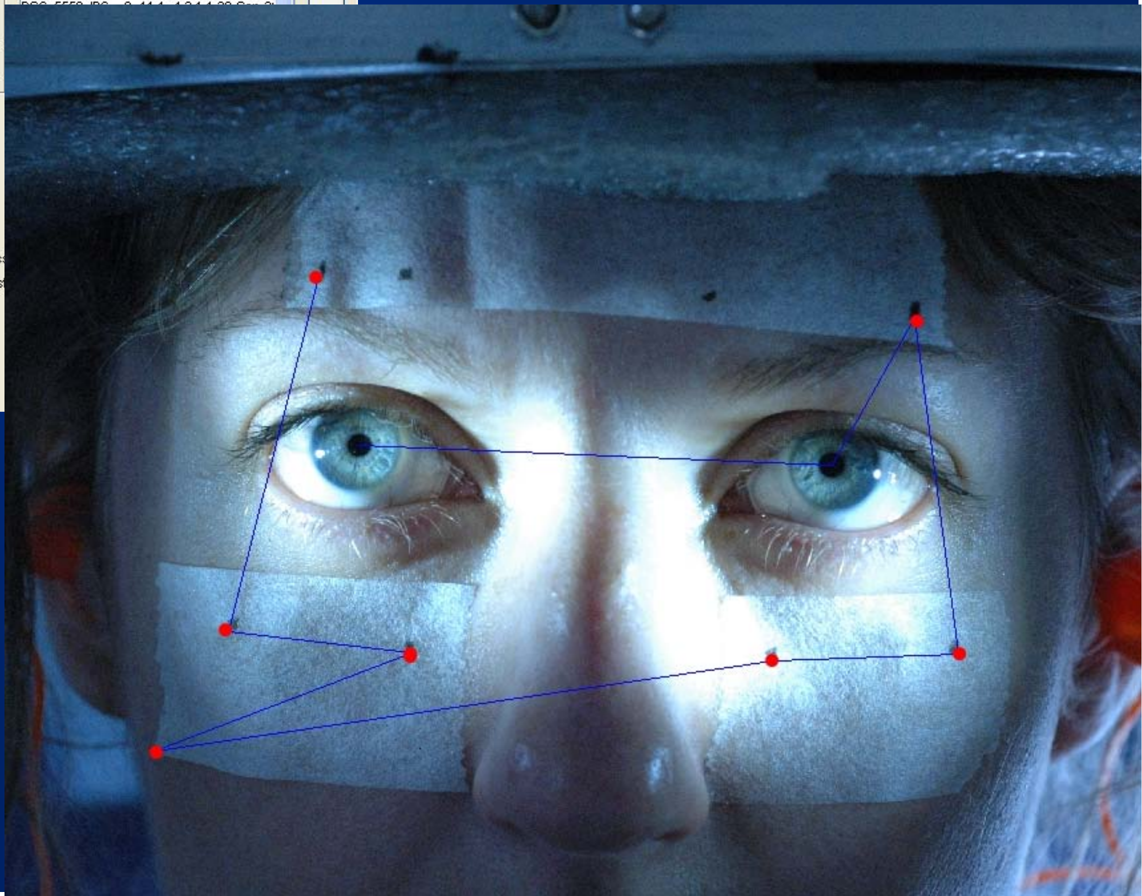
Measuring pitch VOR gain

- Active sine-like head movements
  - 0.3-1.6 Hz. Results based on 0.6-1.3 Hz
  - 20-30º
  - 40-90º/sec
- Fixating stationary point in the light.
- Eye movements were recorded using a head-mounted video system (Chronos).
- Gain computed by least-squares fitting of eye velocity to head velocity, for each cycle of motion.

Measuring static eye position



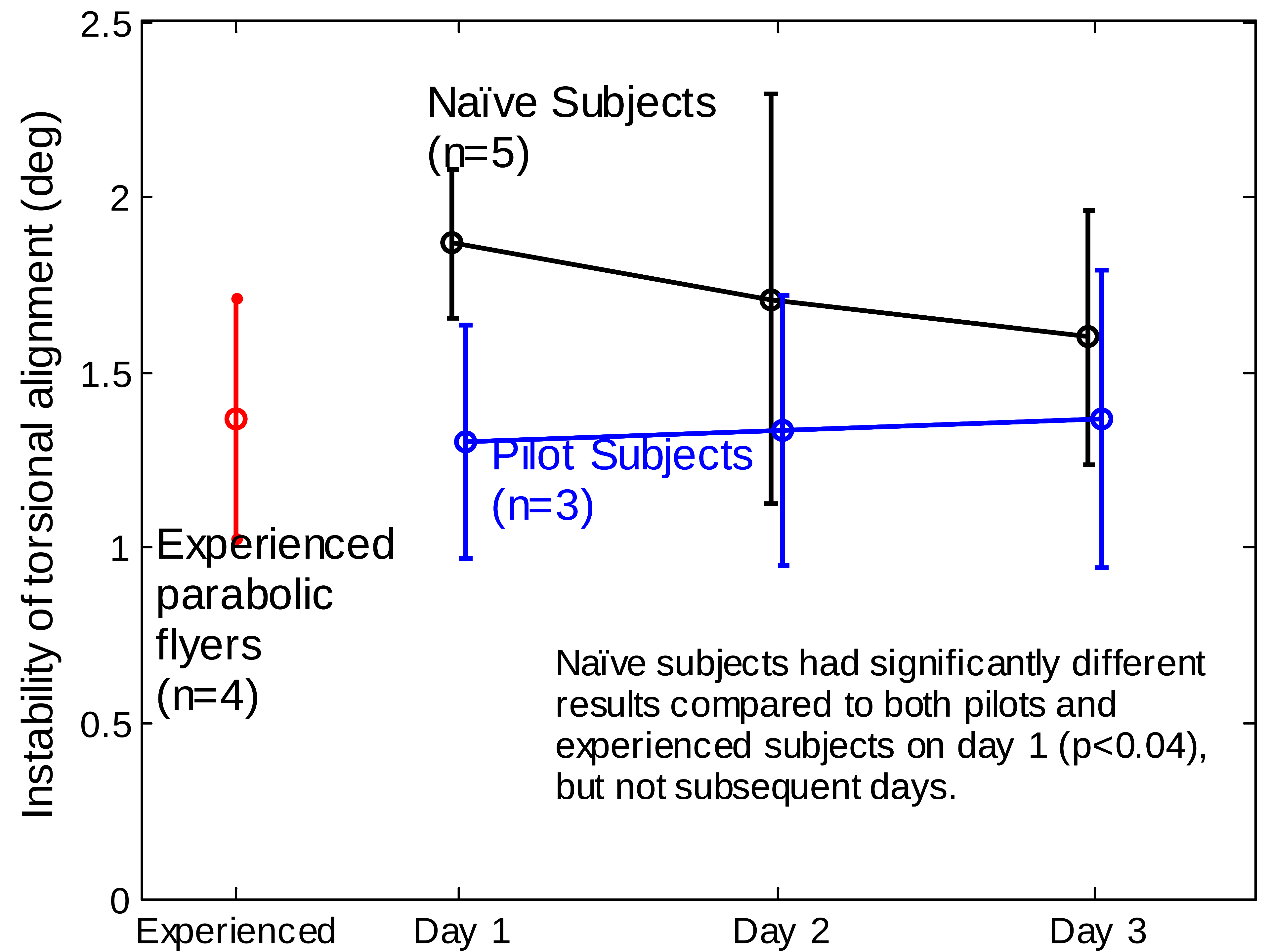
- OCR
- Torsional alignment
- Vertical alignment



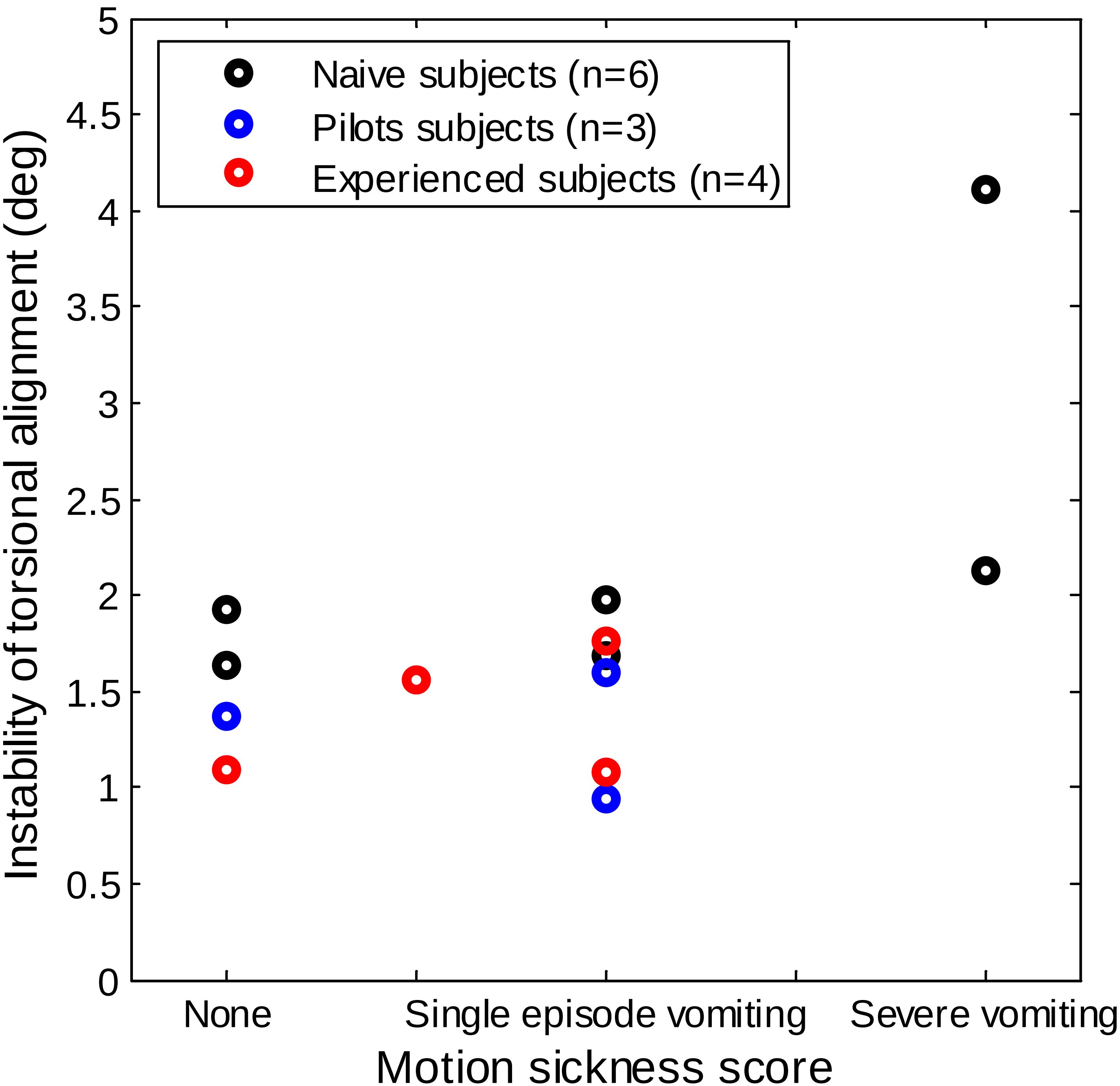
- Nikon D70 digital camera
- Subjects' head upright/ tilted

Results

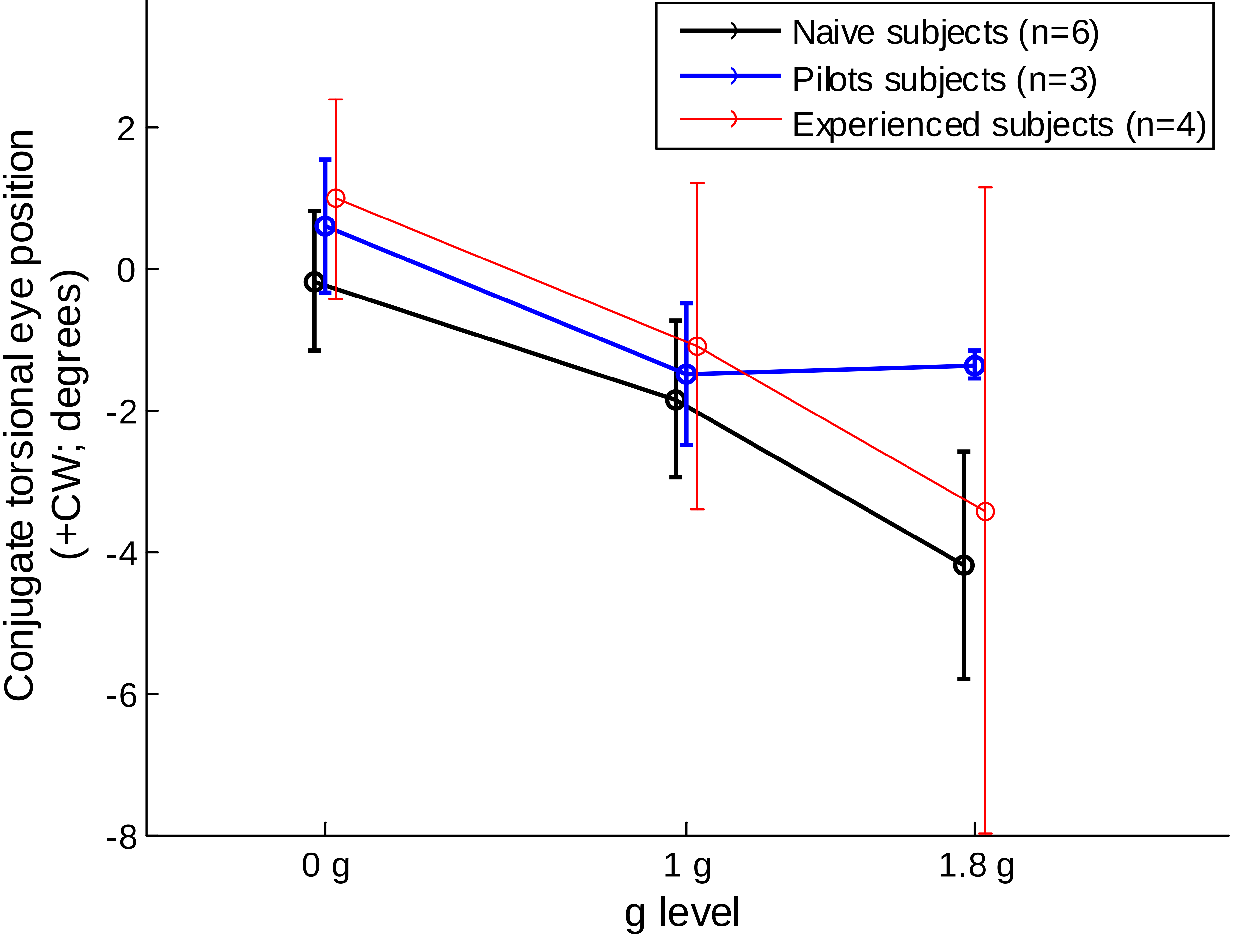
- Torsional alignment instability
- Ocular counterroll (response to head tilt)
- Active pitch VOR



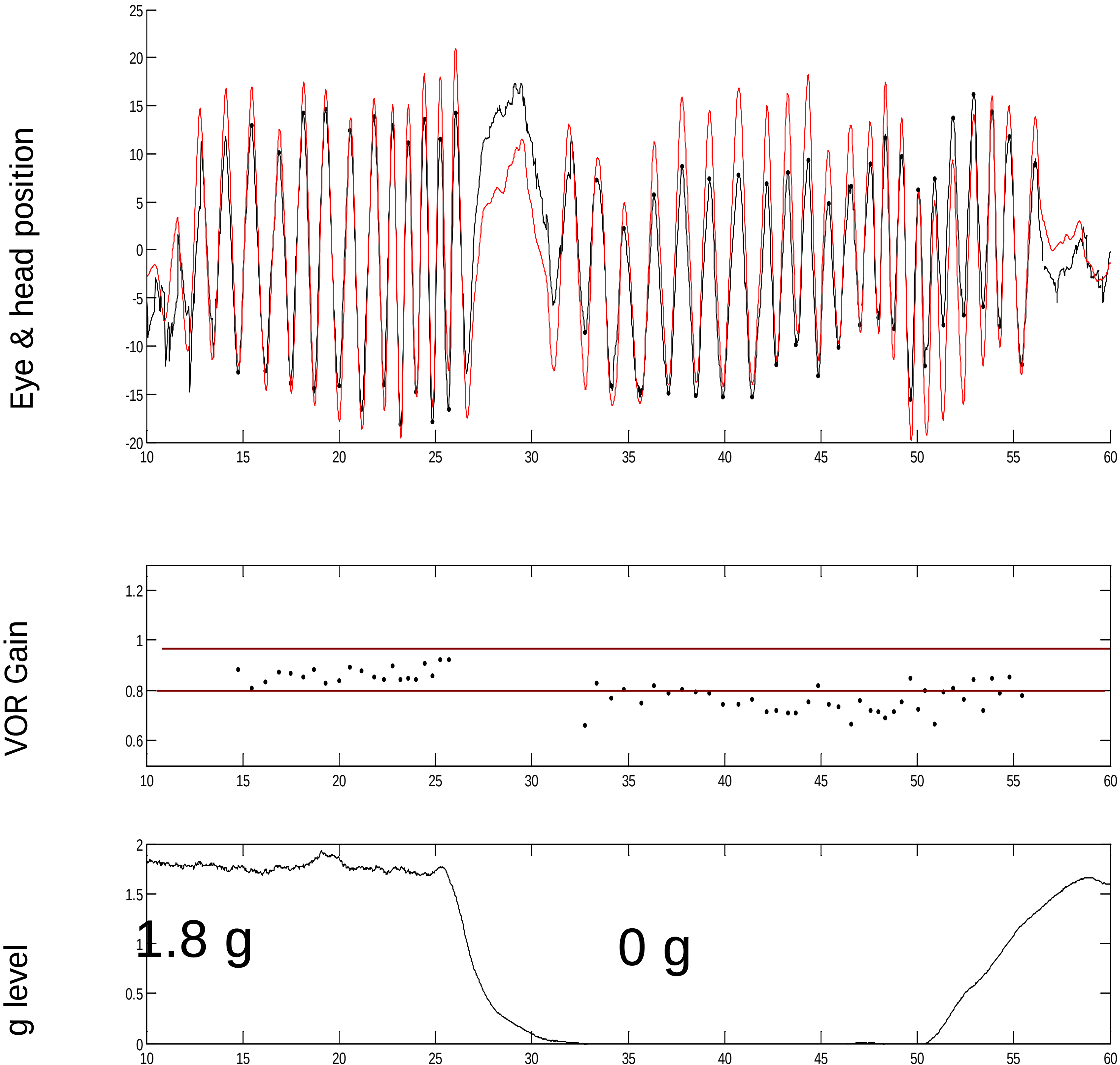
Instability of torsional alignment (deg)
0
0.5
1
1.5
2
2.5
Experienced
Day 1
Day 2
Day 3
Naïve Subjects
(n=5)
Pilot Subjects
(n=3)
Experienced
parabolic
flyers
(n=4)
Naïve subjects had significantly different
results compared to both pilots and
experienced subjects on day 1 (p<0.04),
but not subsequent days.

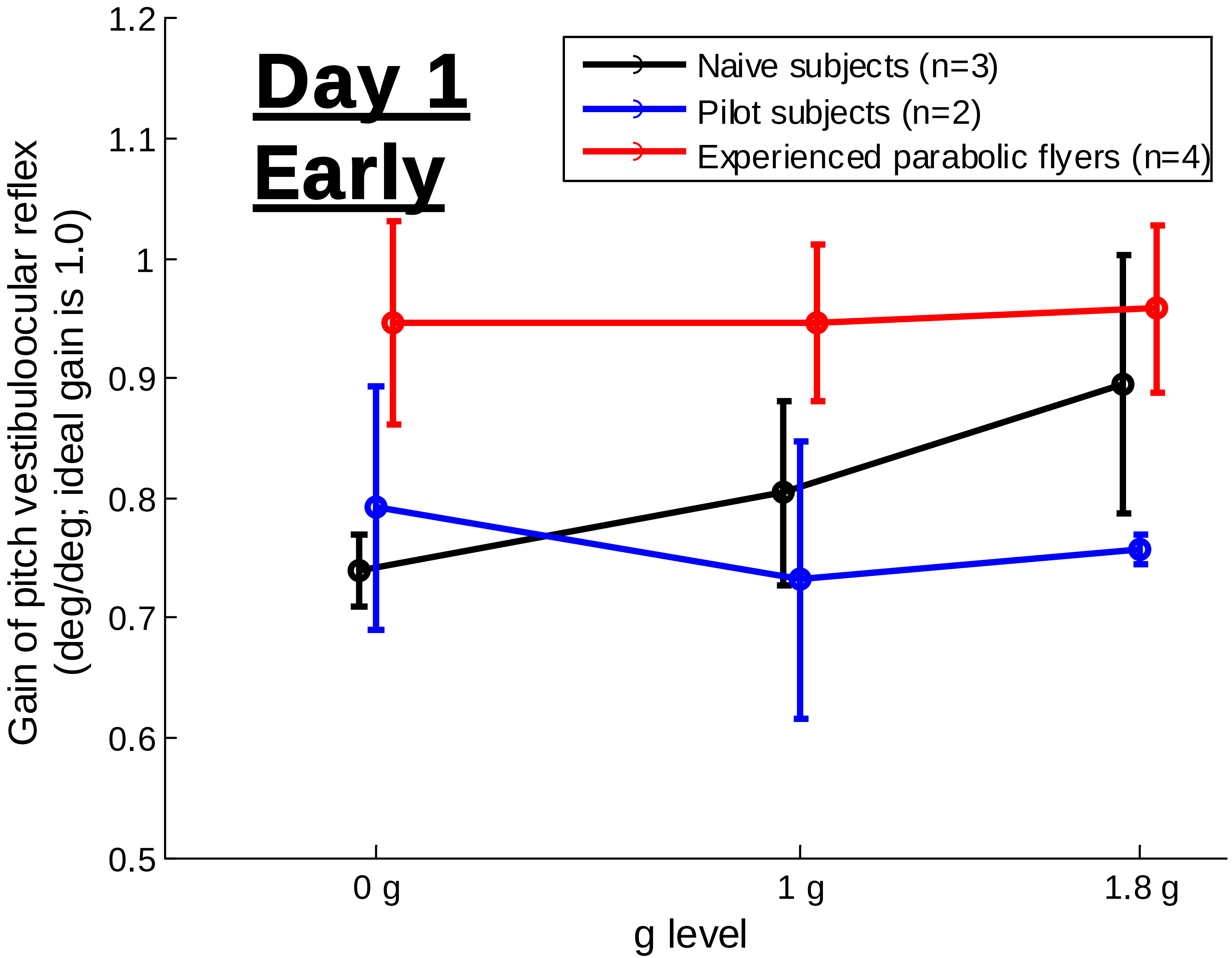


Naive subjects (n=6)
Pilots subjects (n=3)
Experienced subjects (n=4)
Instability of torsional alignment (deg)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
None
Single episode vomiting
Severe vomiting
Motion sickness score

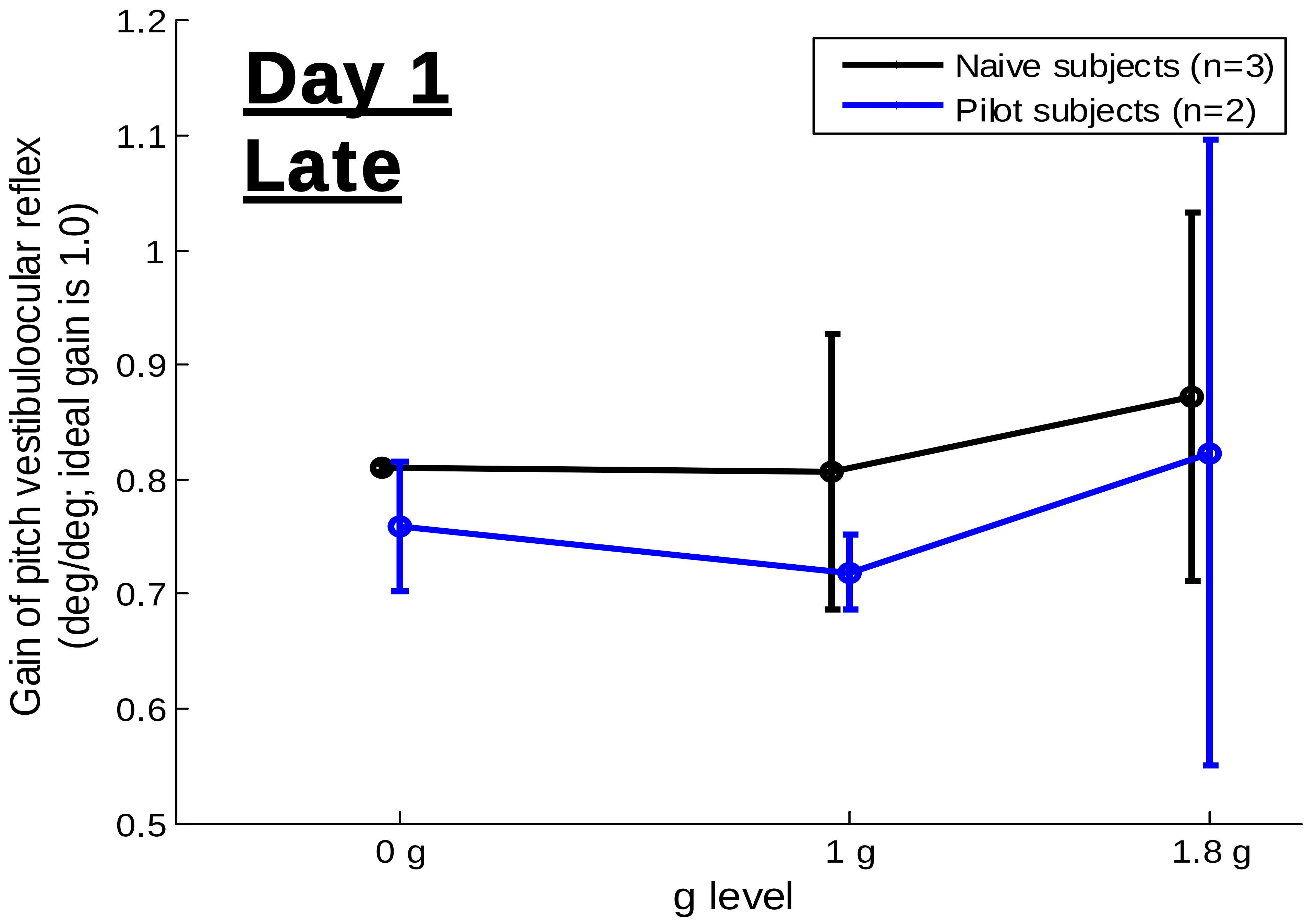


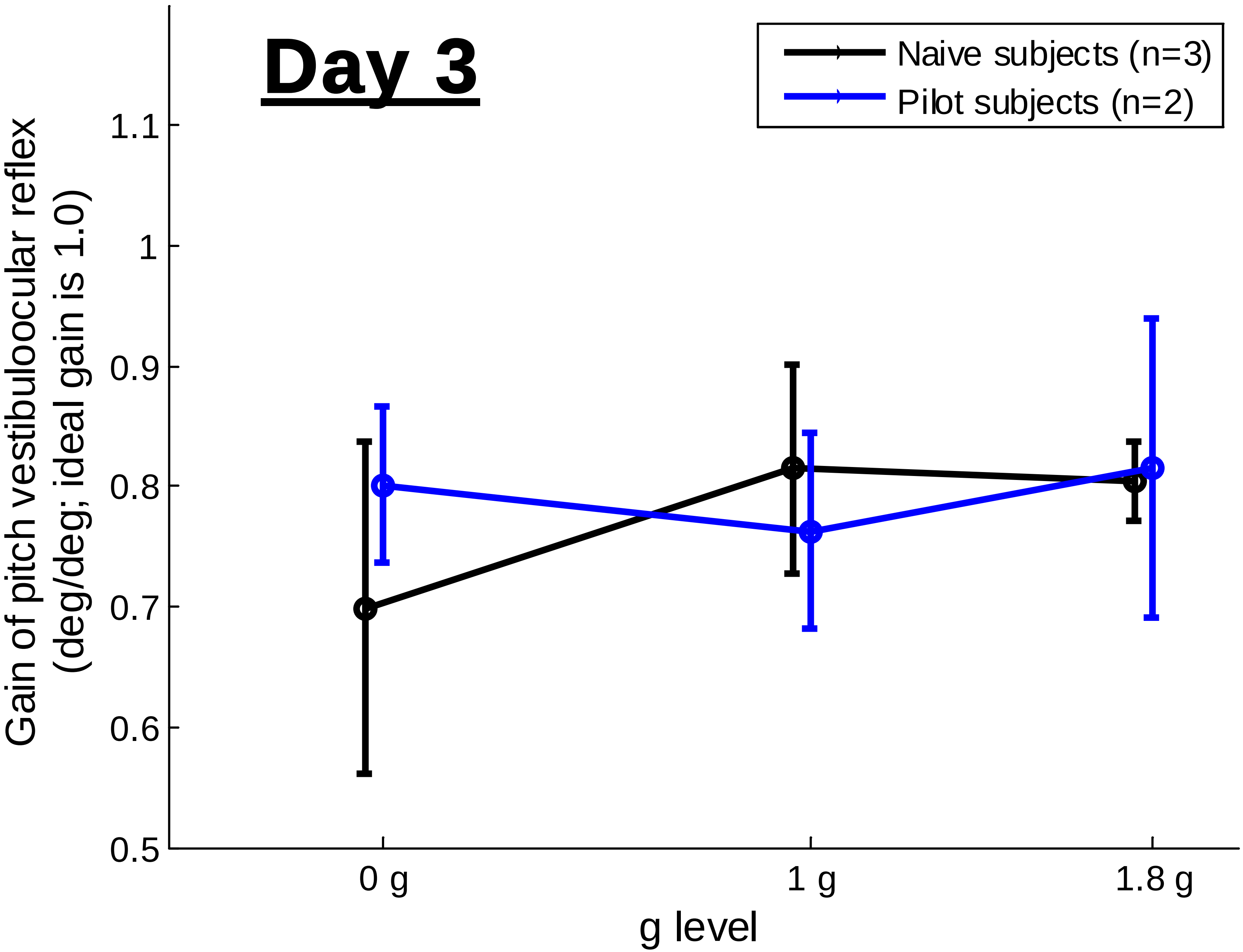
Naive subjects (n=6)
Pilots subjects (n=3)
Experienced subjects (n=4)
Conjugate torsional eye position
(+CW; degrees)
2
0
-2
-4
-6
-8
0 g
1 g
1.8 g
g level


Eye & head position
VOR Gain
g level
1.8 g
0 g



Day 1
Early
Naive subjects (n=3)
Pilot subjects (n=2)
Experienced parabolic flyers (n=4)
Gain of pitch vestibuloocular reflex
(deg/deg; ideal gain is 1.0)
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0 g
1 g
1.8 g
g level


Day 1
Late
Naive subjects (n=3)
Pilot subjects (n=2)
Gain of pitch vestibuloocular reflex
(deg/deg; ideal gain is 1.0)
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0 g
1 g
1.8 g
g level


Day 3
Naive subjects (n=3)
Pilot subjects (n=2)
Gain of pitch vestibuloocular reflex
(deg/deg; ideal gain is 1.0)
1.1
1
0.9
0.8
0.7
0.6
0.5
0 g
1 g
1.8 g
g level

Conclusions

- **All responses showed a g-level dependence early in flight, which decreased with experience.**

- **Rate of adaptation varied between reflexes:** torsional disconjugacy is fastest, then pitch VOR, then ocular counterroll.
  - **Torsional alignment instability rapidly reduced upon exposure to parabolic flight, and adaptation is retained between flights.** The relatively rapid adaptation may be because errors in torsional alignment have greater functional offsets than conjugate changes in torsional eye position and changes in the pitch VOR.
  - **Pitch VOR gain initially dropped in 0 g and increased in 1.8 g**, consistent with an otolith contribution. Difference between g levels decreased with experience and eventually disappeared, showing that the different otolith contributions in the different g levels are correctly processed after adaptation.
  - **Ocular counterroll is initially larger in 1.8 g and smaller in 0 g**. Differences between g levels do not change within 3 days, although pilots show more appropriate responses in 1 g. An explanation for this slow adaptation may be that a well-tuned OCR gain is not critical; it is not compensatory in normal circumstances.
  - **None of the mechanisms show a change in response to 1 g after exposure to parabolic flight.** This suggests that adaptation is context specific.

- **Upon adaptation, torsion, torsional alignment and pitch VOR are correctly calibrated in each g level, supporting the hypothesis of a context-specific adaptation of each response.**

Acknowledgements

- Advisor: Dr. Mark Shelhamer
- Undergraduate researchers: Ondrej Juhasz, Michelle Zwernemann, Anton Aboukhalil
- Technical assistance: Adrian Lasker, Dale Roberts, Dr. Andy Clarke
- NASA staff: Noel Skinner, John Yaniec
- Scientific advise: Dr. Mark Walker, Dr. Howard Ying, SPH Biostats Clinic
- Moral support: Zee lab, friends & family
- Funding: NSBRI, NIH, NSERC

- Compare t-test significance of day 1 vs day 3 naïve
- Change bar graphs to std err instead of std
- Review adapt. Spaceflight
- See MJS PPT
- Inc cool videos
- ~45 slides

- Otolith ambiguity – same sensor transduces tilt and translation of head
- Transduced signal during tilt differs dramatically in weightlessness / high g environments, and changes in otolith-dependent reflexes occur
- Designing a countermeasure to speed adaptation or pre-adapt reflexes could reduce adverse problems during space missions, return to Earth or visiting other celestial bodies
- Characterizing the adaptive characteristics of otolith-dependent reflexes and the relationship between adaptation of translation and tilt important for the design of countermeasures
- To learn more about these pathways, we studied the vestibulo-ocular reflex
- Specifically interested in the pitch VOR, because this is the most common type of head movement in which the otolith organs transduce a changing direction of gravity
- During pitch head movements, three (or more) sensory signals available: otolith-transduced head position; SCC-transduced head velocity; eye position
- Goals:
    - to adapt VOR and show that adaptation is otolith-organ dependent
    - Show that adaptation of VOR transfers from tilt to translation
    - Characterize how the brain processes otolith organ information using the characteristics of the transfer of adaptation
- With pitch head movements, during translation and tilt, the compensatory eye movement is vertical. Makes it impossible to distinguish adaptation that is dependent on eye- vs. head- motion-dependent adaptation. Using vertical eye misalignment allows dependency on velocity and position to be better discriminated.
- Methods
    - How to adapt VOR / eye misalignment?
- Results / Discussion
- Conclusions
    - The evidence that Cartesian components of the g vector are used as adaptive cues is important because it suggests that countermeasures on Earth can adapt some responses without changing the magnitude of the g vector. That means adaptation of otolith-dependent reflexes could occur in a 1 g field, which allows longer, cheaper adaptation sessions than jet or parabolic flight.

Transfer of oculomotor adaptation between otolith-dependent tilt and translation reflexes

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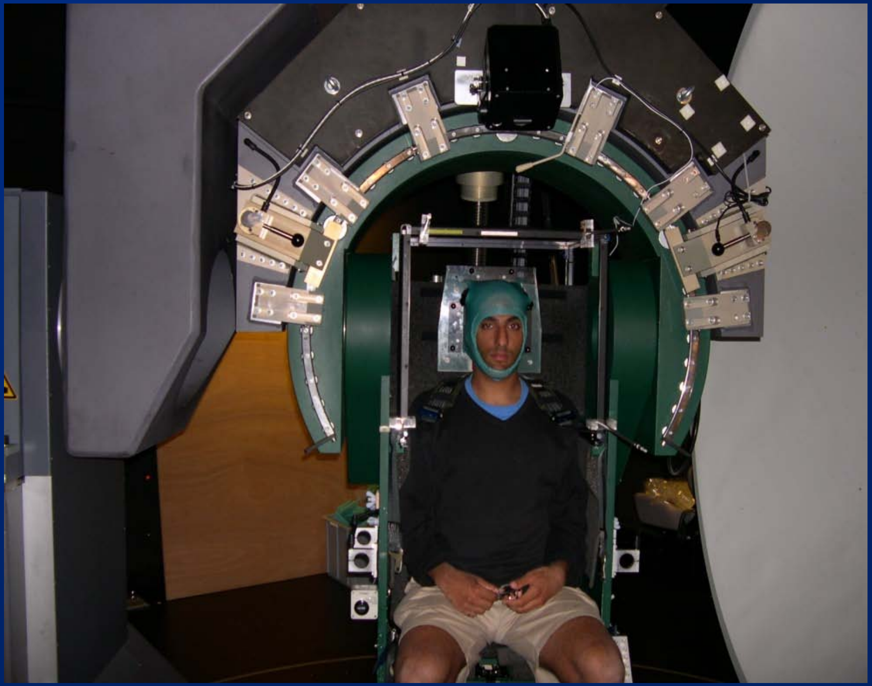


MVL, MIT
November 14, 2007

The bottom line…

1. A vertical misalignment between the eyes can be adapted that is dependent on otolith-transduced head tilt during pitch head rotation using a visual-vestibular mismatch

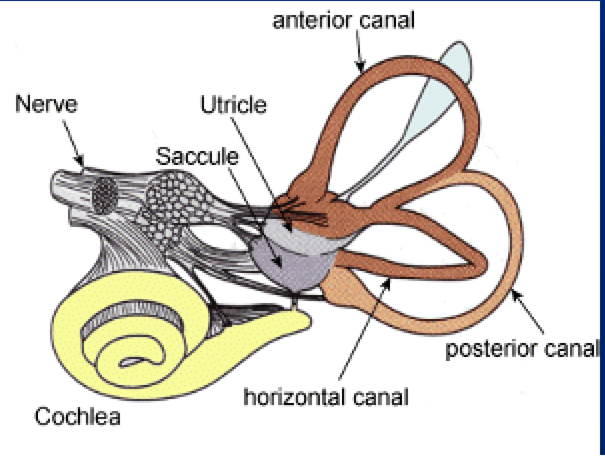
2. Modification of the response to otolith-transduced head tilt also modifies the response to vertical translation

3. Modeling shows that for adaptation, the brain processes the g vector as Cartesian components, rather than in polar coordinates

Background

Vestibular-Ocular Reflexes

- **Otolith organs** measure linear acceleration and gravity (contains **utricle** and **saccule)**
- **Semicircular canals (SCC)** measure angular velocity



- Eye movements opposite of head movements
- **Conjugate:** eyes move together
- **Disconjugate**: difference between left and right eyes

VOR gain=Eye velocity / head velocity

Eye movements and otolith organs

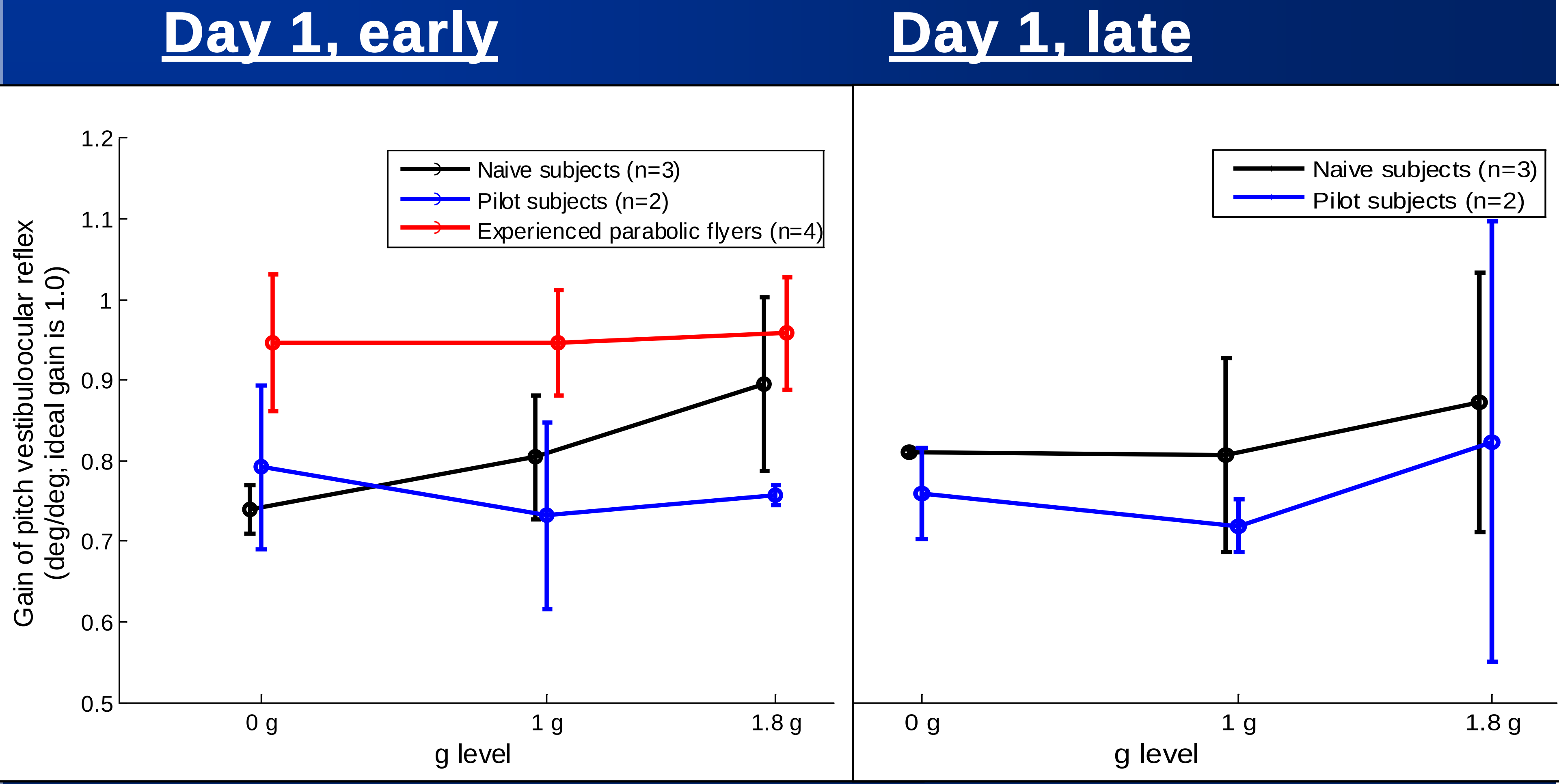
- Eye misalignments occur in parabolic flight and whole-body pitch rotation – otolith implicated (Markham, Diamond, Karmali)
- Amount of misalignment decreases with experience in parabolic flight – shows adaptation of pathway occurs
- Pitch VOR gain changes with g level – otolith implicated
- Pitch VOR still exists when canals deactivated (Angelaki)
- Otolith-dependent misalignments can be adapted with static head positioning using a visual-vestibular mismatch (Schor)

Previous studies of transfer between translation and rotation

- Yaw adaptation affects interaural translation response (Koizuka *et al.*)
- Interaural adaptation affects yaw response (Koizuka *et al.*)
- Yaw adaptation affects response to constant-velocity pitch rotation (Petropoulos, Wall III, Oman)

- These studies suggest adaptation of a pathway common to the SCC and otolith reflexes
- In contrast, we find adaptation specific to the otolith pathway

Pitch VOR gain is dependent on g level in parabolic flight



Experimental Design

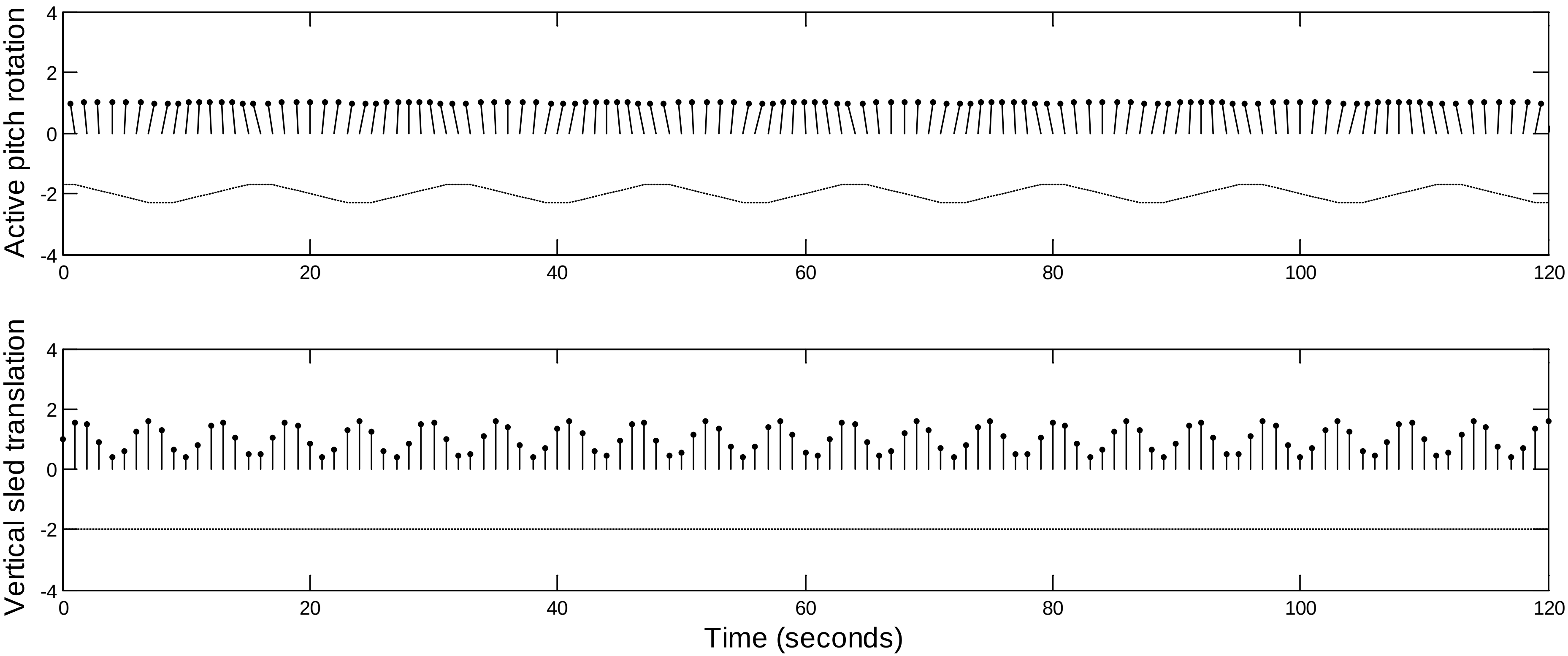
Aims

1. Show that a misalignment between the eyes can be adapted that it dependent on otolith-transduced tilt during dynamic pitch rotation using a visual-vestibular mismatch

2. Determine if modification of the response to otolith-transduced head tilt also modifies the response to vertical translation

3. Develop a model to understand how the brain processes otolith information during adaptation of otolith-ocular responses

Motion profiles



Sensory environment during motion profiles

	Motion profile	
Sensory receptor	*Active pitch rotation*	*Vertical translation*
Otolith organs	Changing orientation relative to gravity	Linear acceleration
Semicircular canals (SCC)	Yes	No
Orbital eye position	Yes	Yes
Collic (neck) reflex	Yes	No

Sensory environment during motion profiles

	Motion profile		
Sensory receptor	*Passive pitch rotation* (full body)	*Active pitch rotation*	*Vertical translation*
Otolith organs	Changing orientation relative to gravity	Changing orientation relative to gravity	Linear acceleration
Semicircular canals (SCC)	Only before vestibular time constant exceeded	Yes	No
Orbital eye position	Yes, due to counterpitch response	Yes	Yes
Collic (neck) reflex	No	Yes	No
Cognitive intent	No	Yes	No
Cognitive anticipation	Some situations	Yes	Yes

Study procedures

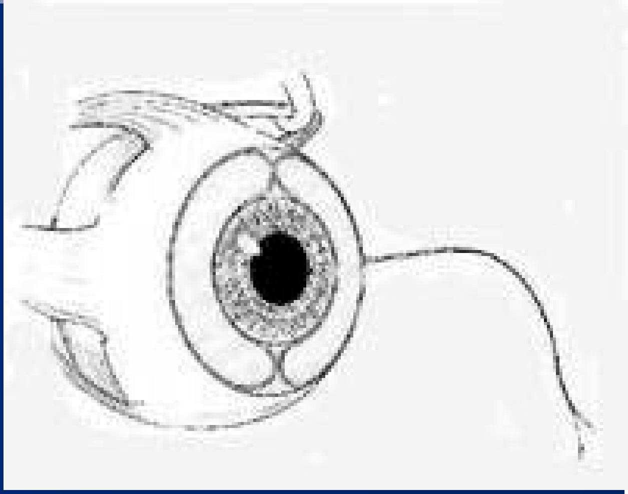
The *pitch plasticity study*

Pre-test Pitch (monocular targets) → **Adapt Pitch** (20 min) → **Post-test Pitch** (monocular targets)

The *vertical translate study*

Pre-test Vertical (monocular target) → **Pre-test Pitch** (monocular target) → **Adapt Pitch** (15 min) → **Post-test Pitch** (monocular target) → **Adapt Pitch** (5 min) → **Post-test vertical** (monocular target)

Scleral contact lens coils



- Coil frame in a cube that consists of three orthogonal magnetic fields oscillating at different frequencies
- Coil acts as antenna that picks up a linear combination of the three that depends on its orientation
- Accuracy <0.01º
- Wire is fragile, and often breaks
- Small coil frame used on vertical sled – data for pitch not usable during the *vertical translate study*

Generalized Estimating Equations

- *t*-test is often used to compare time-series data in two different conditions
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Pitch plasticity study

- Goal: understand the nature of central compensation
- Study the ability of the brain to learn an otolith organ-dependent misalignment during <u>dynamic</u> head movements
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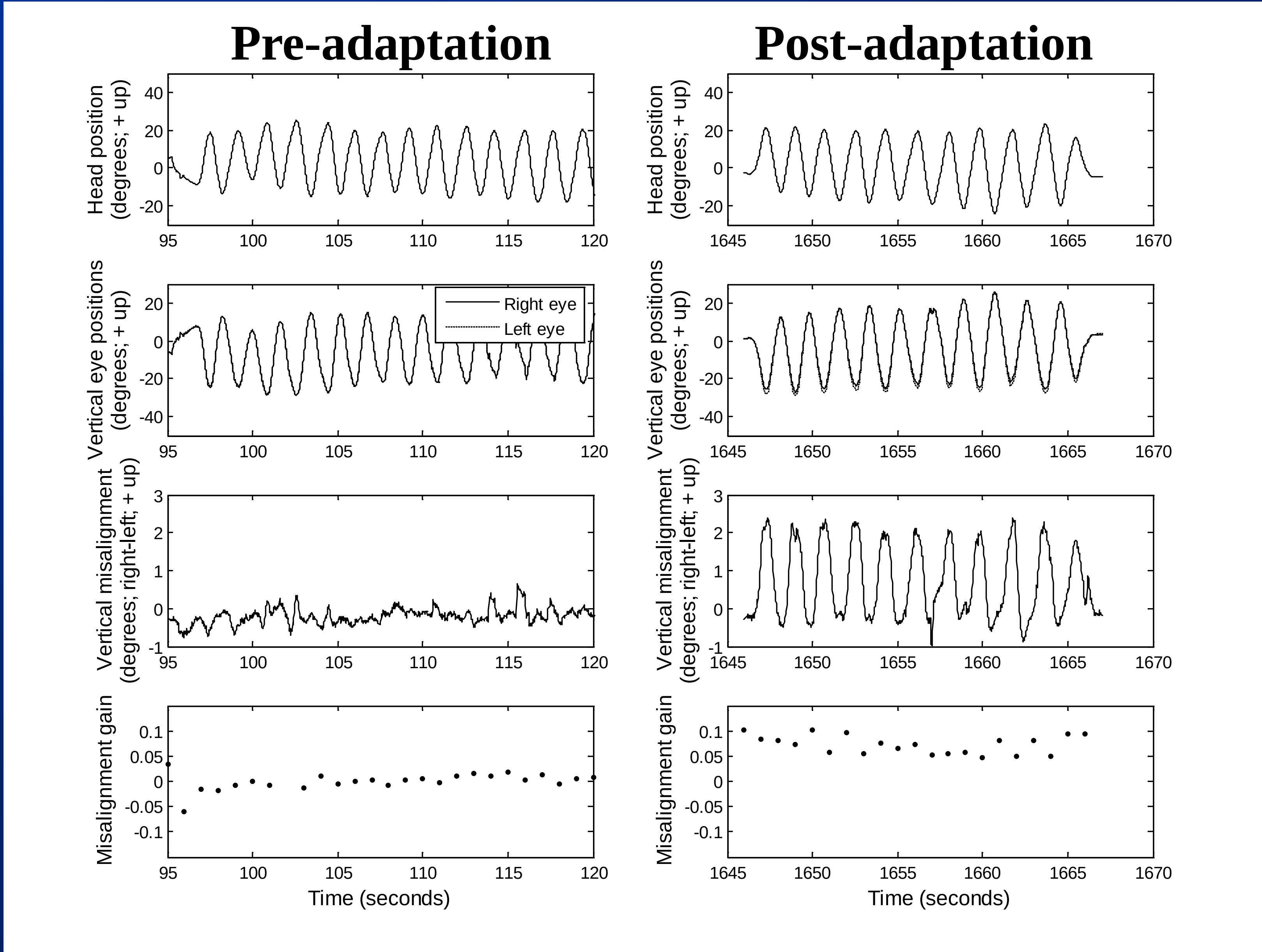
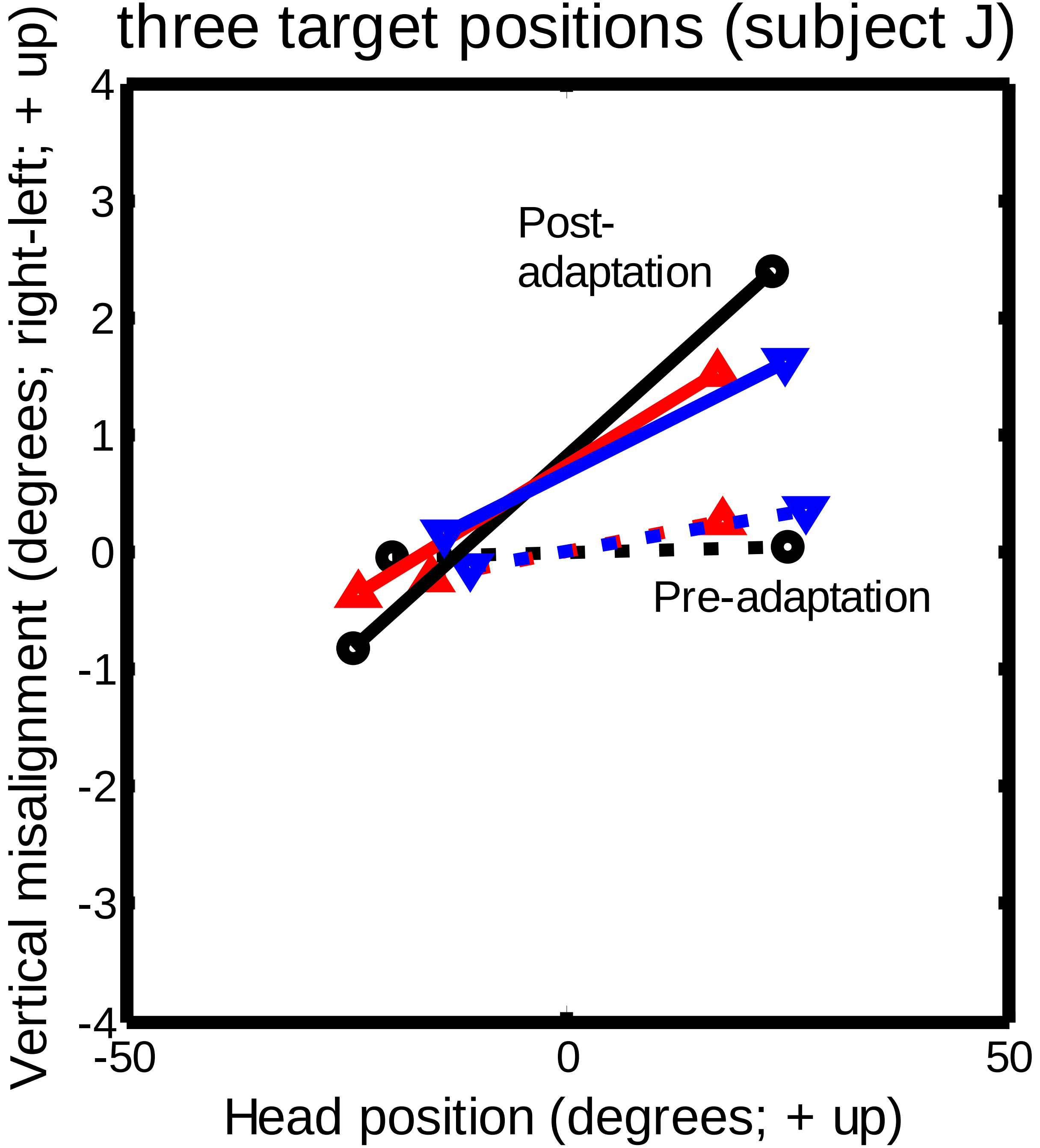
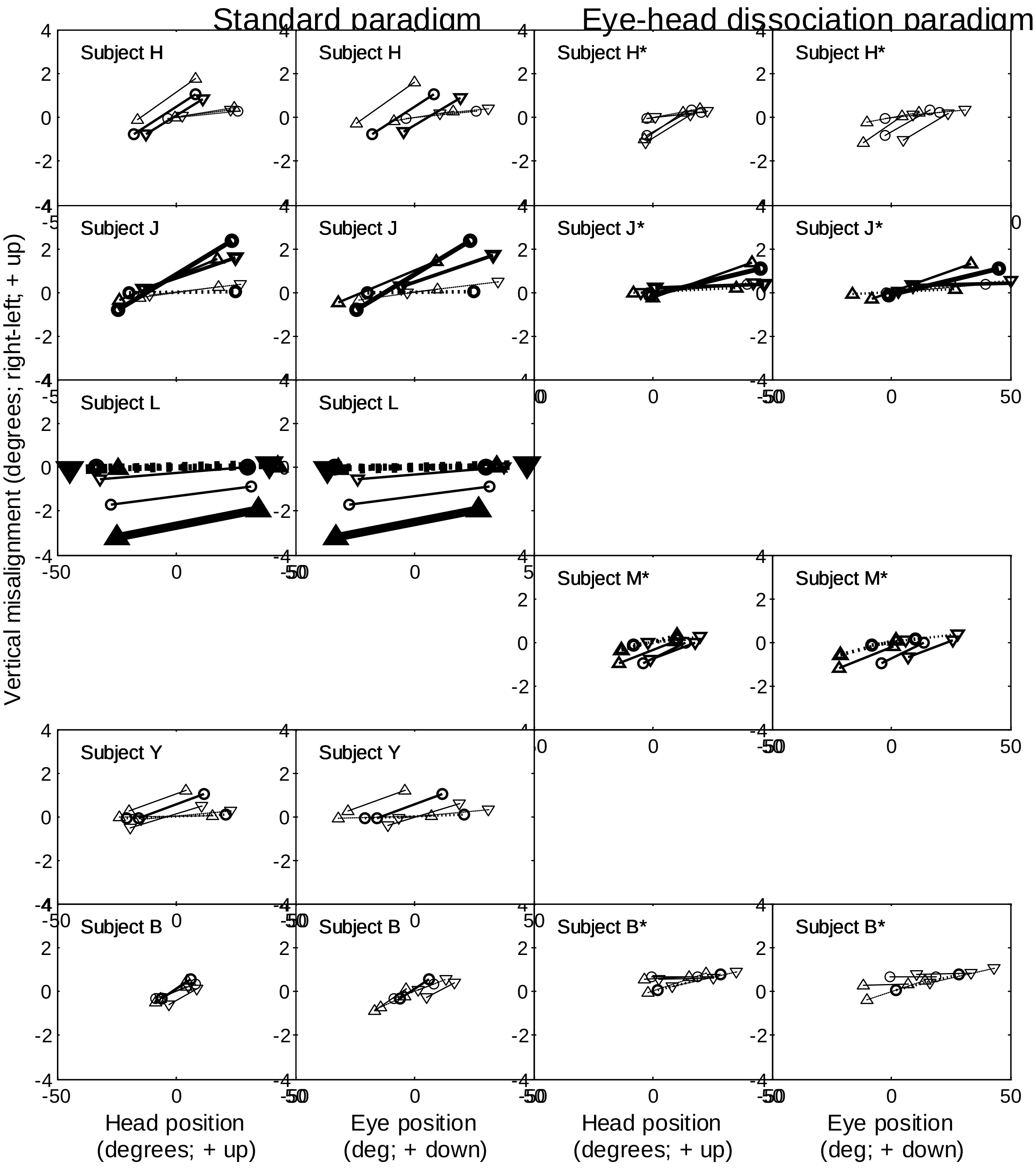
- The dots have a vertical disparity between left and right eyes
- *Regular* & *eye-head dissociation* paradigms

Pitch plasticity study

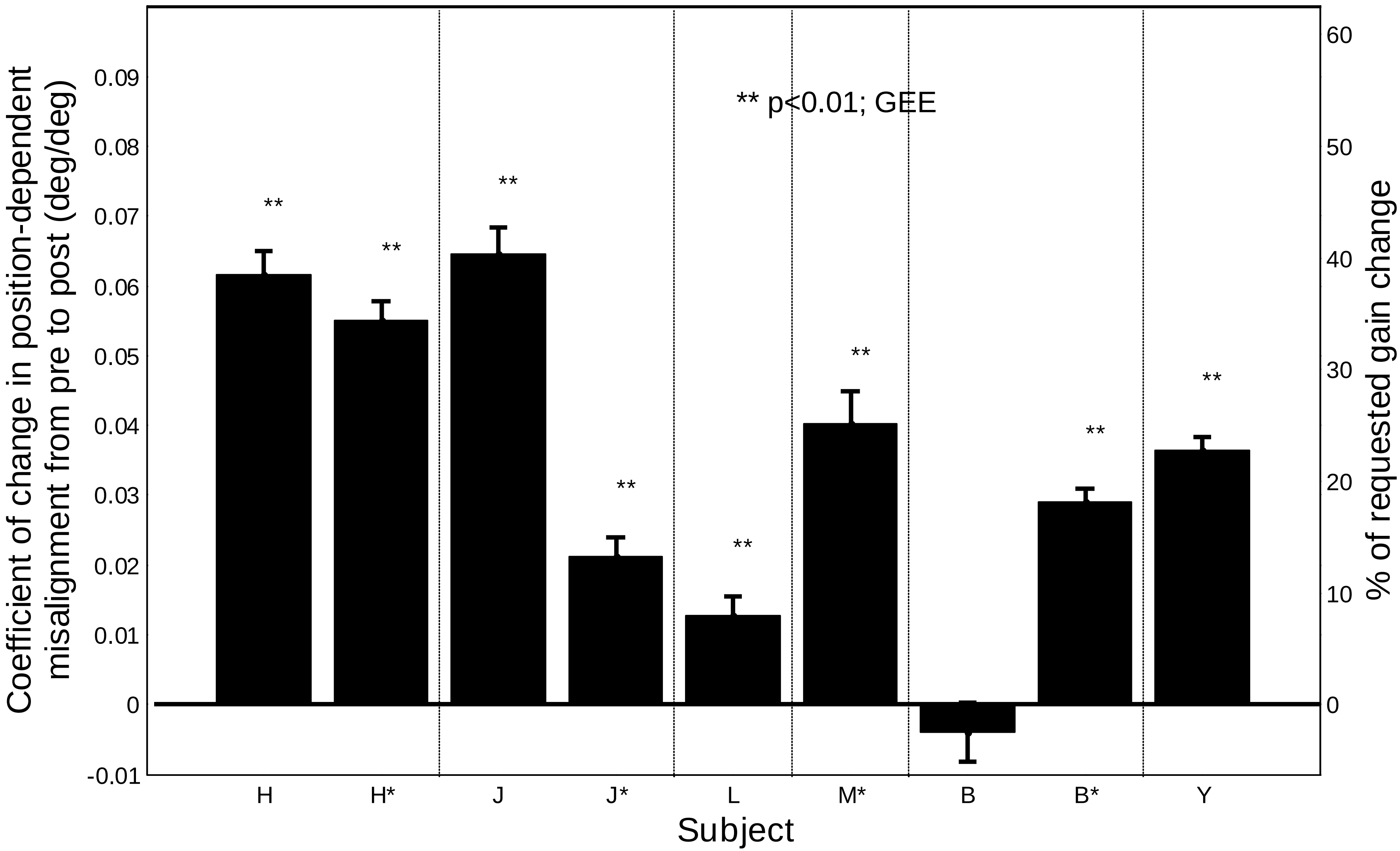


Misalignment vs. head position for three target positions (subject J)



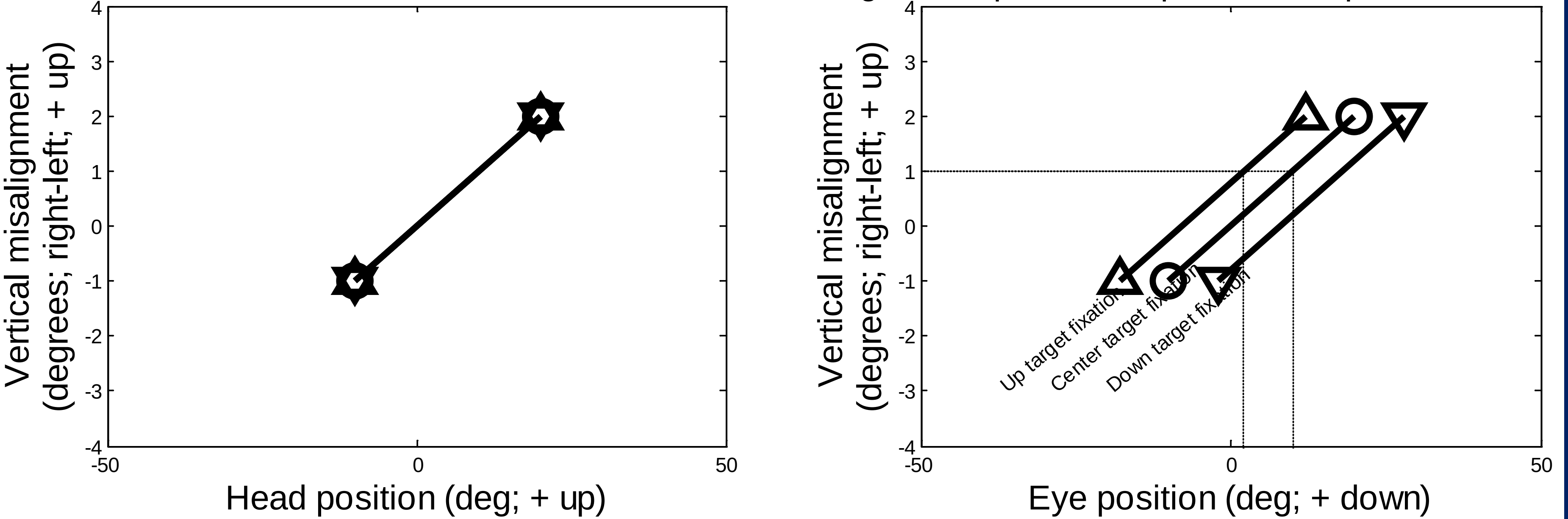

Standard paradigm
Eye-head dissociation paradigm
Subject H
Subject H*
Subject J
Subject J*
Subject L
Subject M*
Subject Y
Subject B
Subject B*
Vertical misalignment (degrees; right-left; + up)
Head position (degrees; + up)
Eye position (deg; + down)

Position-dependent misalignment increased in most experiments

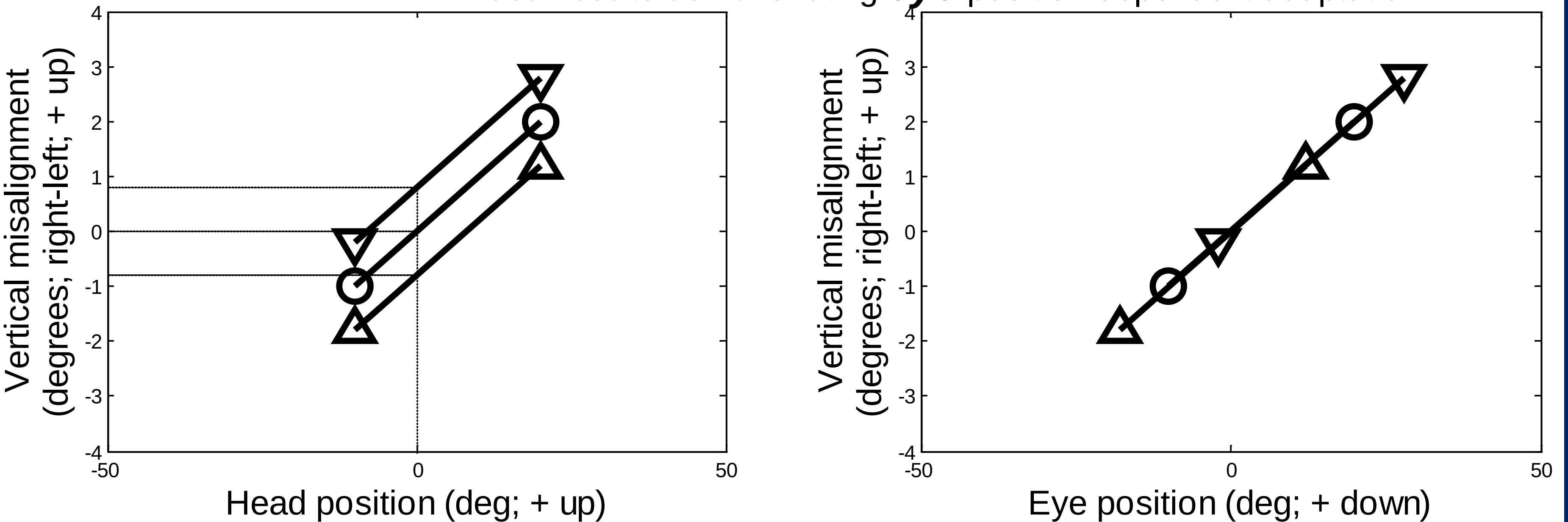


* *eye-head dissociation* paradigm

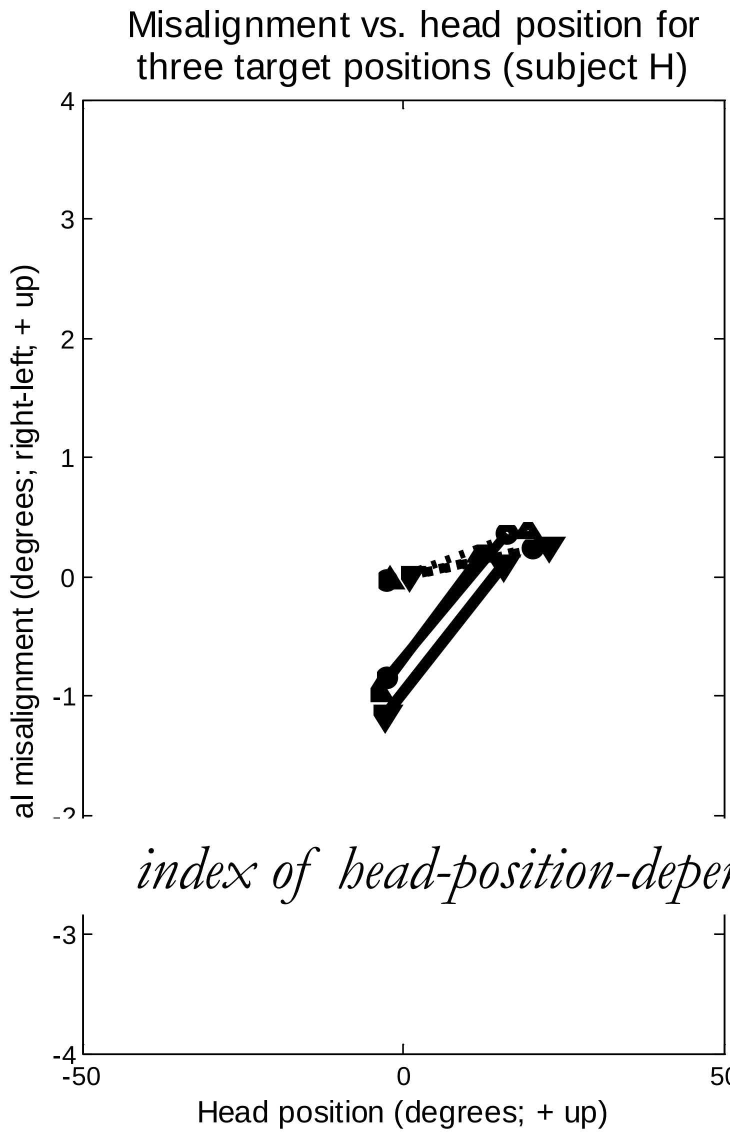
Ideal results demonstrating ***head*** position-dependent adaptation

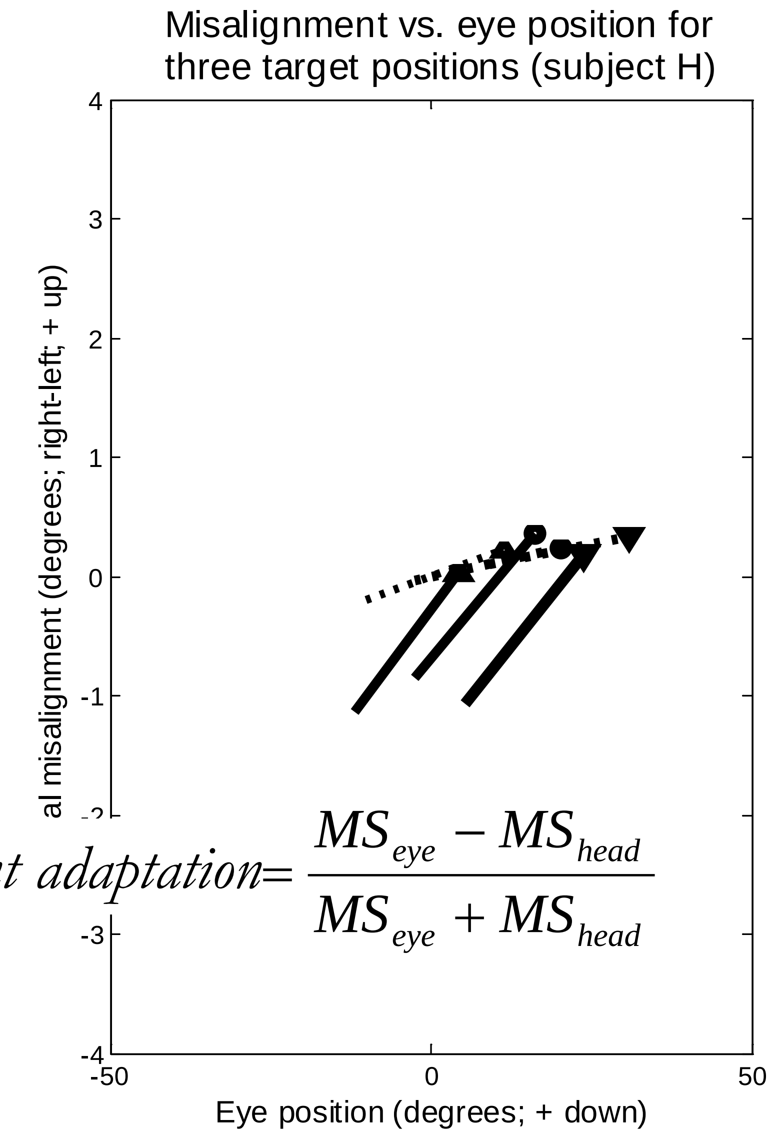


Ideal results demonstrating ***eye*** position-dependent adaptation



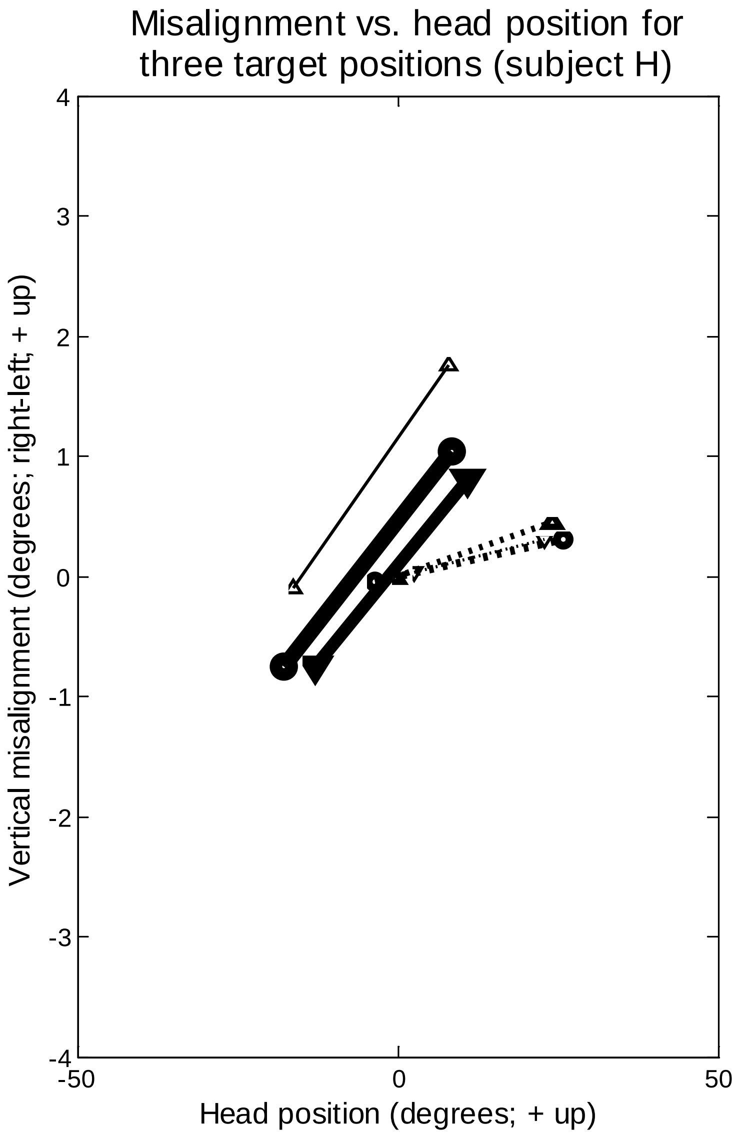
Example: misalignment dependent on head position

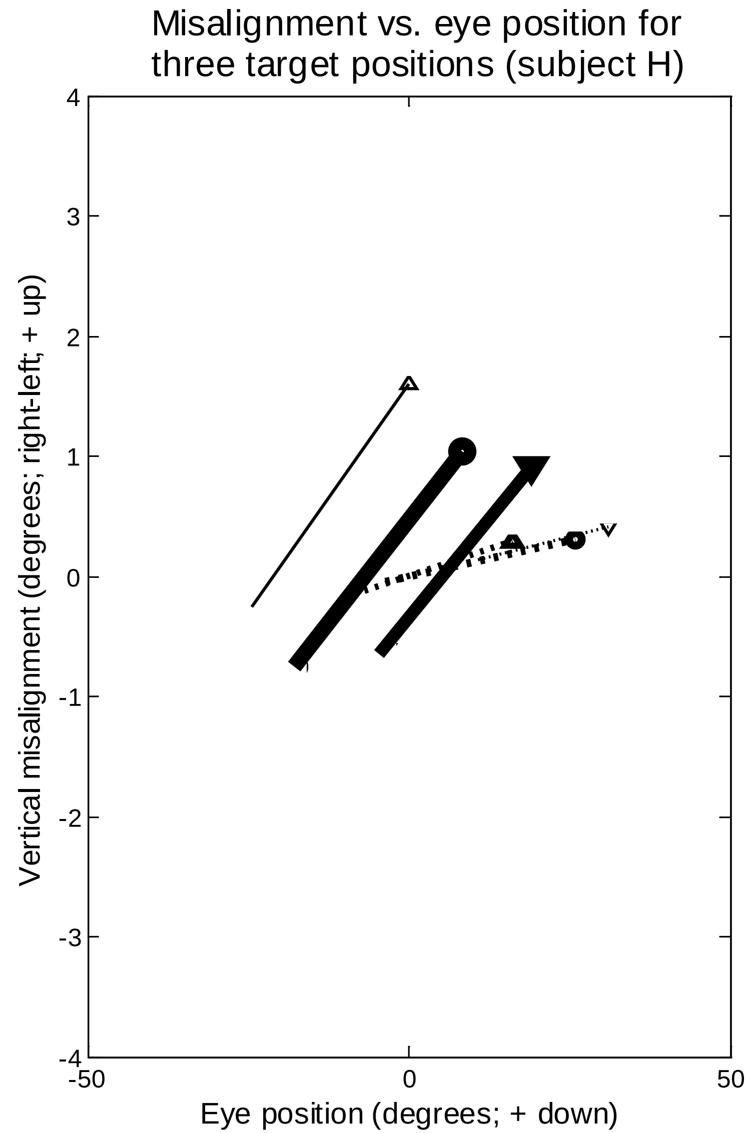




$$\textit{index of head-position-dependent adaptation} = \frac{MS_{eye} - MS_{head}}{MS_{eye} + MS_{head}}$$

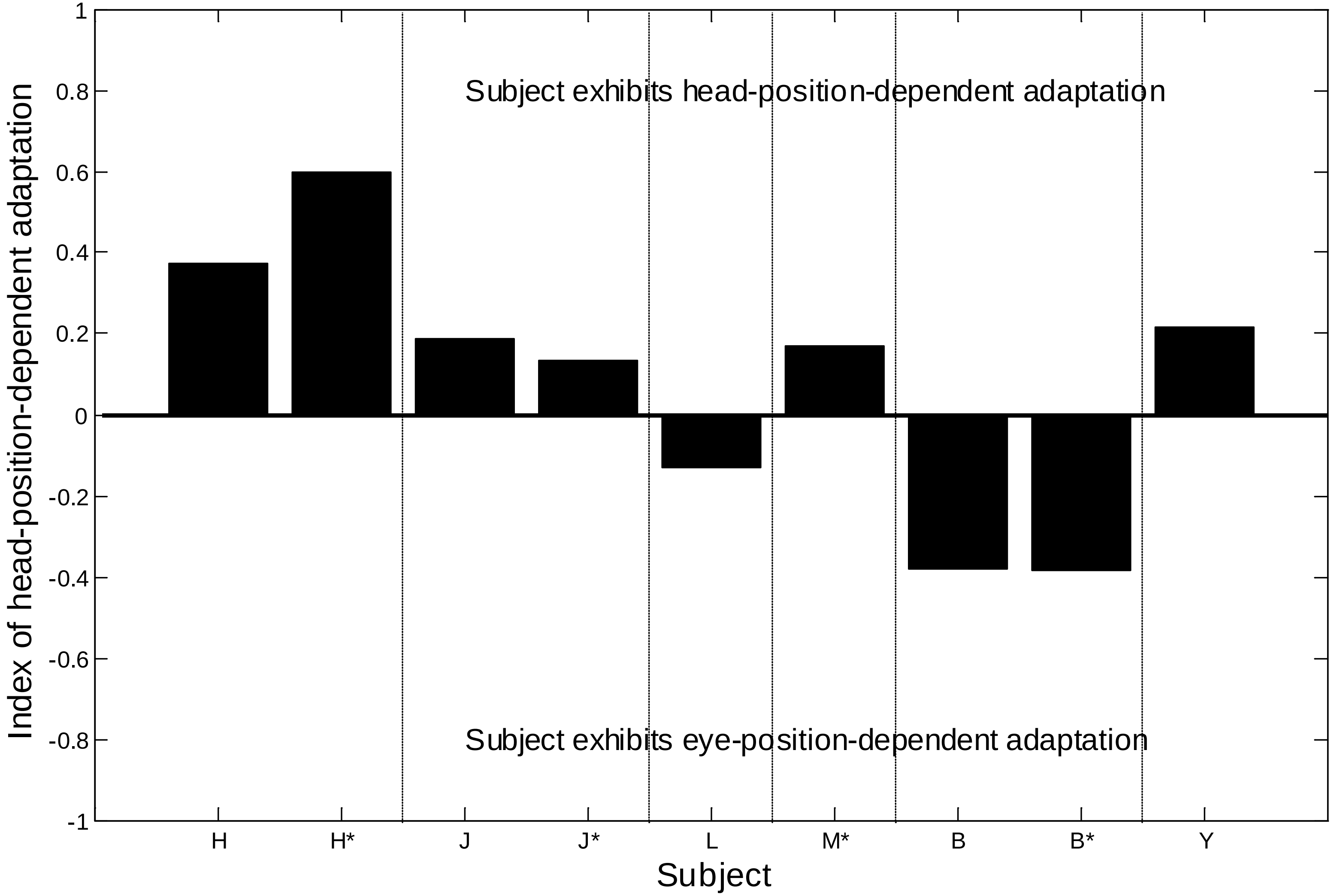
Example: misalignment partly dependent on eye position





Is adaptation dependent on eye or head?

- Compare mean sum-of-squares of regression for misalignment on eye, and misalignment on head

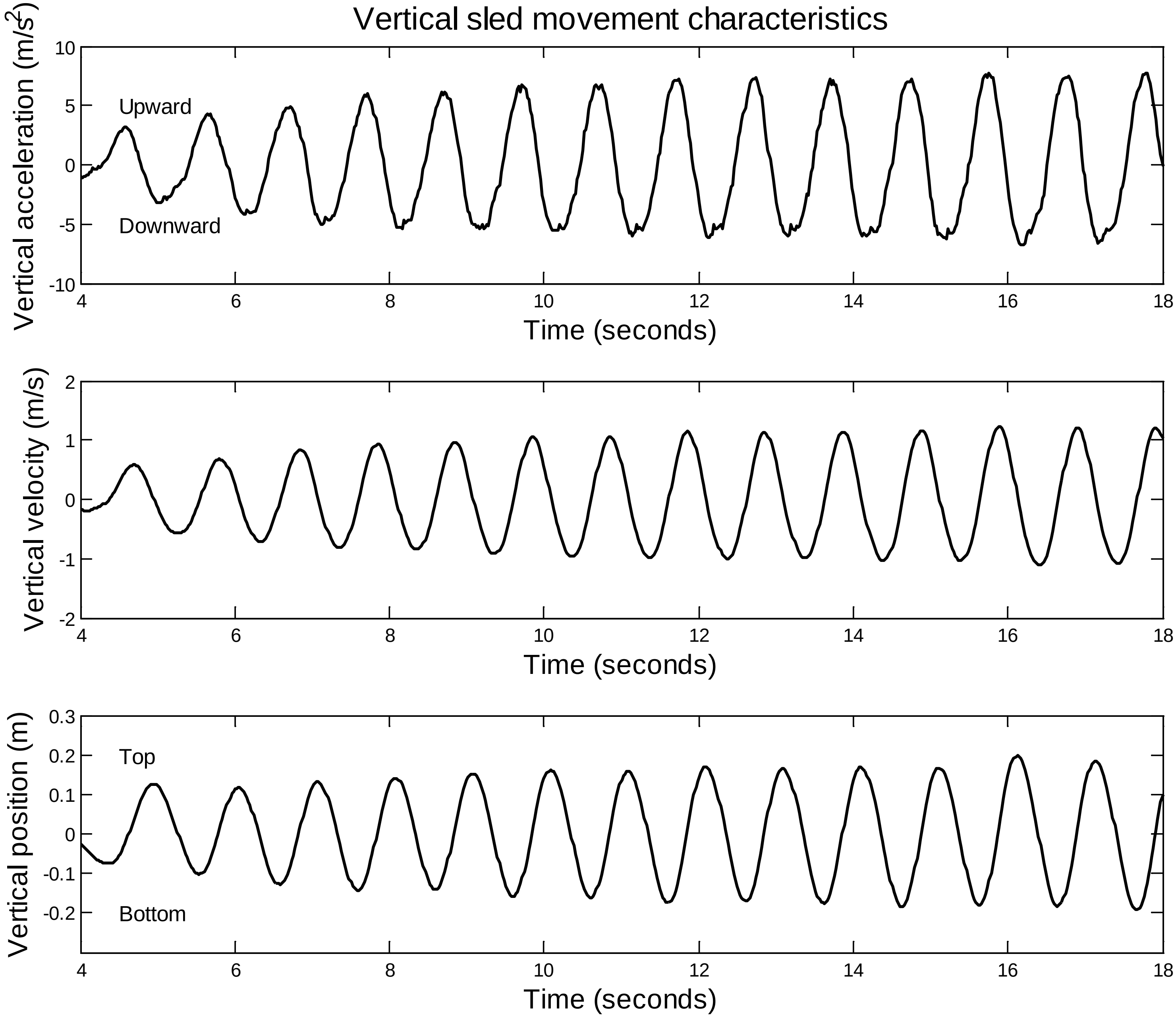


Pitch plasticity study – summary

- Position-dependent misalignments were adapted in all subjects
- Head position was implicated as the adaptation cue in most subjects
- Otolith organs or SCC could be driving adaptation
- In the next study, we performed the same adaptation and also tested in *vertical translation*, which stimulated the otolith organs but not the SCC

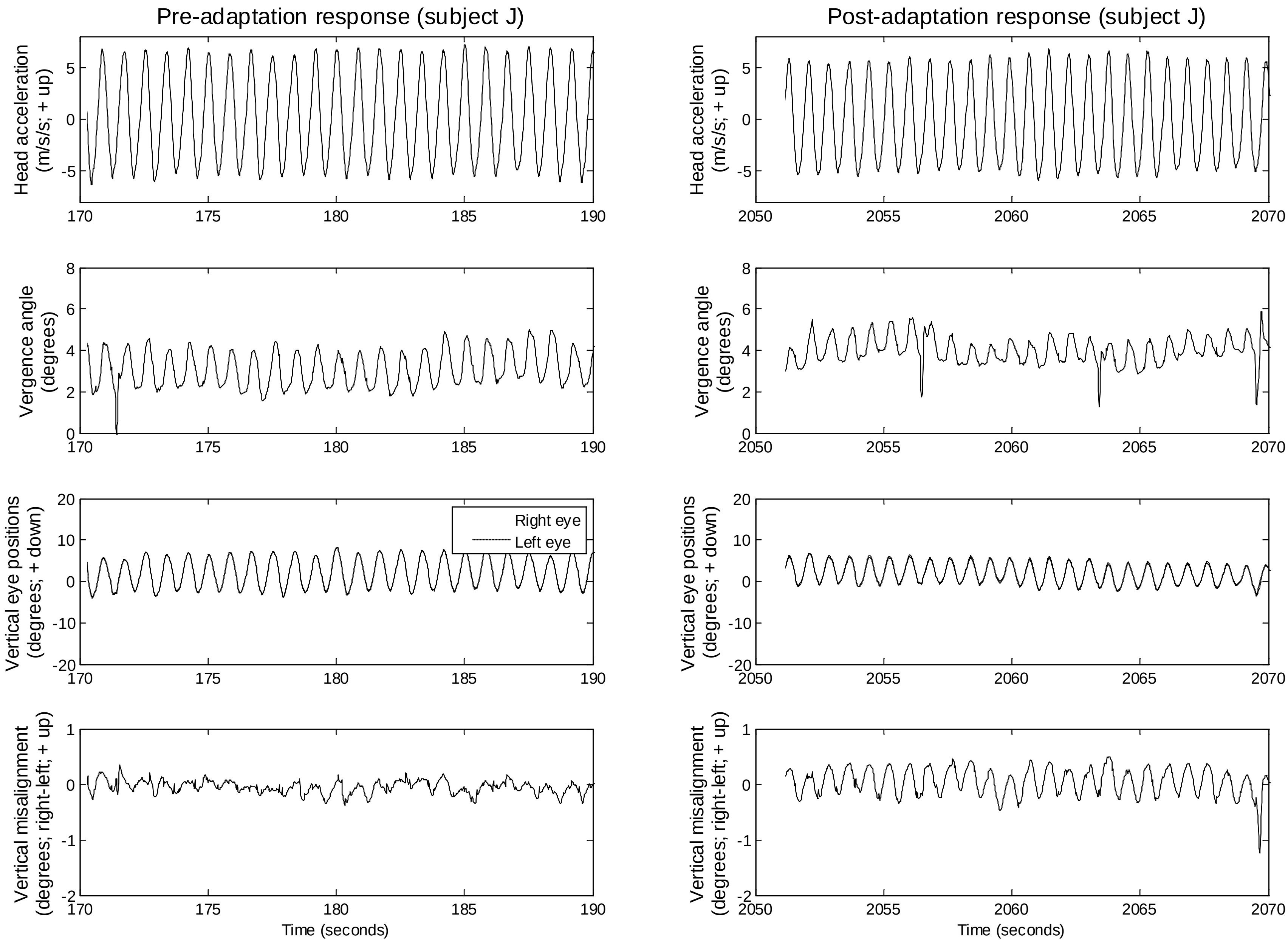
Vertical translate study

Pre-test Vertical (monocular target) → **Pre-test Pitch** (monocular target) → **Adapt Pitch** (15 min) → **Post-test Pitch** (monocular target) → **Adapt Pitch** (5 min) → **Post-test vertical** (monocular target)

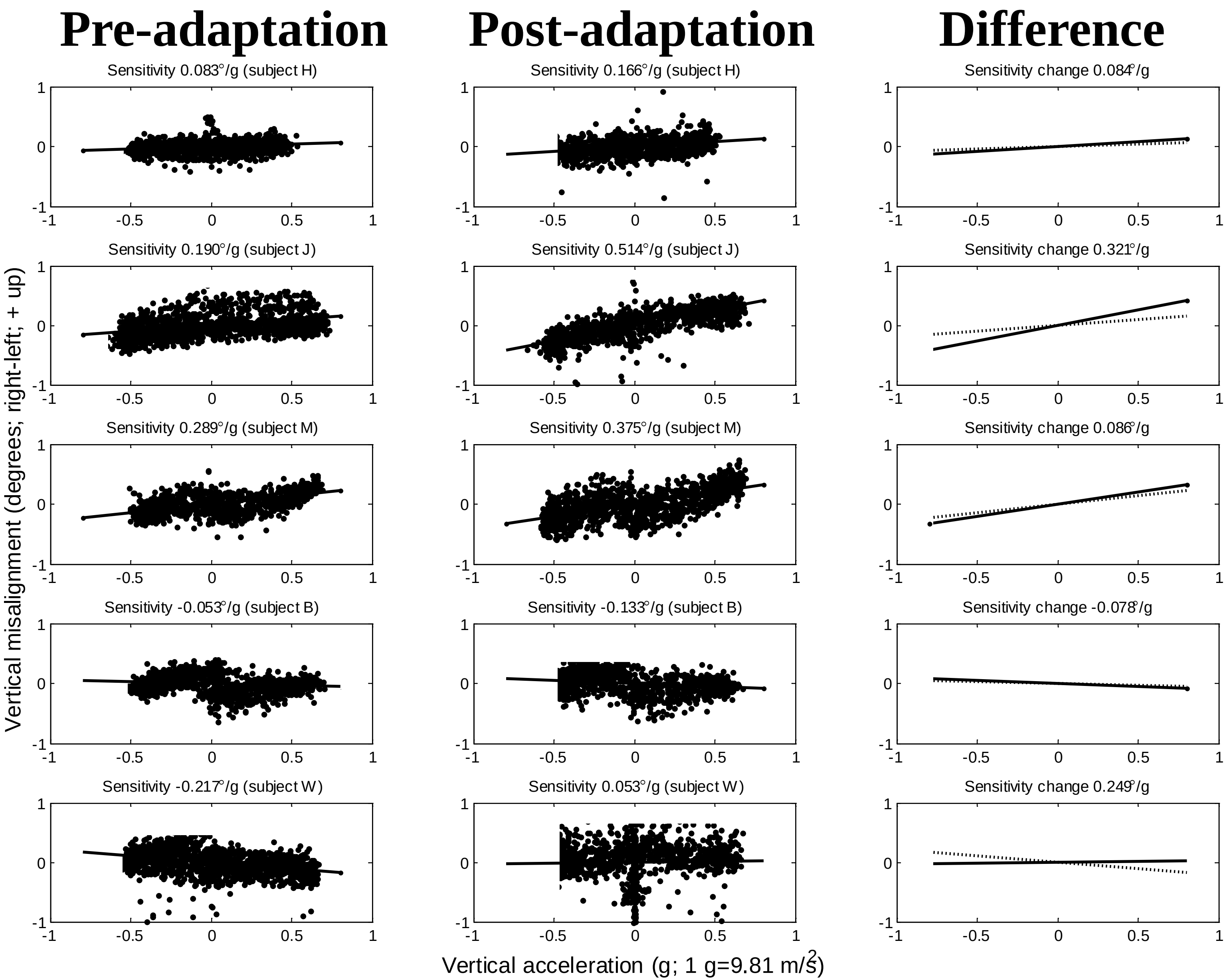


0.95 Hertz ±0.7 g peak acceleration

Response to vertical translation

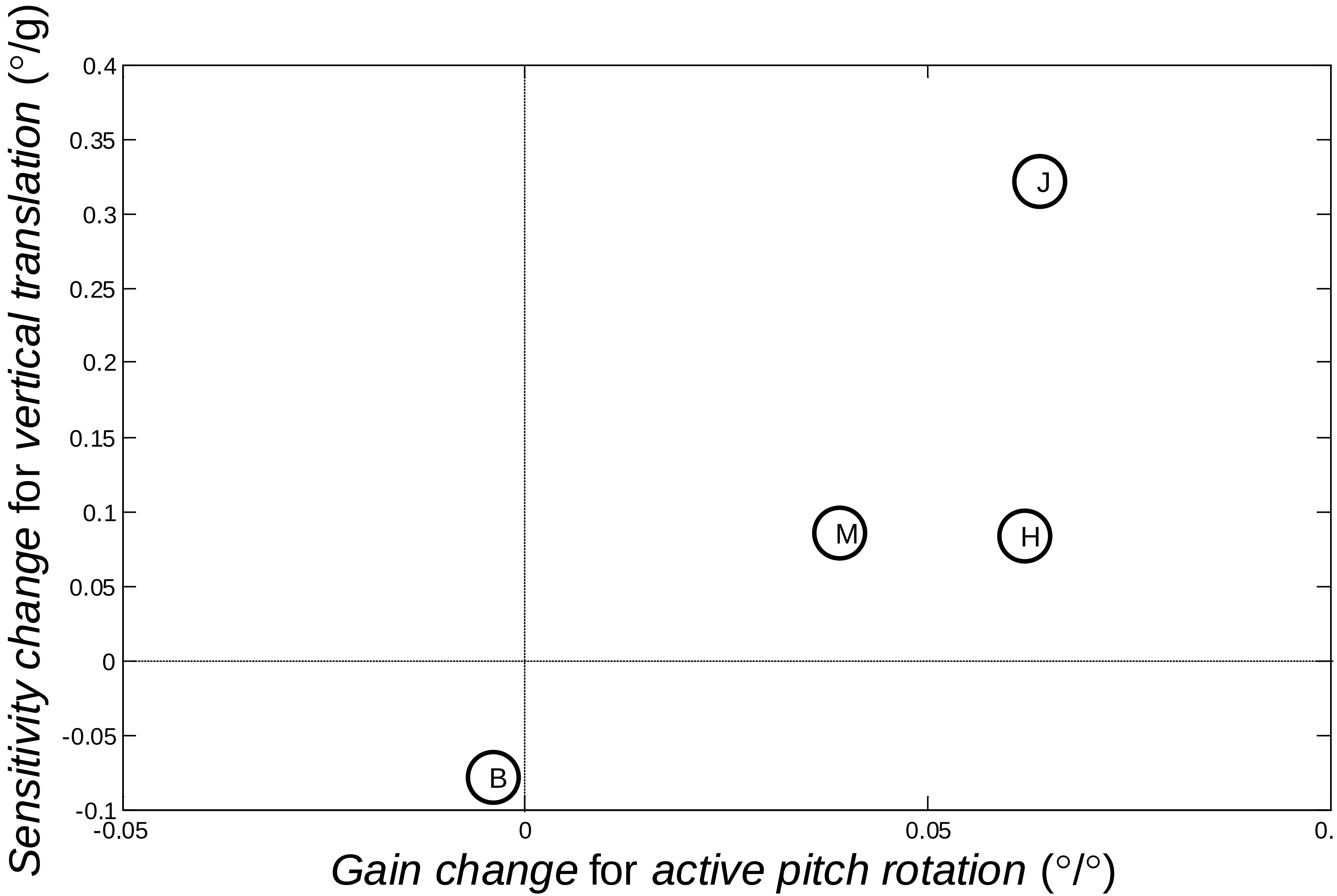


Sensitivity to vertical translation increases after adaptation of pitch response



- Increase in sensitivity increases for 4 of 5 subjects
- Change statistically significant in all subjects (GEE)

Sensitivity to vertical translation increases after adaptation of pitch response



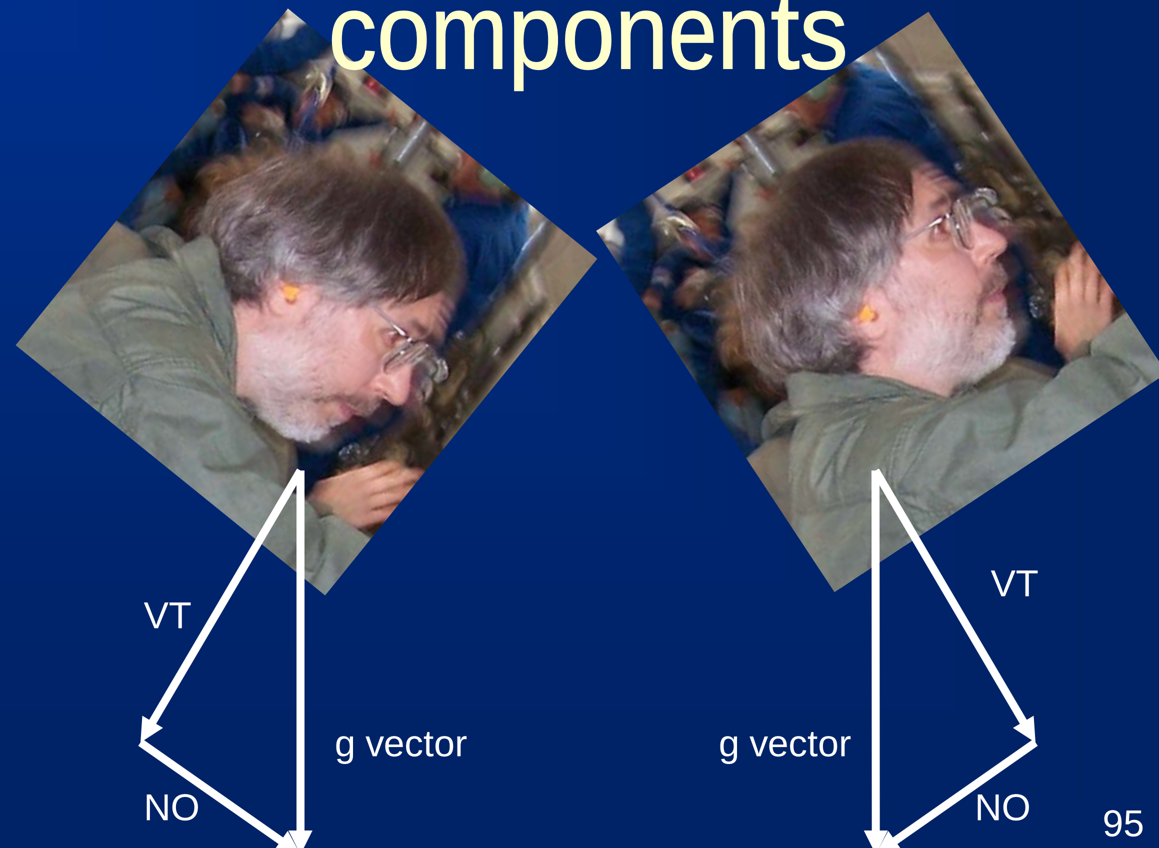
Vertical translate study – summary

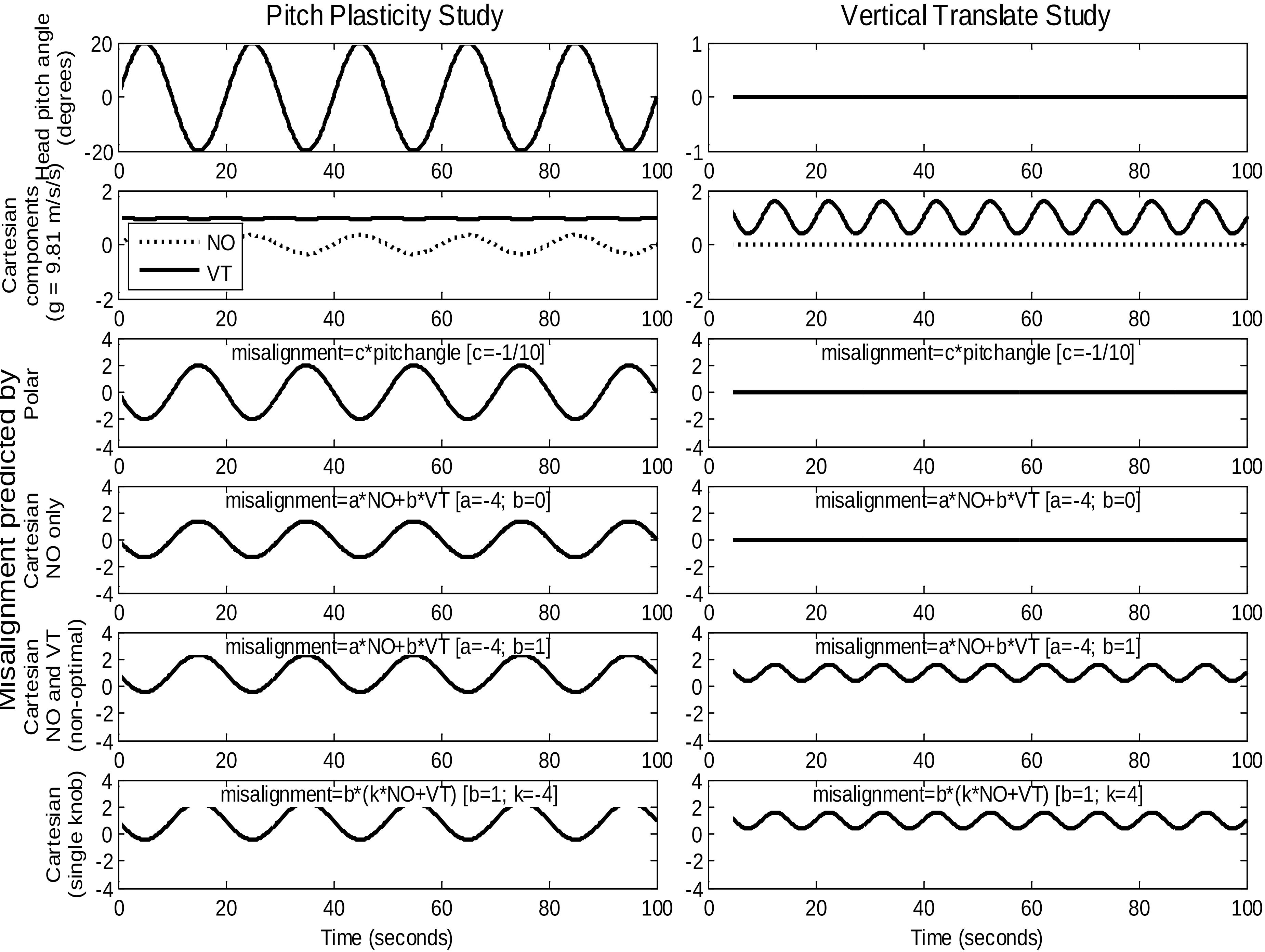
- Head-position-dependent adaptation of misalignment during pitch rotation was otolith organ dependent
- Adaptation transferred from otolith-dependent tilt response to otolith-dependent translation response
- Misalignment is a tool to study the otolith-ocular pathway: it allows questions to be asked about tilt/translation which are difficult to answer using conjugate eye movements

What model of otolith organ information processing explains the transfer of adaptation from *pitch* to *vertical translation?*

Polar coordinates

Cartesian components




Pitch Plasticity Study
Vertical Translate Study
Head pitch angle (degrees)
Cartesian components (g = 9.81 m/s/s)
NO
VT
Misalignment predicted by
Polar
Cartesian NO only
Cartesian NO and VT (non-optimal)
Cartesian (single knob)
misalignment=c*pitchangle [c=-1/10]
misalignment=a*NO+b*VT [a=-4; b=0]
misalignment=a*NO+b*VT [a=-4; b=1]
misalignment=b*(k*NO+VT) [b=1; k=-4]
misalignment=b*(k*NO+VT) [b=1; k=4]
Time (seconds)

Modeling – summary

- Otolith organ information is processed in Cartesian components
- Adaptation affects all g vector components equally

Conclusions

- Otolith-dependent eye misalignments can be adaptively created during dynamic pitch rotation using a visual-vestibular mismatch
- Adaptation transfers from otolith-transduced tilt responses to translation responses
- Components of the g vector are used to determine the ocular response; adaptation affects all components equally

Application to countermeasures

- Adapting otolith reflexes during weightlessness is expensive and of a short duration
- Countermeasures can focus on adapting responses of individual Cartesian components
- When appropriate g vector cannot be provided using translation, it can be provided using tilt

Future work

- Test for transfer when adapted Cartesian components are the same
- The relationship between head position and misalignment in the adaptive paradigm was linear – a parabolic relationship would separate otolith and SCC contributions
- Transfer of adaptation from *vertical translation* to *pitch rotation*

Future work

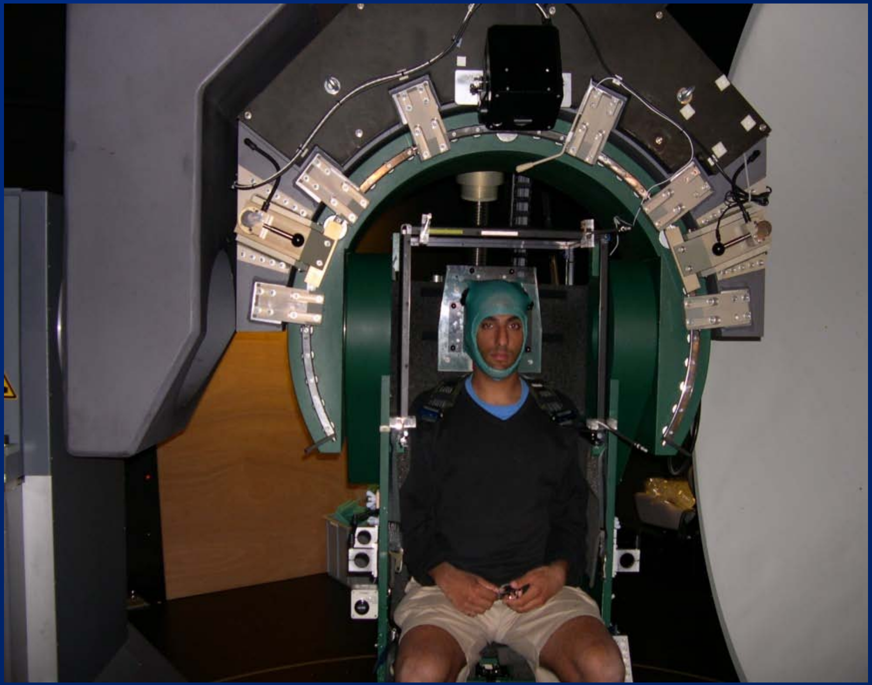
Head orientation during adaptation		during first test		during second test	
rotation axis	g vector components stimulated	rotation axis	g vector components stimulated	rotation axis	g vector components stimulated
Pitch upright	VT & NO	Roll onside	VT (&IA)	Yaw onside	NO (&IA)
Roll upright	VT & IA	Pitch supine	VT (&NO)	Yaw supine	IA (&NO)
Yaw supine	NO & IA	Pitch upright	NO (&VT)	Roll upright	IA (&VT)

Acknowledgements

- Advisor: Dr. Mark Shelhamer
- Committee members: Drs. Paul Fuchs, David Solomon, David Zee, Kechen Zhang
- Technical assistance: Adrian Lasker, Dale Roberts, NASA staff, Dr. Andy Clarke
- Scientific advise: Dr. Mark Walker, Dr. Howard Ying, School of Public Health Biostats Clinic
- Funding: NSBRI, NIH, NSERC

Vertical eye misalignments during pitch rotation and vertical translation: Evidence for bilateral asymmetries and plasticity in the otolith-ocular reflex

Dr. Faisal Karmali
MEEI
September 10, 2007



Publications

- 12 conference abstracts
- Peer-reviewed publications

  - Karmali F, Ramat S, Shelhamer M. *Vertical skew due to changes in gravitoinertial force: A possible consequence of otolith asymmetry*. Journal of Vestibular Research. 2006 Dec;16:117-125.
  - Karmali F, Shelhamer M. *Automatic Detection of Camera Translation in Eye Video Recordings using Multiple Methods*. Annals of the New York Academy of Sciences. 2005 Apr;1039:470-6.
  - Karmali F, Shelhamer M. *Compensating for camera translation in video eye movement recordings by tracking a landmark selected automatically by a genetic algorithm*. (submitted)
  - Karmali F, Shelhamer M. *The dynamics of parabolic flight: flight characteristics and passenger percepts.* (submitted)
  - Grabherr L, Karmali F, Bach S, Indermaur K, Metzler S, Mast FW. *Mental Rotation of Bodies and Body-parts in Microgravity*. Journal of Vestibular Research. 2007. (accepted)
  - Karmali F, Ramat S, Straumann D, Shelhamer M. *Binocular disconjugacy in slow and fast pitch vestibulo-ocular reflex: Evidence for otolithic influence.* (in preparation)

Background

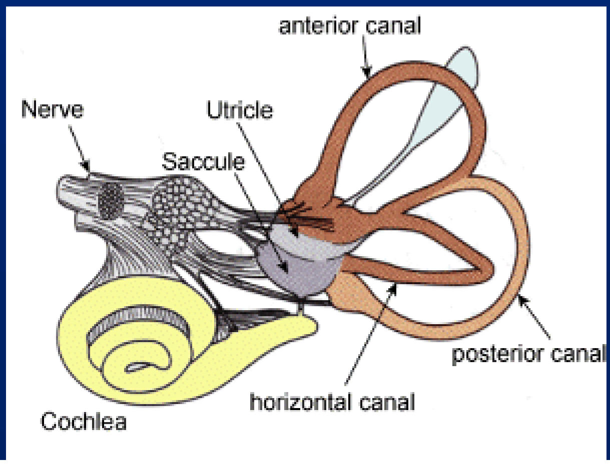
The Vestibular System

- “Sixth sense” that keeps us balanced
- Stops us from falling when we stumble
- Helps move eyes (“gaze stabilization”)

Patients with Vestibular Disease or stroke	Astronauts affected by weightlessness
Vertigo Difficulty walking Eyes move incorrectly	Vertigo and motion sickness Difficulty walking upon return Eyes move incorrectly

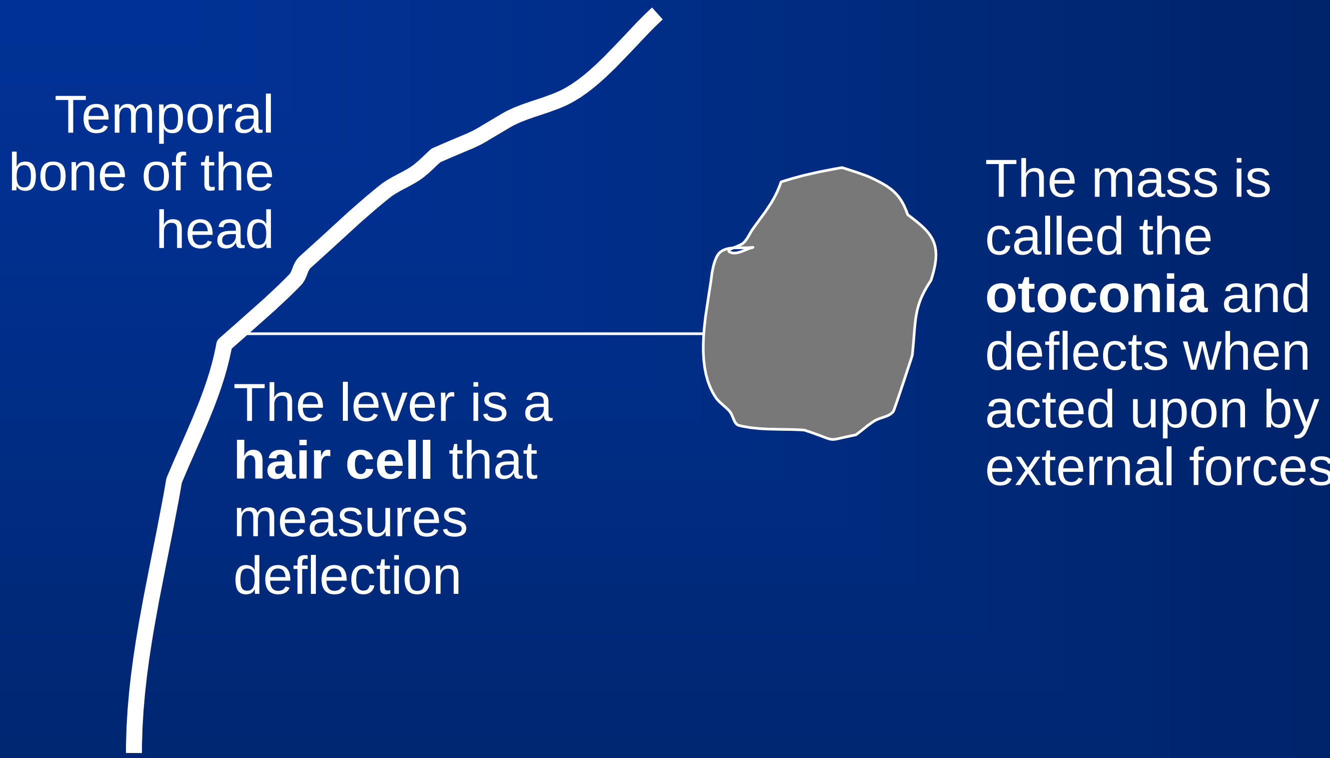
Vestibular-Ocular Reflexes

- **Otolith organs** measure linear acceleration and gravity (contains **utricle** and **saccule)**
- **Semicircular canals (SCC)** measure angular velocity



- Eye movements opposite of head movements
- **Torsion** is rotation of eye about the line of sight
- **Conjugate:** eyes move together
- **Disconjugate**: difference between left and right eyes

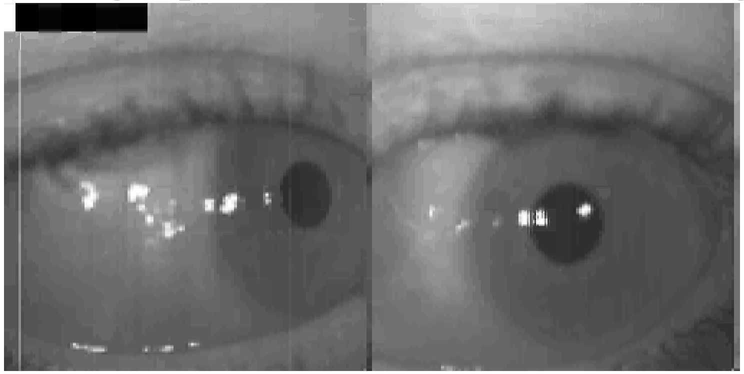
The otolith organ: a mass on a lever

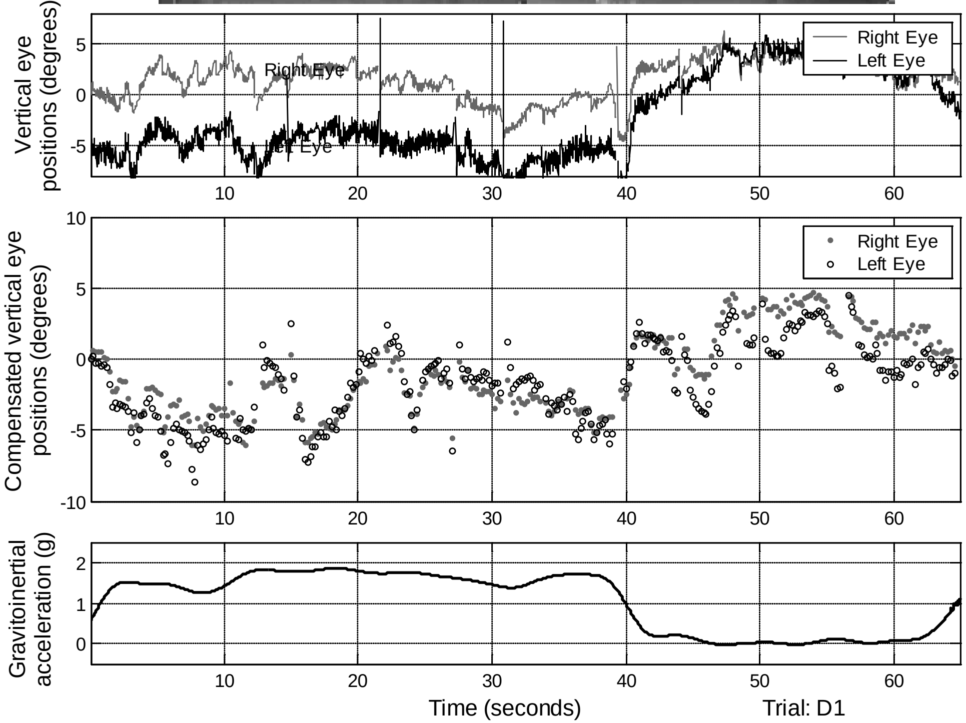


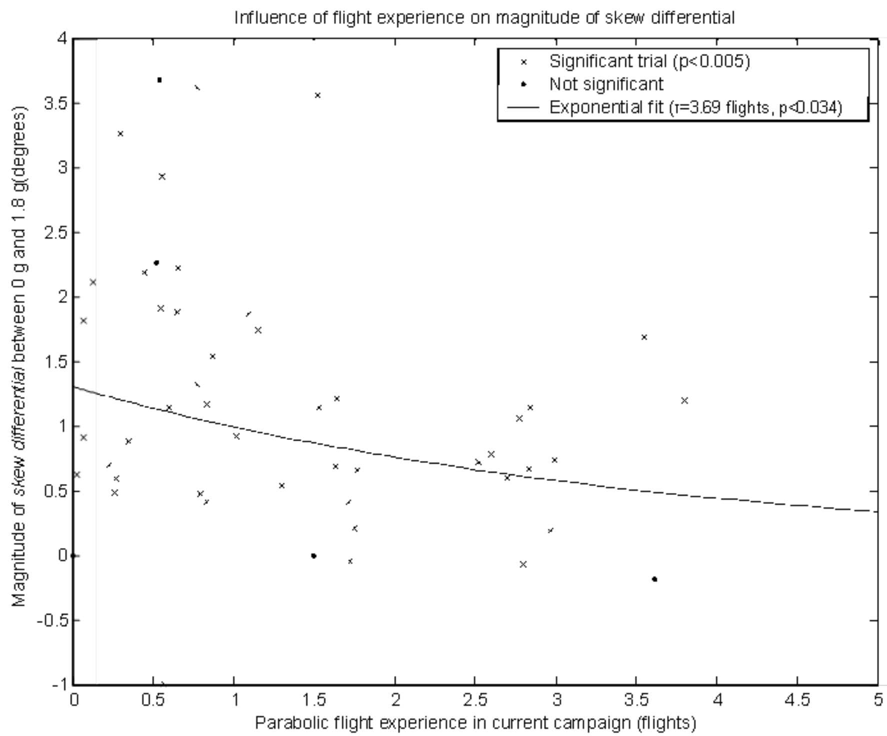
g vector: the sum of linear acceleration and gravity

1 g of downward gravity is indistinguishable from 1 g of upward acceleration of the head

Vertical misalignments during parabolic flight

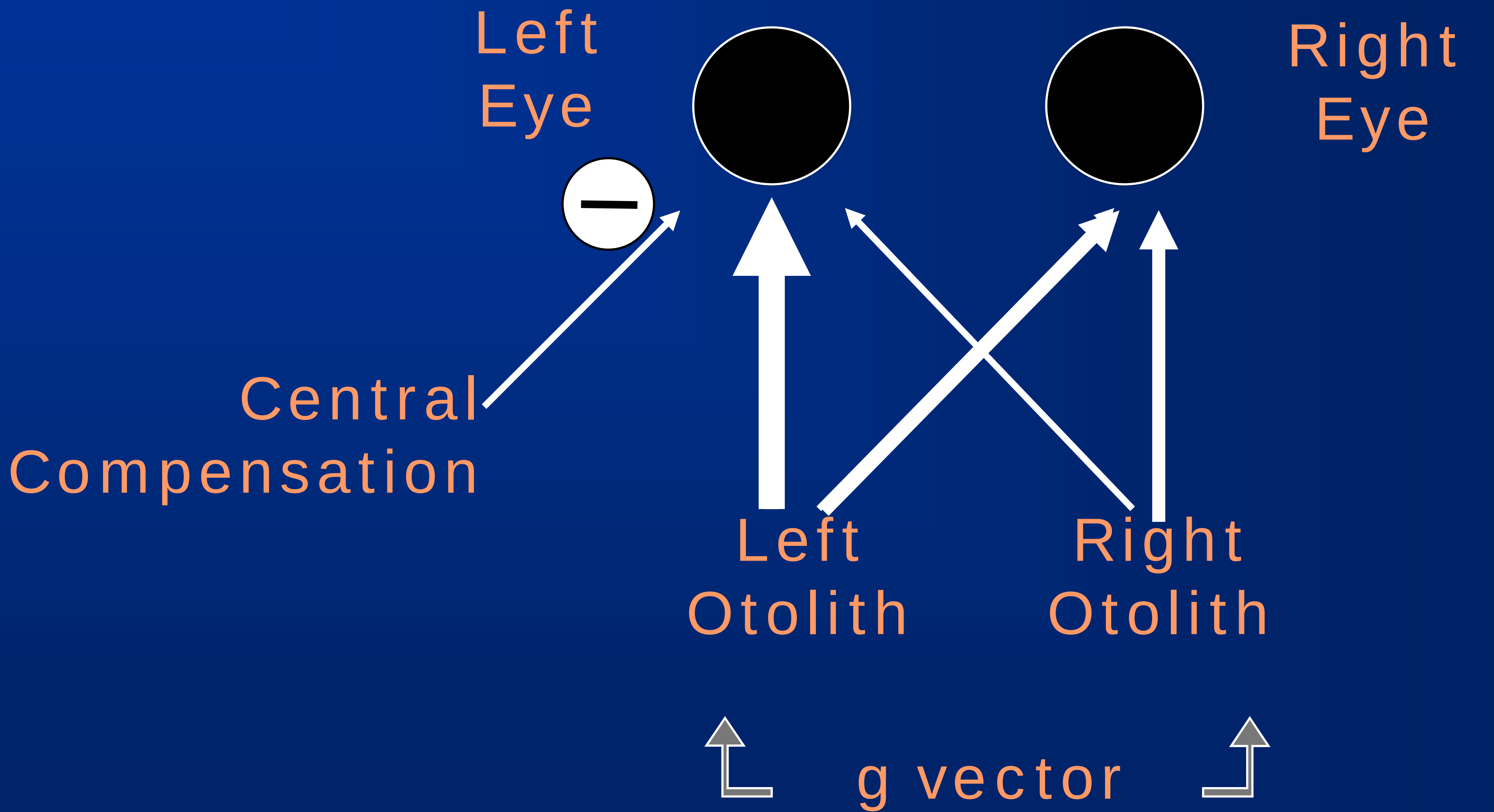






Karmali, Ramat, Shelhamer, Journal of Vestibular Research. 2006 Dec;16:117-125

Otolith Asymmetry Hypothesis



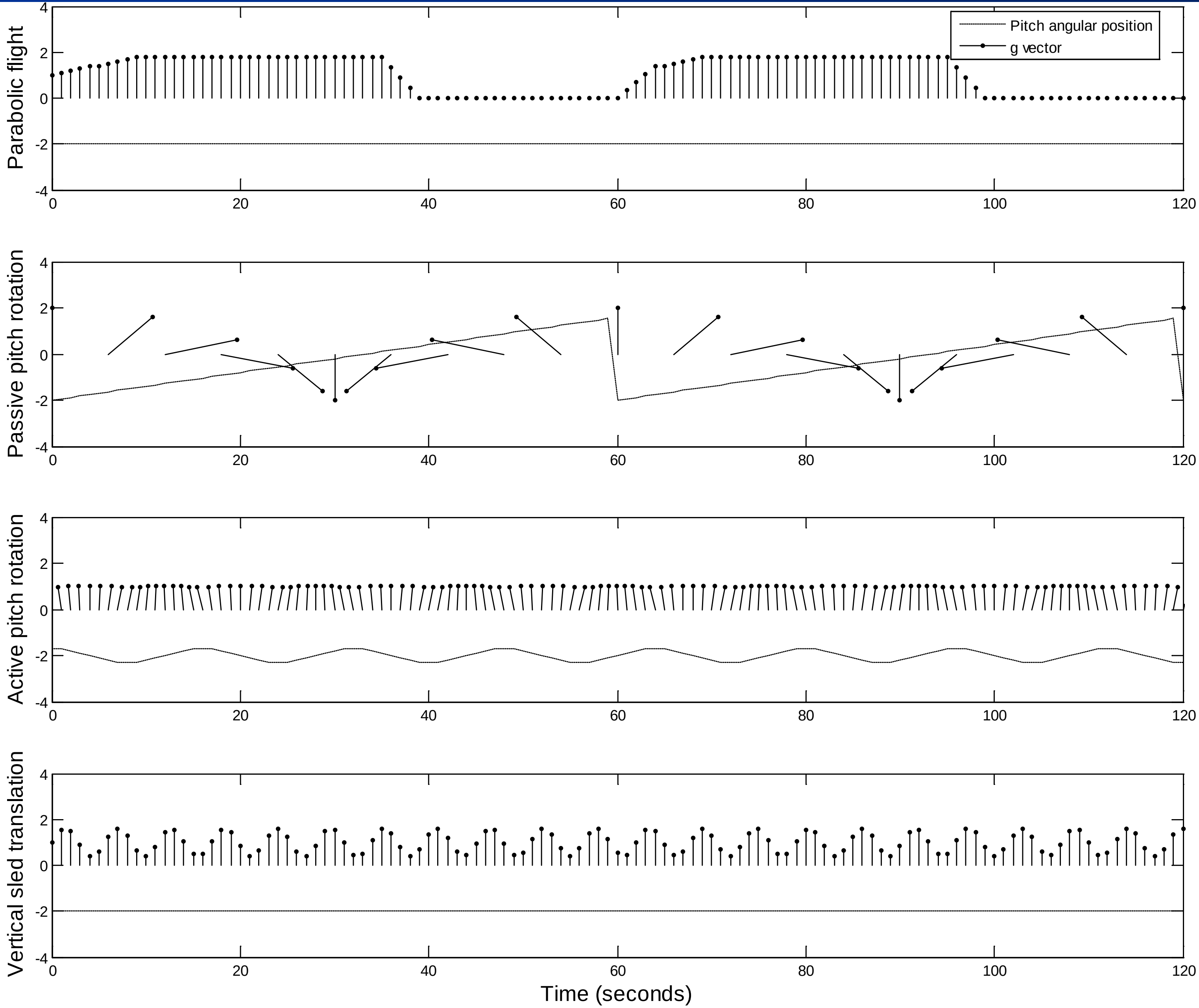
- “Over 50% of utricular-activated, second-order vestibular neurons received commissural inhibition from the contralateral utricular nerve.”
- “Almost all the saccular-activated, second-order vestibular neurons exhibit no response to stimulation of the contralateral saccular nerve.”
- Uchino, 2004

Implications of otolith asymmetry

1. It can predict space sickness: a better understanding of the mechanisms may help to improve screening and produce simpler screening tests
2. It may reduce task performance by creating a sensory conflict or misaligning the eyes
3. Understanding how it adapts may be useful in training including partial adaptation before flight

Experimental Design

Motion profiles



Sensory environment during motion profiles

	Motion profile		
Sensory receptor	*Passive pitch rotation* (full body)	*Active pitch rotation*	*Vertical translation*
Otolith organs	Changing orientation relative to gravity	Changing orientation relative to gravity	Linear acceleration
Semicircular canals (SCC)	Only before vestibular time constant exceeded	Yes	No
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The *pitch innate study*

Slow test Pitch → *Medium* test Pitch → *Fast* test Pitch

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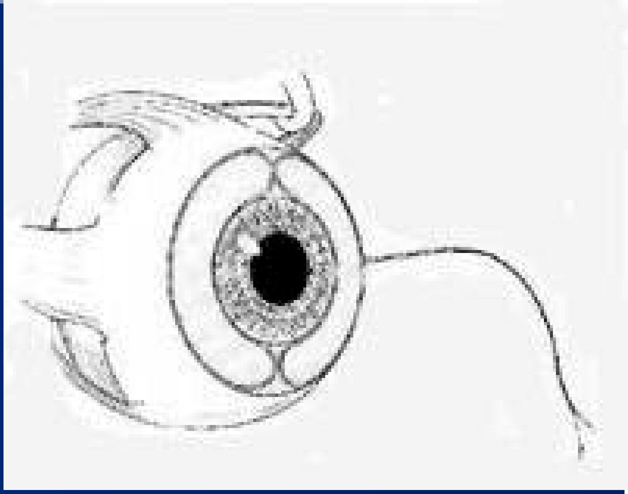

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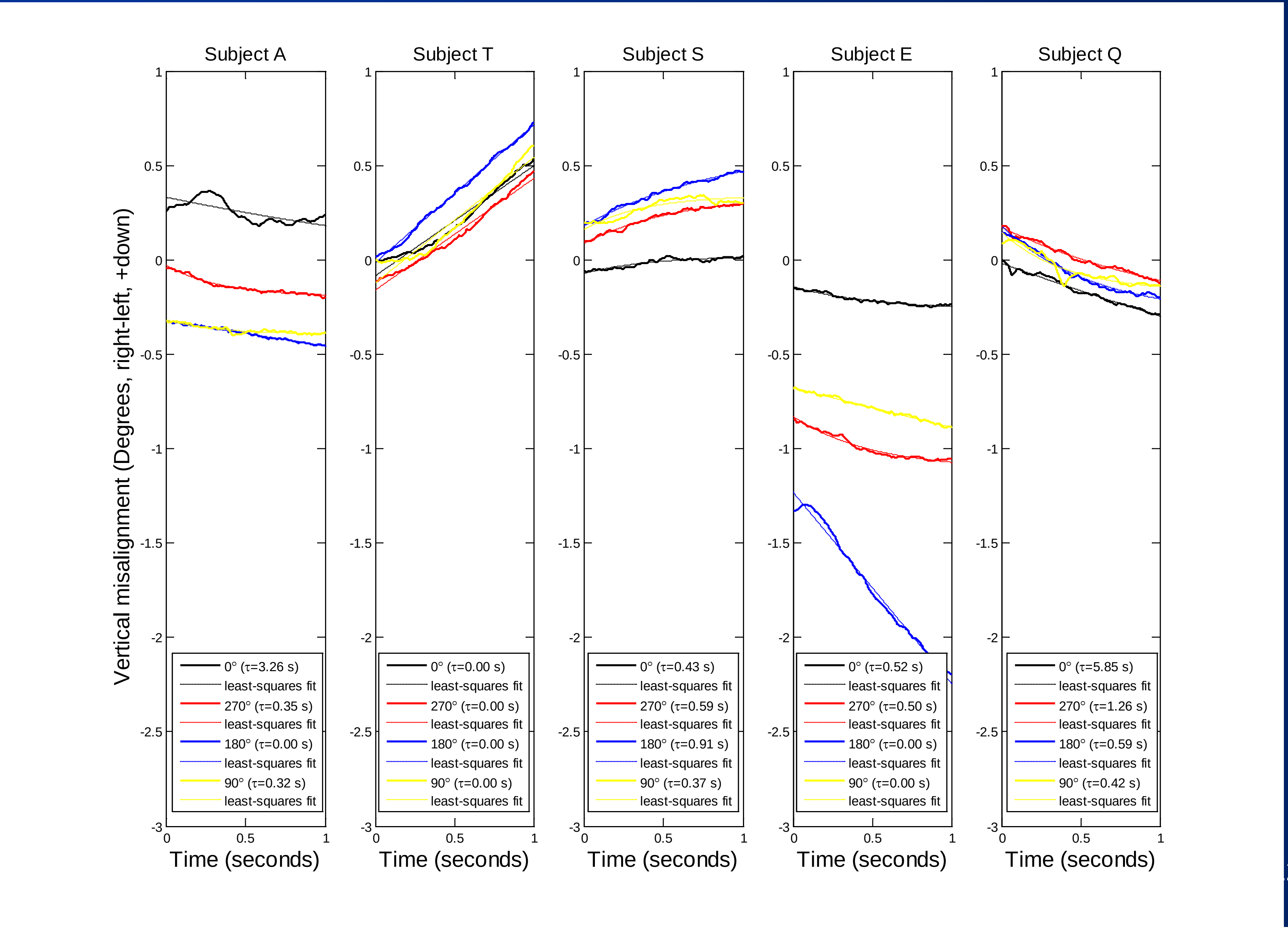
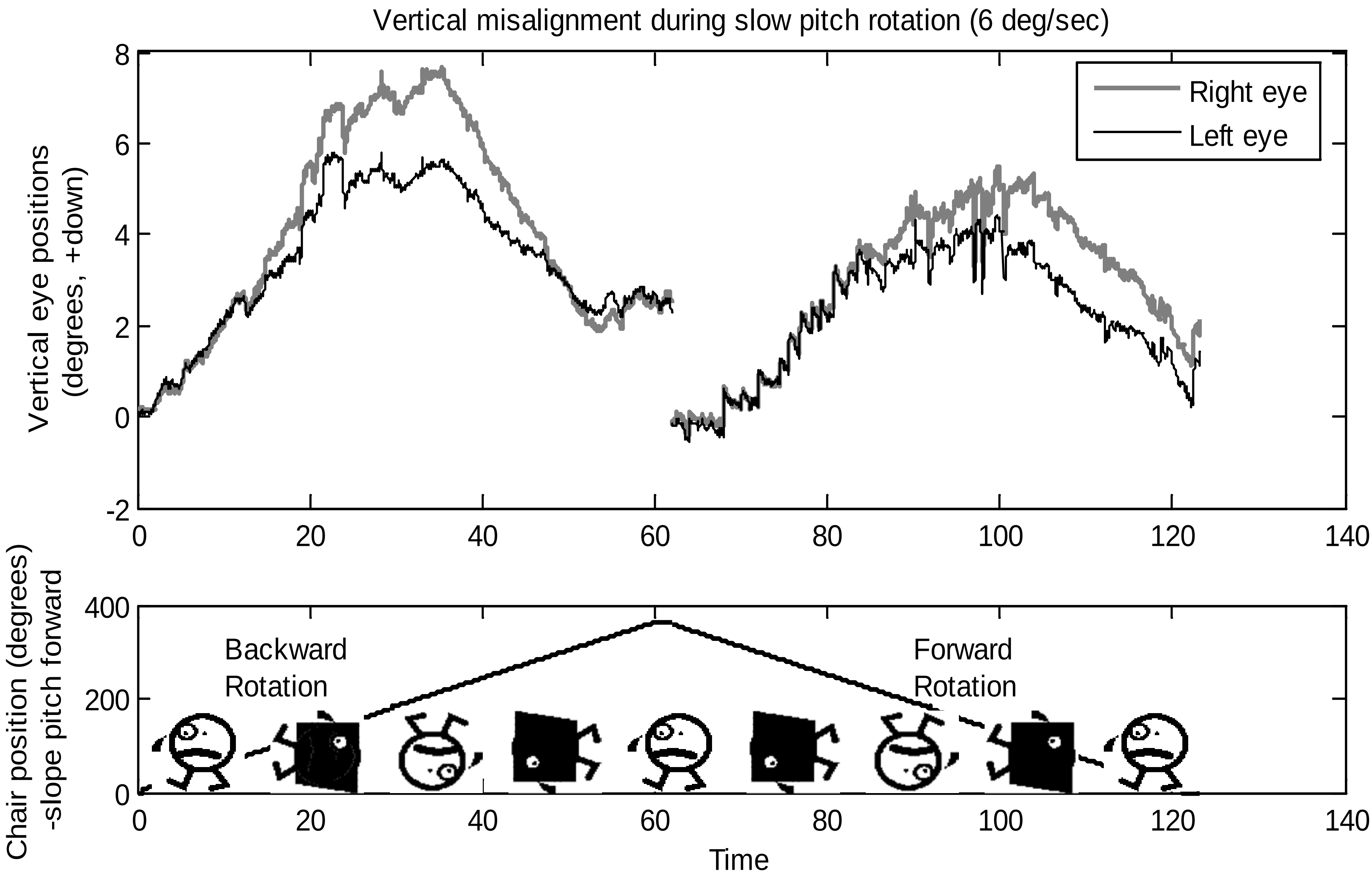
Pitch innate study

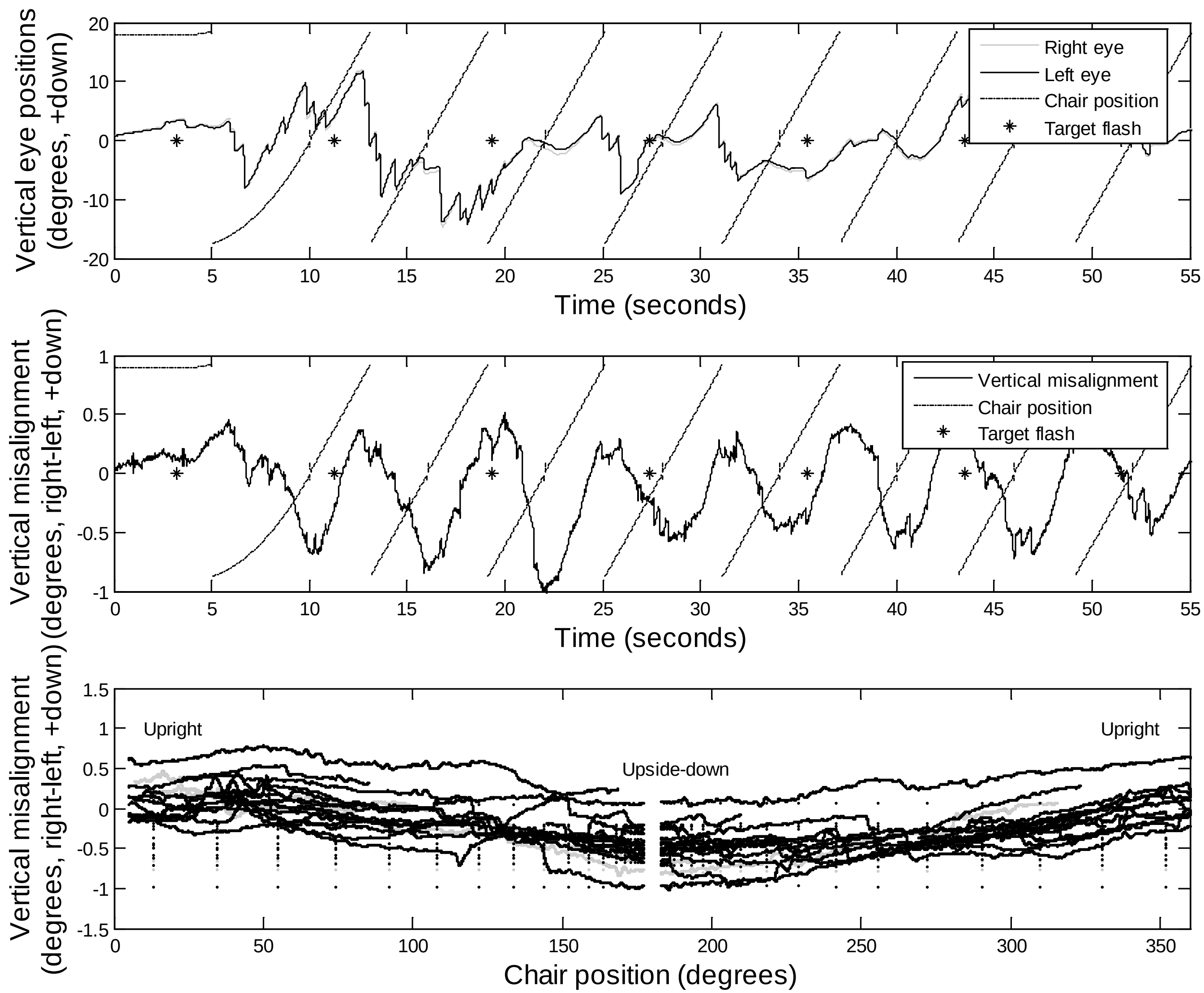
Static alignment



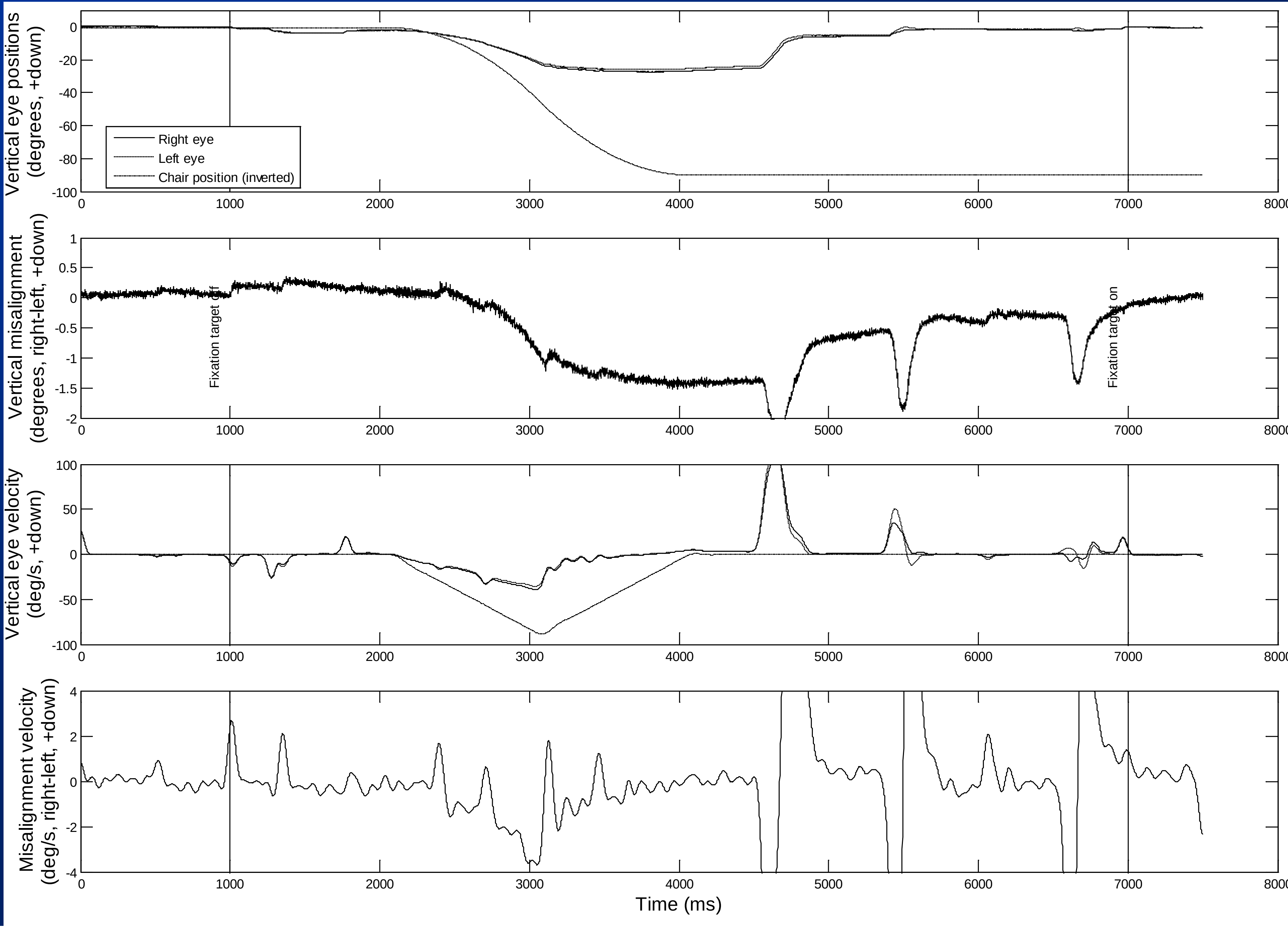
Slow rotation – 6º/sec



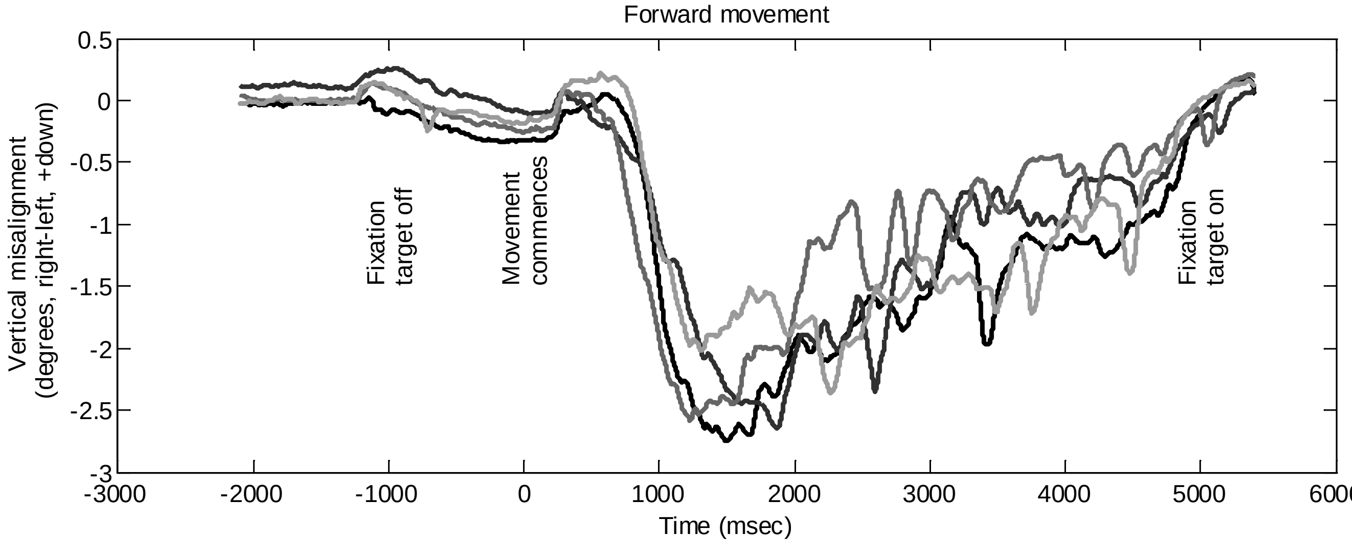
Medium rotation – 60º/sec

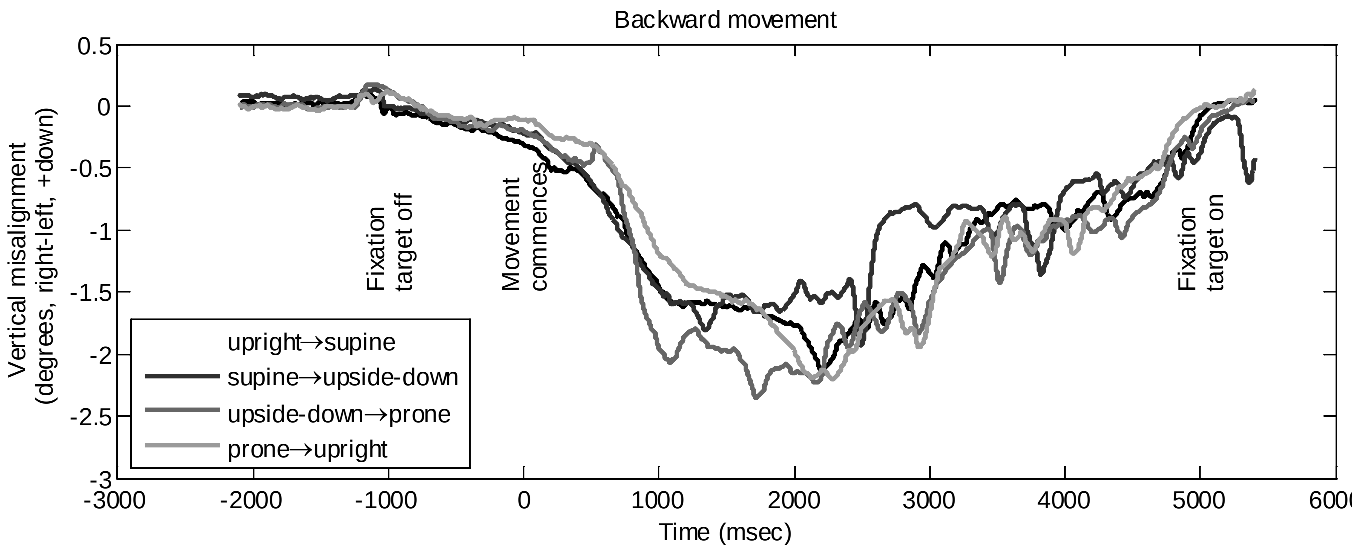


Fast rotation – 2 second steps



Fast rotation – 2 second steps





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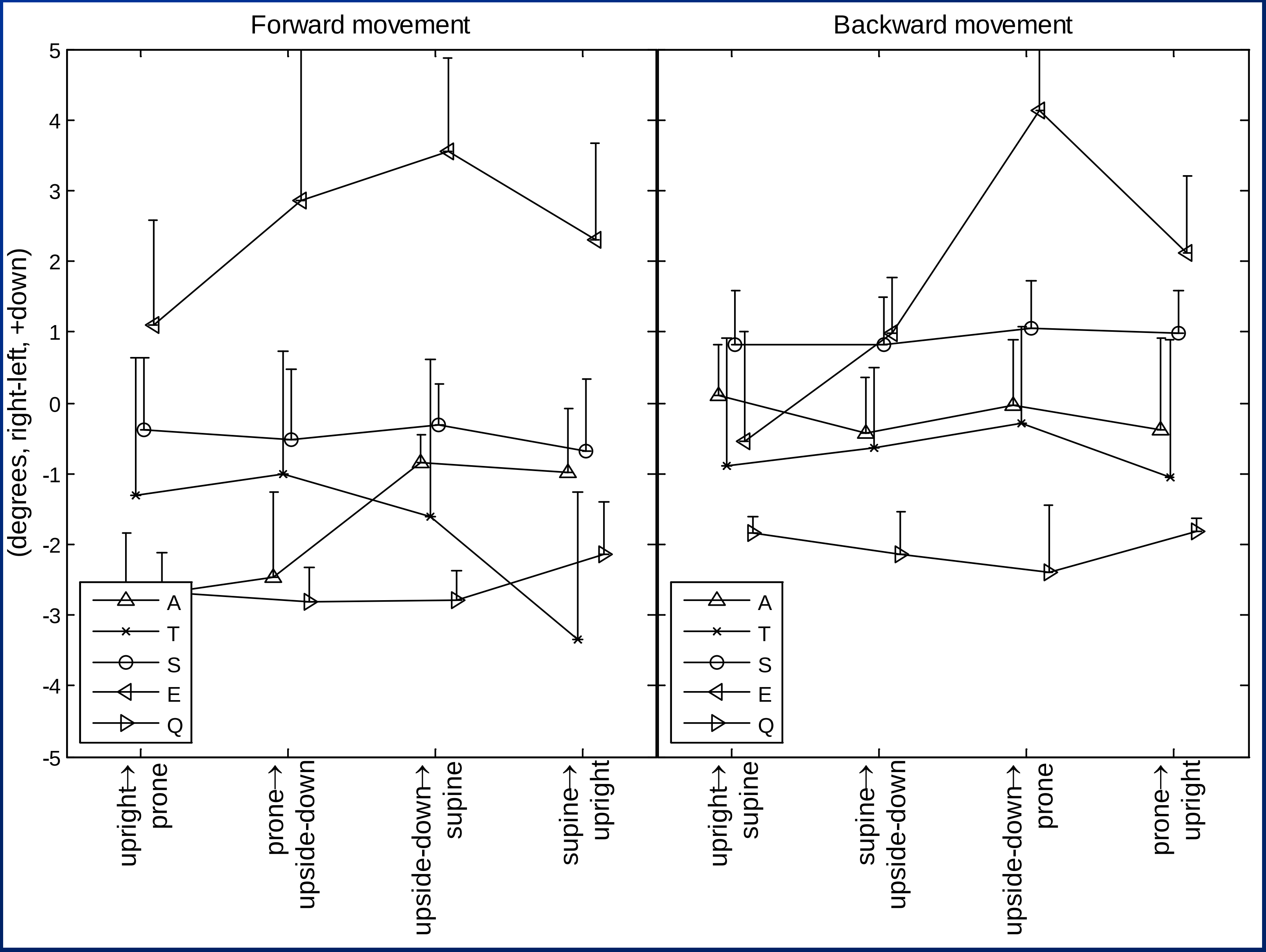
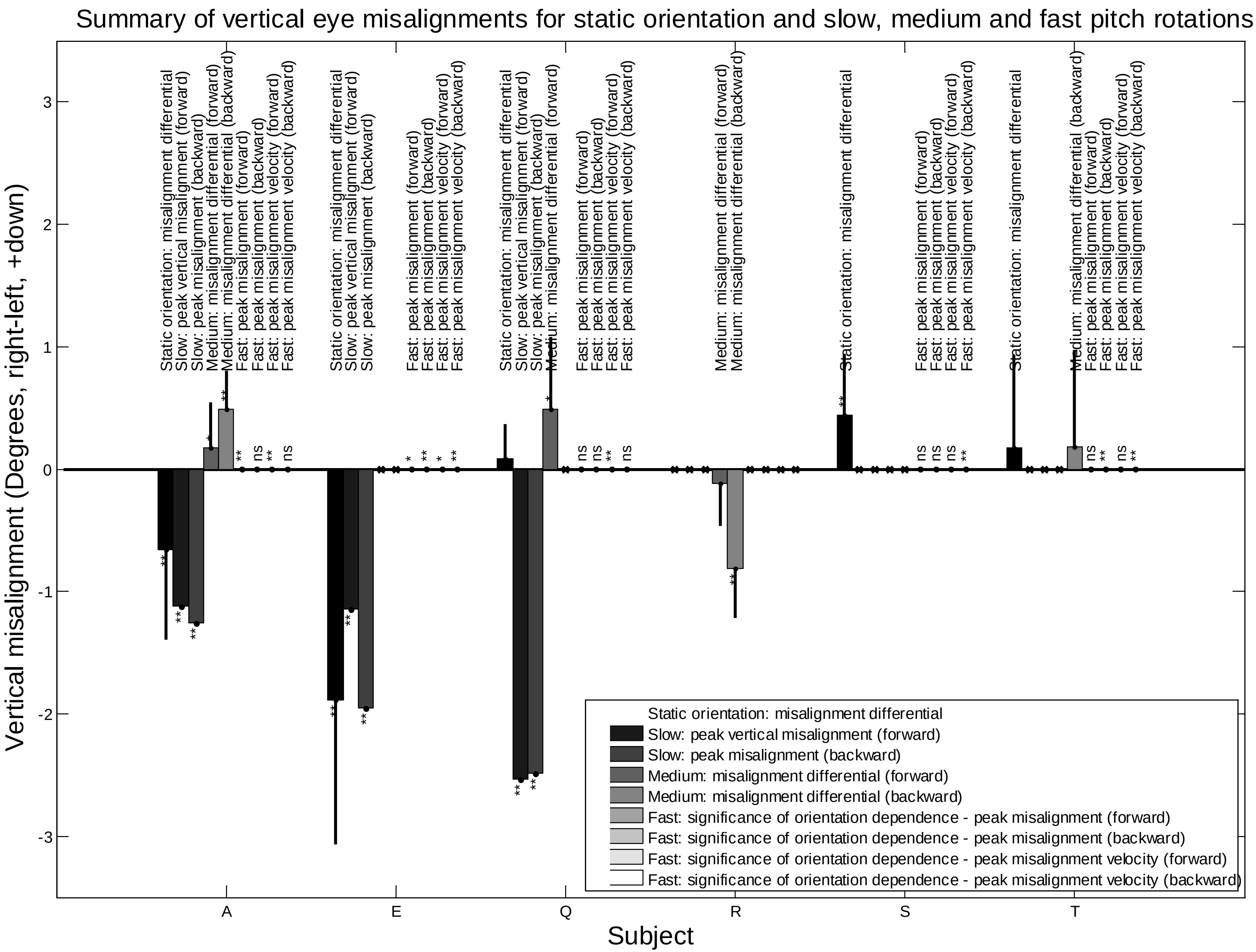




Summary of vertical eye misalignments for static orientation and slow, medium and fast pitch rotations
Vertical misalignment (Degrees, right-left, +down)
Subject
A
E
Q
R
S
T
Static orientation: misalignment differential
Slow: peak vertical misalignment (forward)
Slow: peak misalignment (backward)
Medium: misalignment differential (forward)
Medium: misalignment differential (backward)
Fast: peak misalignment (forward)
Fast: peak misalignment (backward)
Fast: peak misalignment velocity (forward)
Fast: peak misalignment velocity (backward)
Fast: significance of orientation dependence - peak misalignment (forward)
Fast: significance of orientation dependence - peak misalignment (backward)
Fast: significance of orientation dependence - peak misalignment velocity (forward)
Fast: significance of orientation dependence - peak misalignment velocity (backward)

Pitch innate study - summary

	Misalignment determined by	Average misalignment difference between upright & upside-down	Number of significant subjects ($p<0.01$; GEE)
Static	Orientation	0.99º	3/5
Slow	Orientation	1.74º	3/3
Medium	Orientation	0.39º	3/4
Fast	Angular velocity (orientation significant in 1/5 subjects)	1.86º (peak misalignment)	

Orientation-dependent misalignments implicate asymmetry in otolith pathway

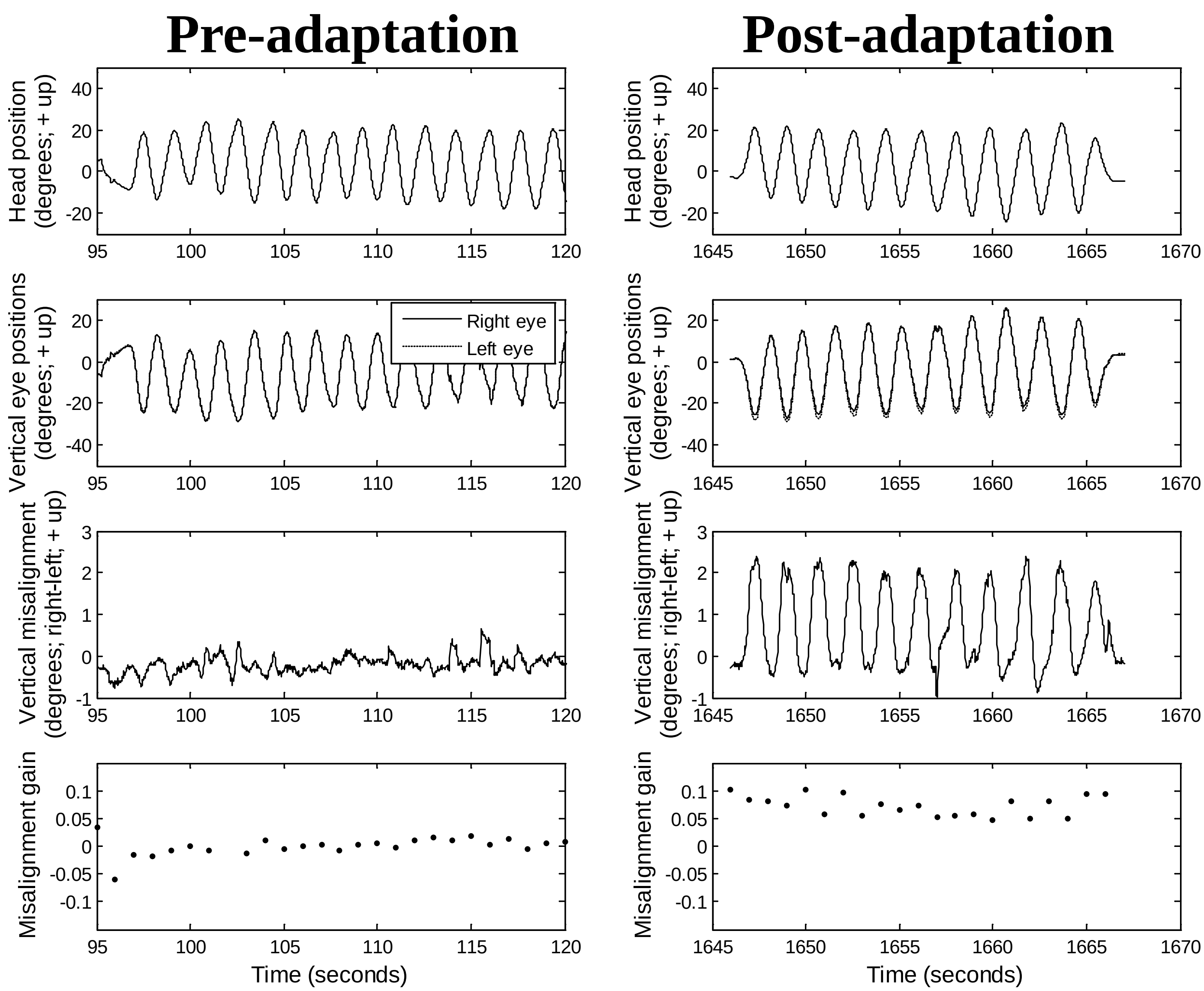
Velocity-dependent misalignments implicate SCC pathway

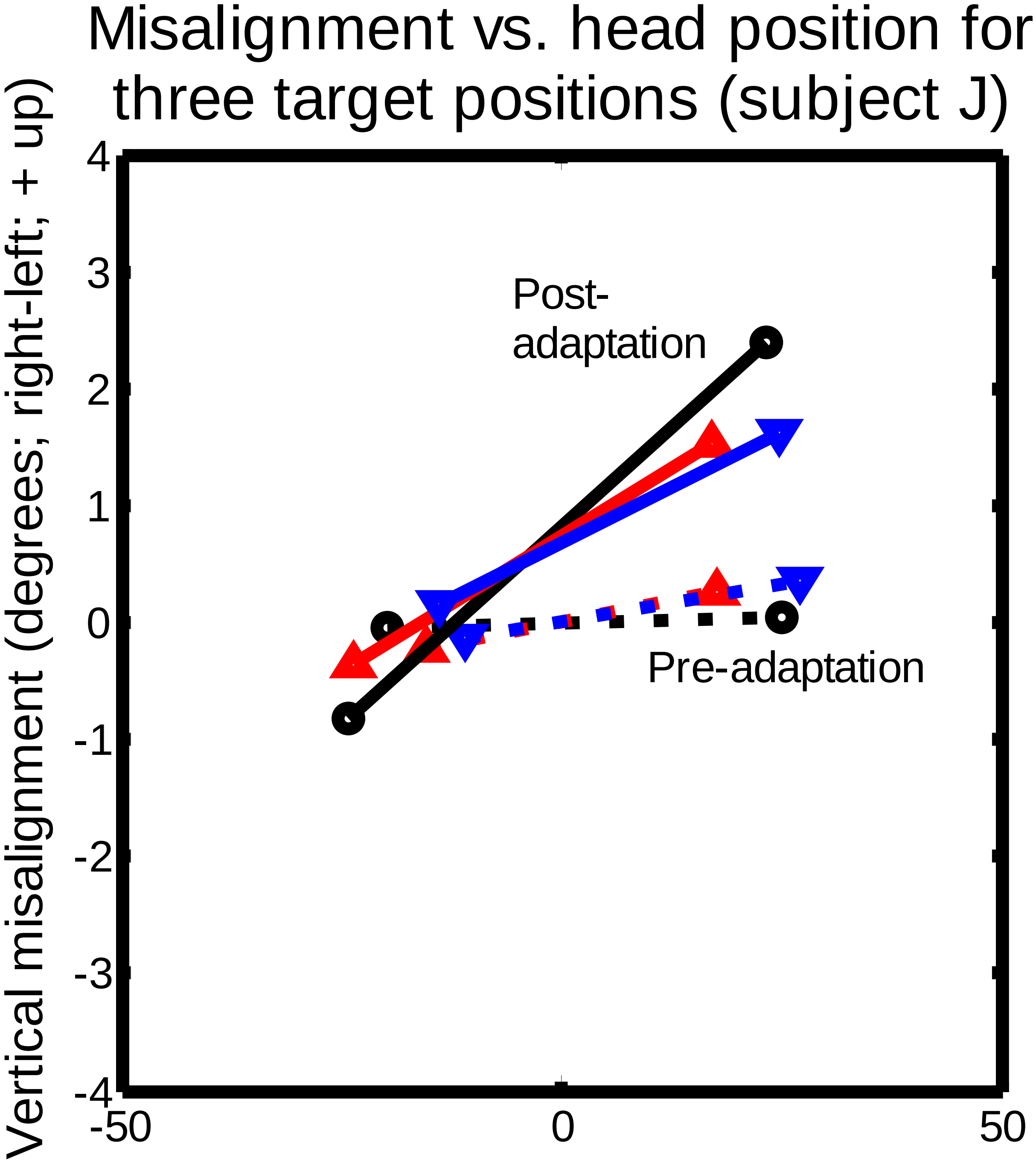
- Otolith asymmetry acts in both:
  - pitch rotation - g vector direction changing
  - vertical acceleration - g vector magnitude changing

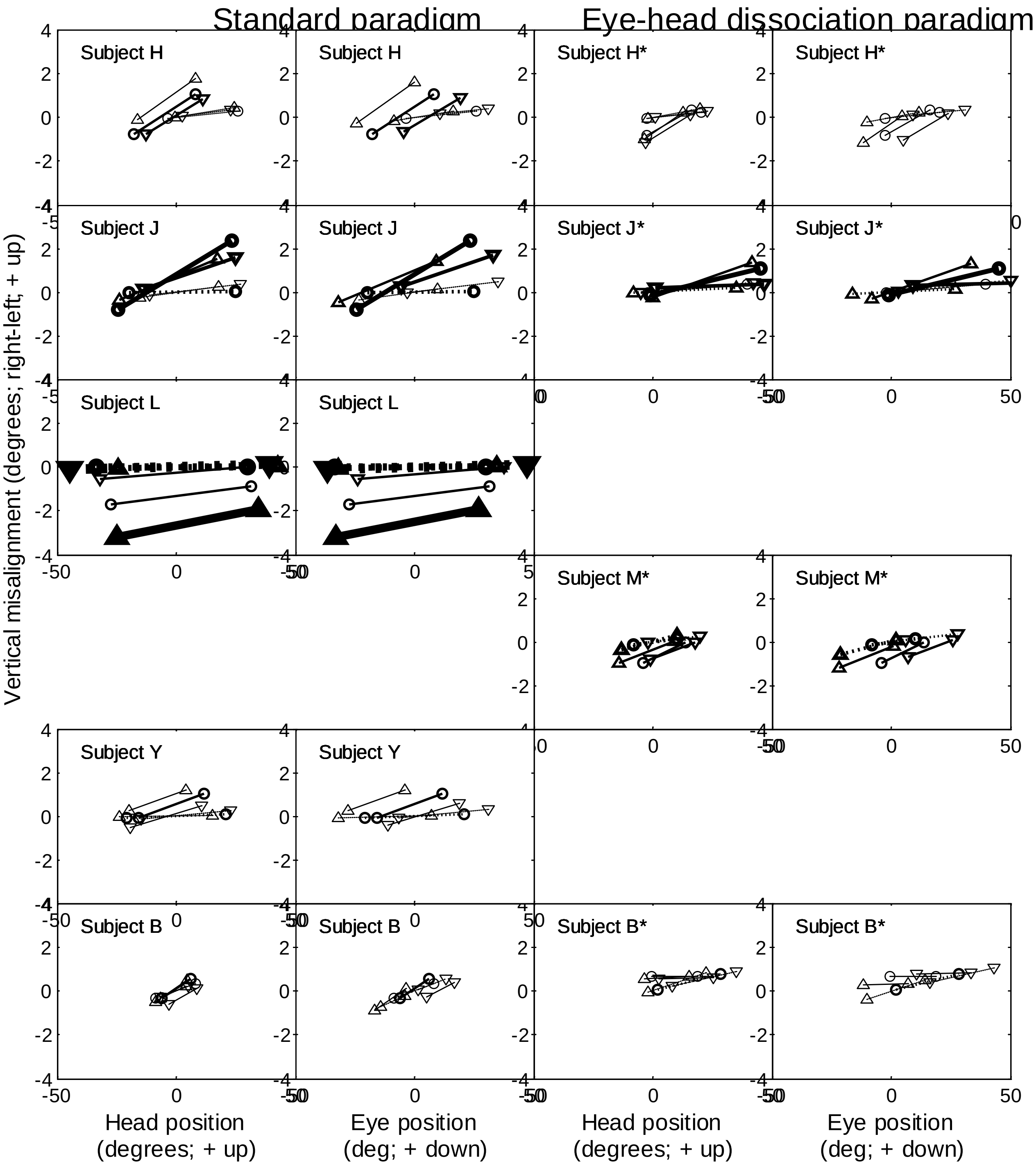
Pitch plasticity study

- Goal: understand the nature of central compensation
- Study the ability of the brain to learn an otolith organ-dependent misalignment during <u>dynamic</u> head movements
- Subject performs *active pitch rotation*
- Induced a vertical misalignment of the eye by presenting a visual disparity between the left and right eyes
- Subject wears red-blue glasses
- Real-time head position is fed to laptop which projects a field of dots onto a screen
- The dots have a vertical disparity between left and right eyes
- *Regular & eye-head dissociation* paradigms

Pitch plasticity study

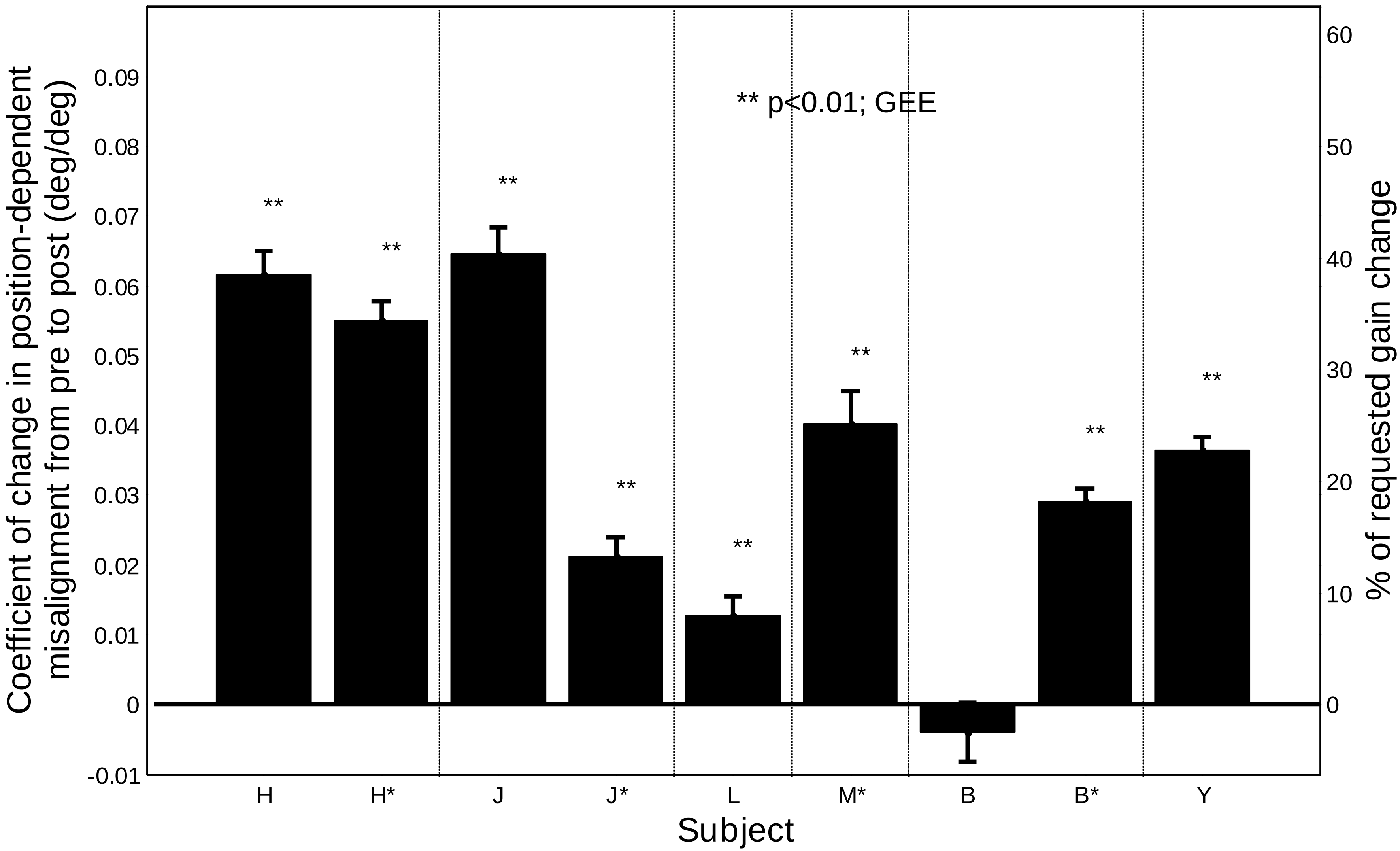



Misalignment vs. head position for three target positions (subject J)
Vertical misalignment (degrees; right-left; + up)
Head position (degrees; + up)
Post-adaptation
Pre-adaptation
4
3
2
1
0
-1
-2
-3
-4
-50
0
50



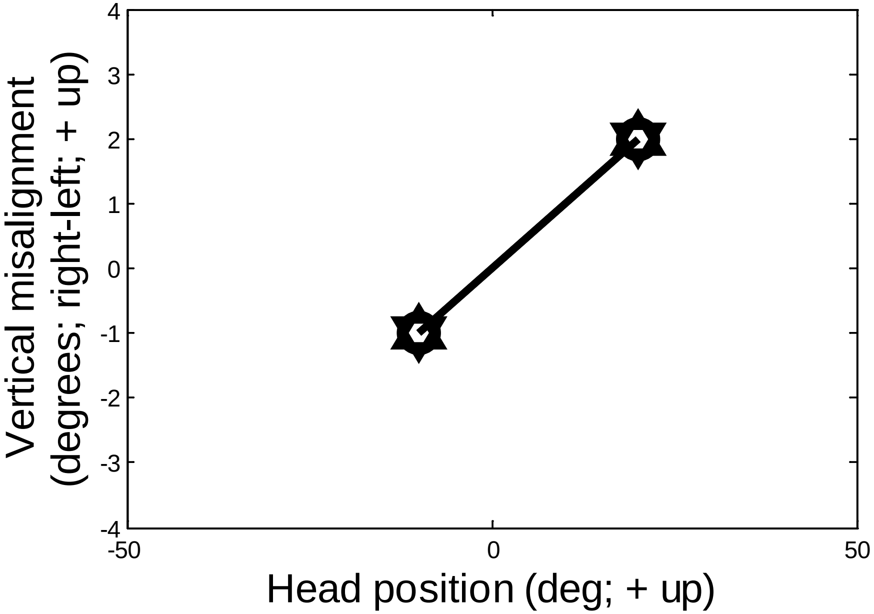
Standard paradigm
Eye-head dissociation paradigm
Subject H
Subject H
Subject H*
Subject H*
Subject J
Subject J
Subject J*
Subject J*
Subject L
Subject L
Subject M*
Subject M*
Subject Y
Subject Y
Subject B
Subject B
Subject B*
Subject B*
Vertical misalignment (degrees; right-left; + up)
Head position (degrees; + up)
Eye position (deg; + down)
Head position (degrees; + up)
Eye position (deg; + down)

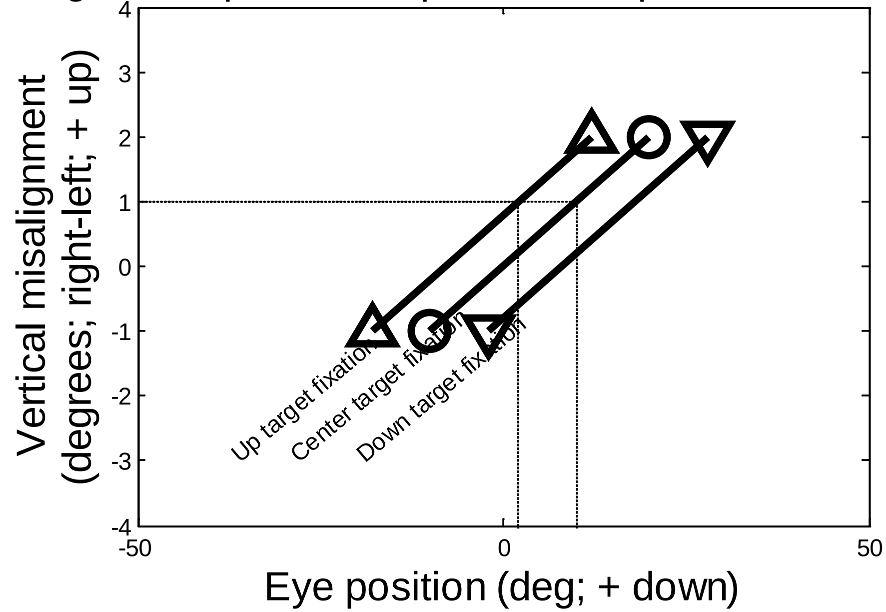
Position-dependent misalignment increased in most experiments



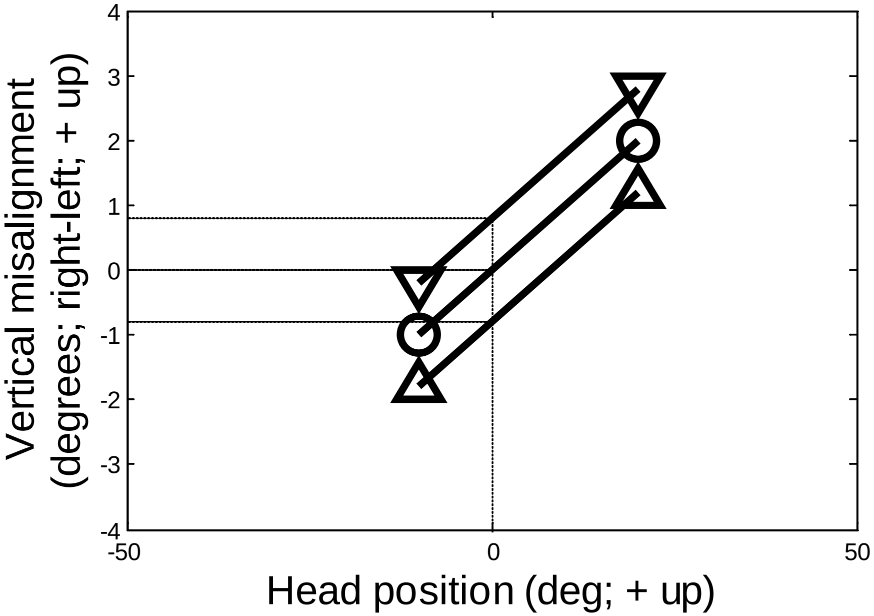
* *eye-head dissociation* paradigm

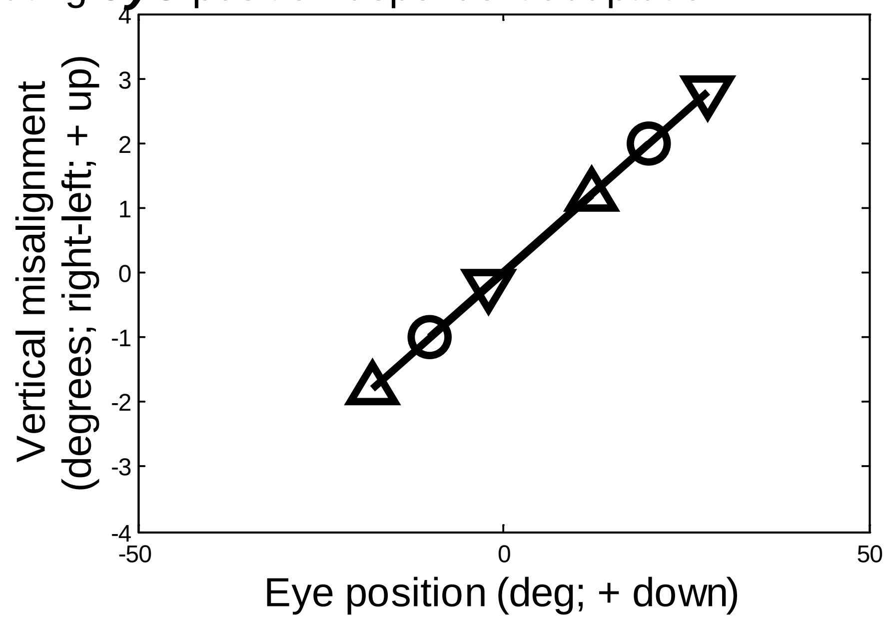
Ideal results demonstrating ***head*** position-dependent adaptation



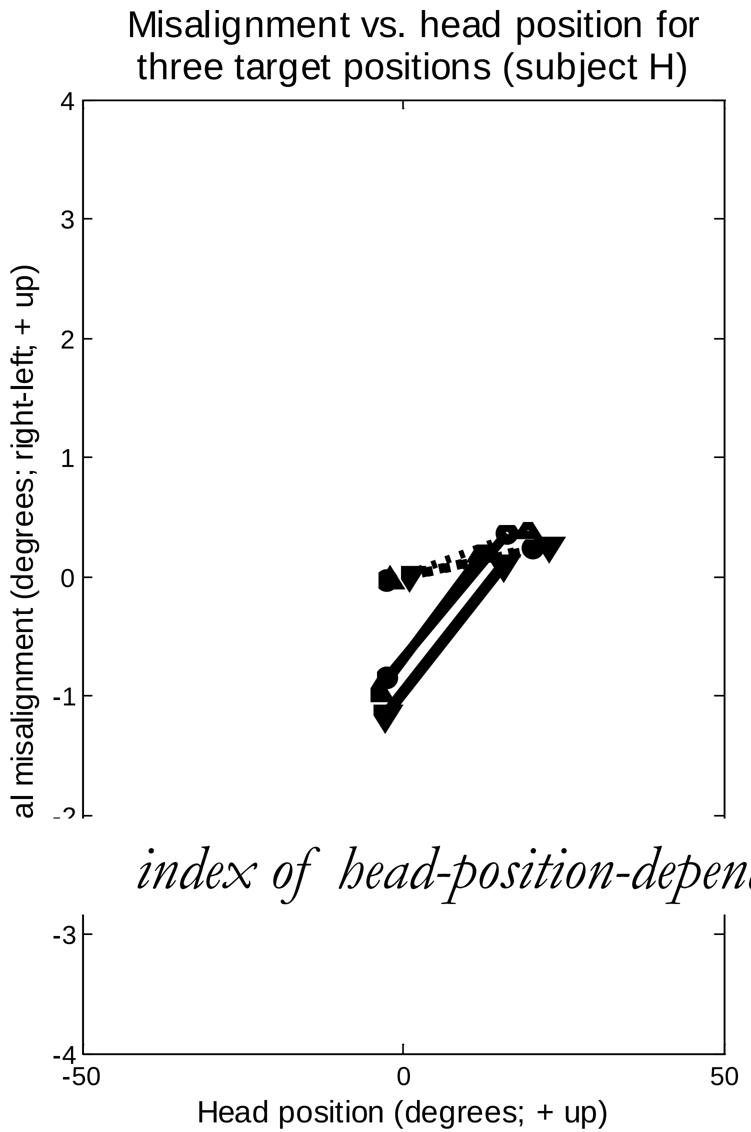


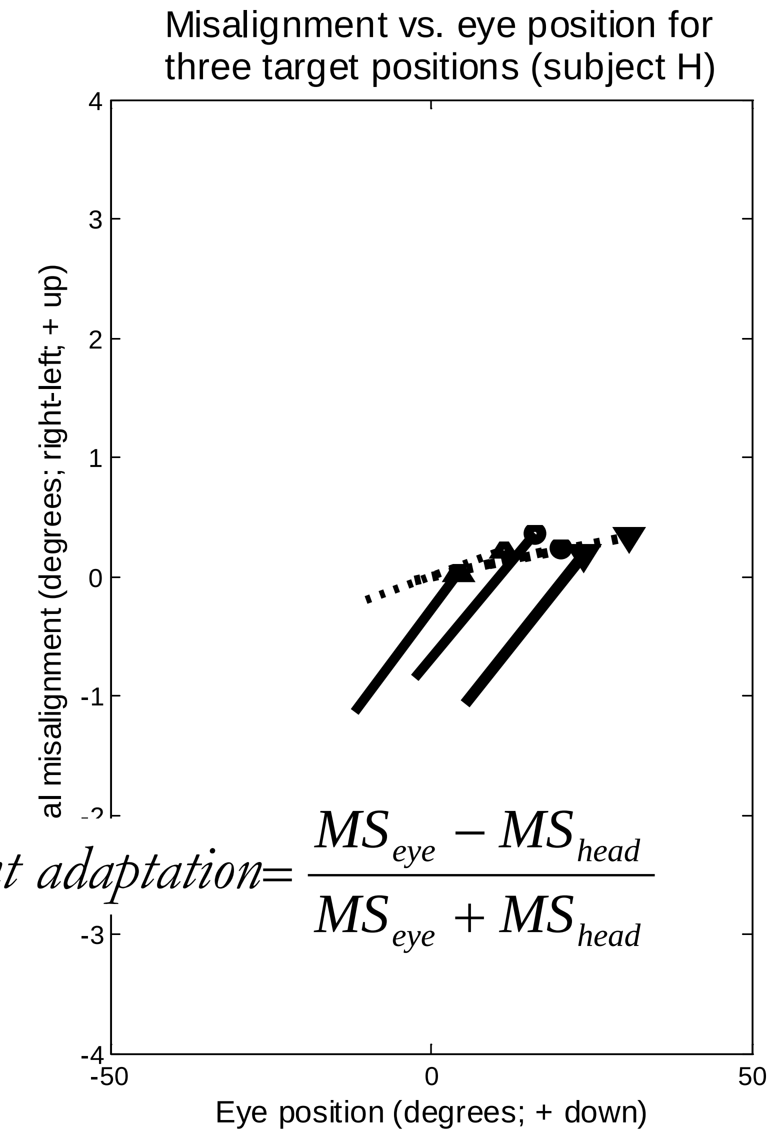
Ideal results demonstrating ***eye*** position-dependent adaptation





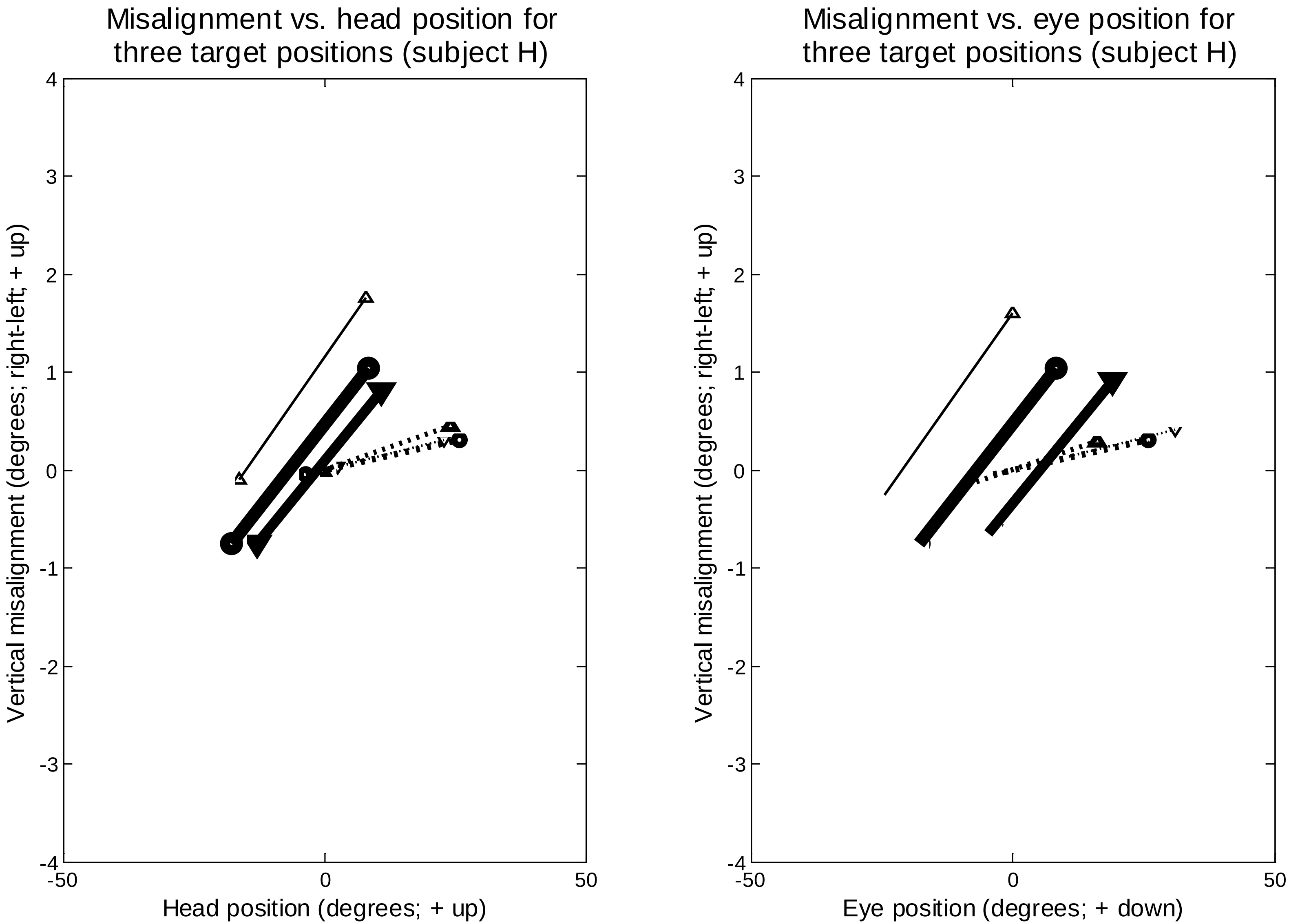
Example: misalignment dependent on head position





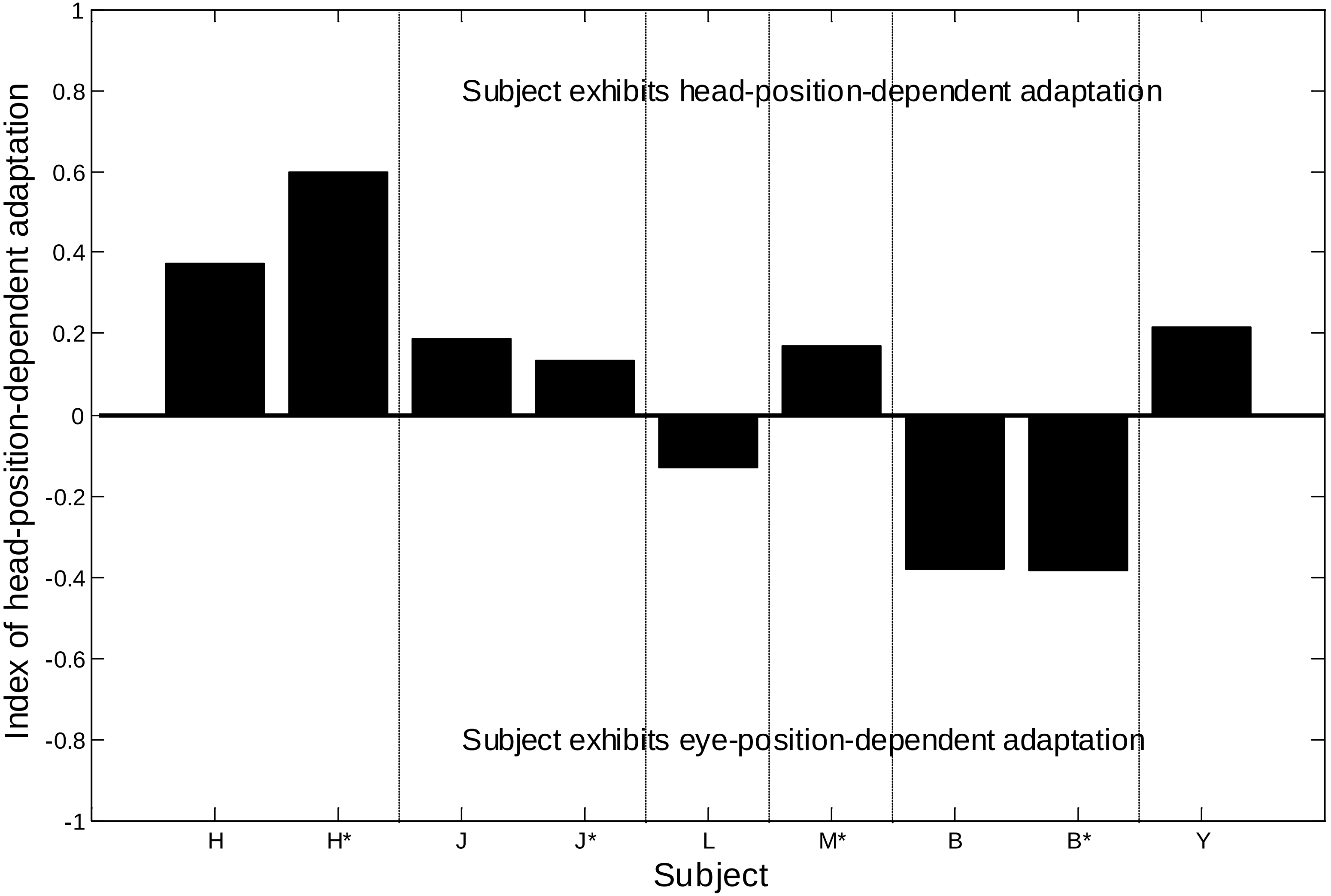
$$\textit{index of head-position-dependent adaptation} = \frac{MS_{eye} - MS_{head}}{MS_{eye} + MS_{head}}$$

Example: misalignment partly dependent on eye position



Is adaptation dependent on eye or head?

- Compare mean sum-of-squares of regression from misalignment on eye and misalignment on head



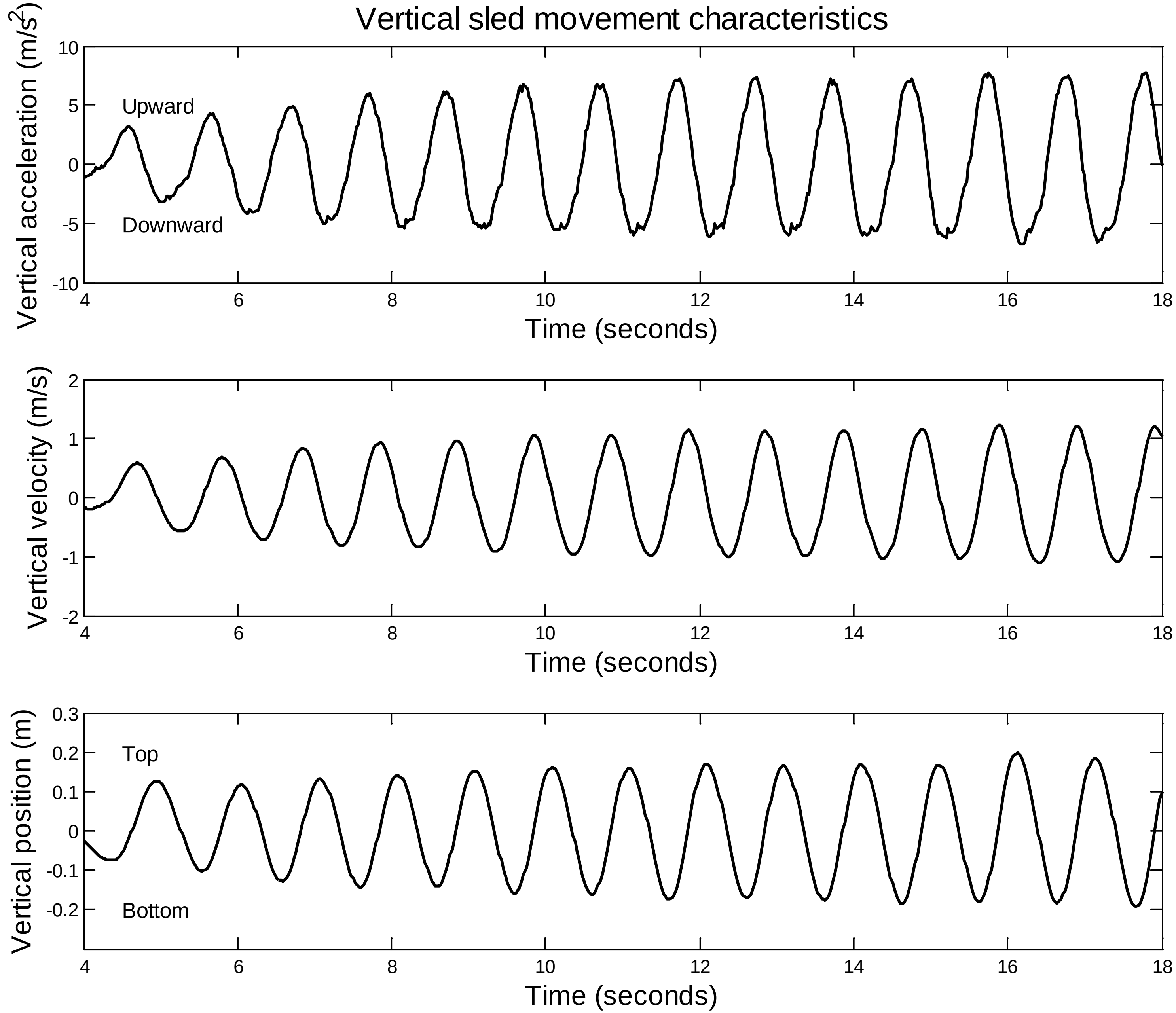
Pitch plasticity study – summary

- Position-dependent misalignments were adapted in all subjects
- Head position was implicated as the adaptation cue in most subjects
- Otolith organs or SCC could be driving adaptation
- In the next study, we performed this experiment and tested in *vertical translation*, which stimulated the otolith organs but not the SCC

Vertical translate study

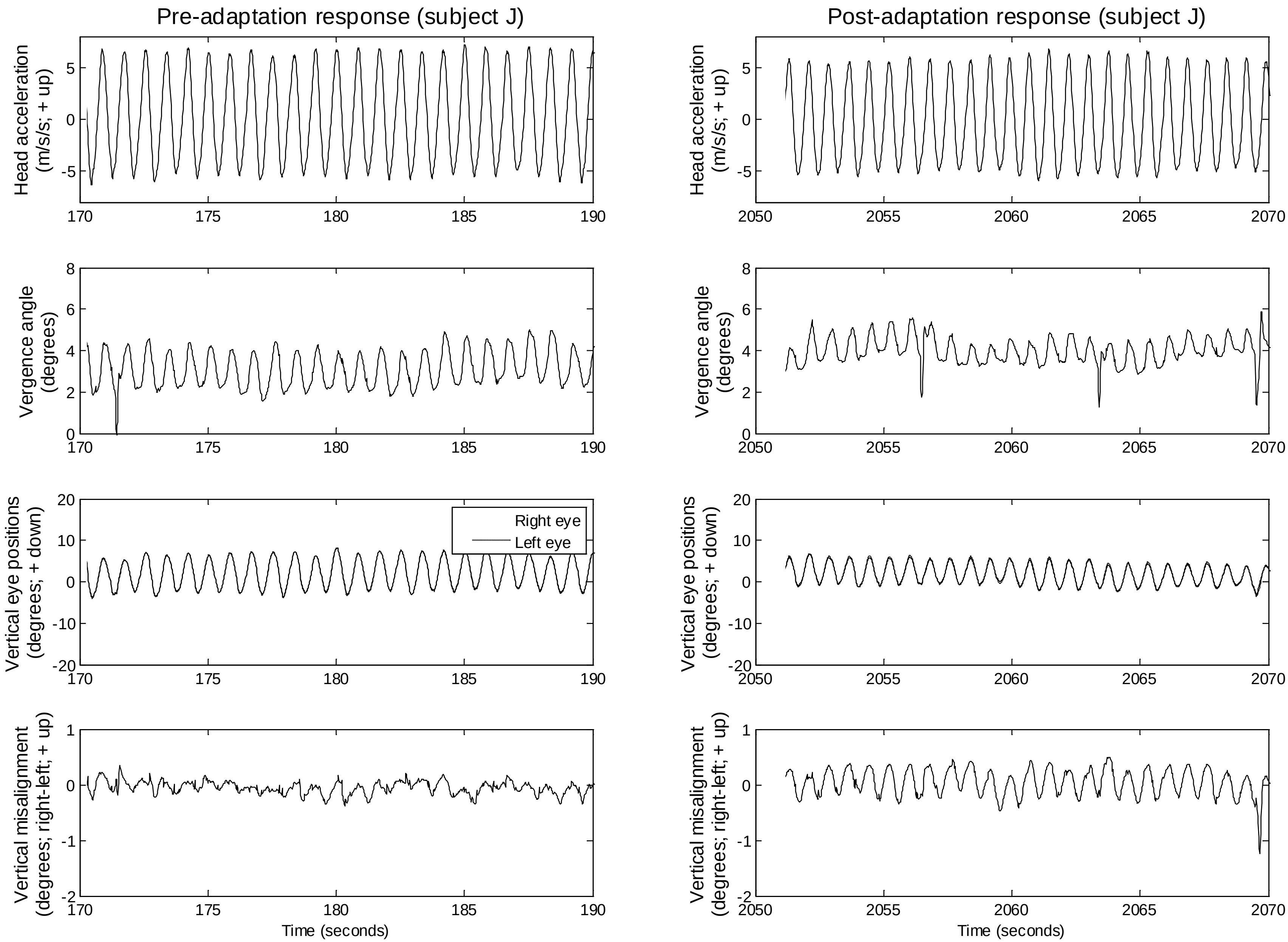
The *vertical translate study*

Pre-test Vertical (monocular target) → Pre-test Pitch (monocular target) → Adapt Pitch (15 min) → Post-test Pitch (monocular target) → Adapt Pitch (5 min) → Post-test vertical (monocular target)

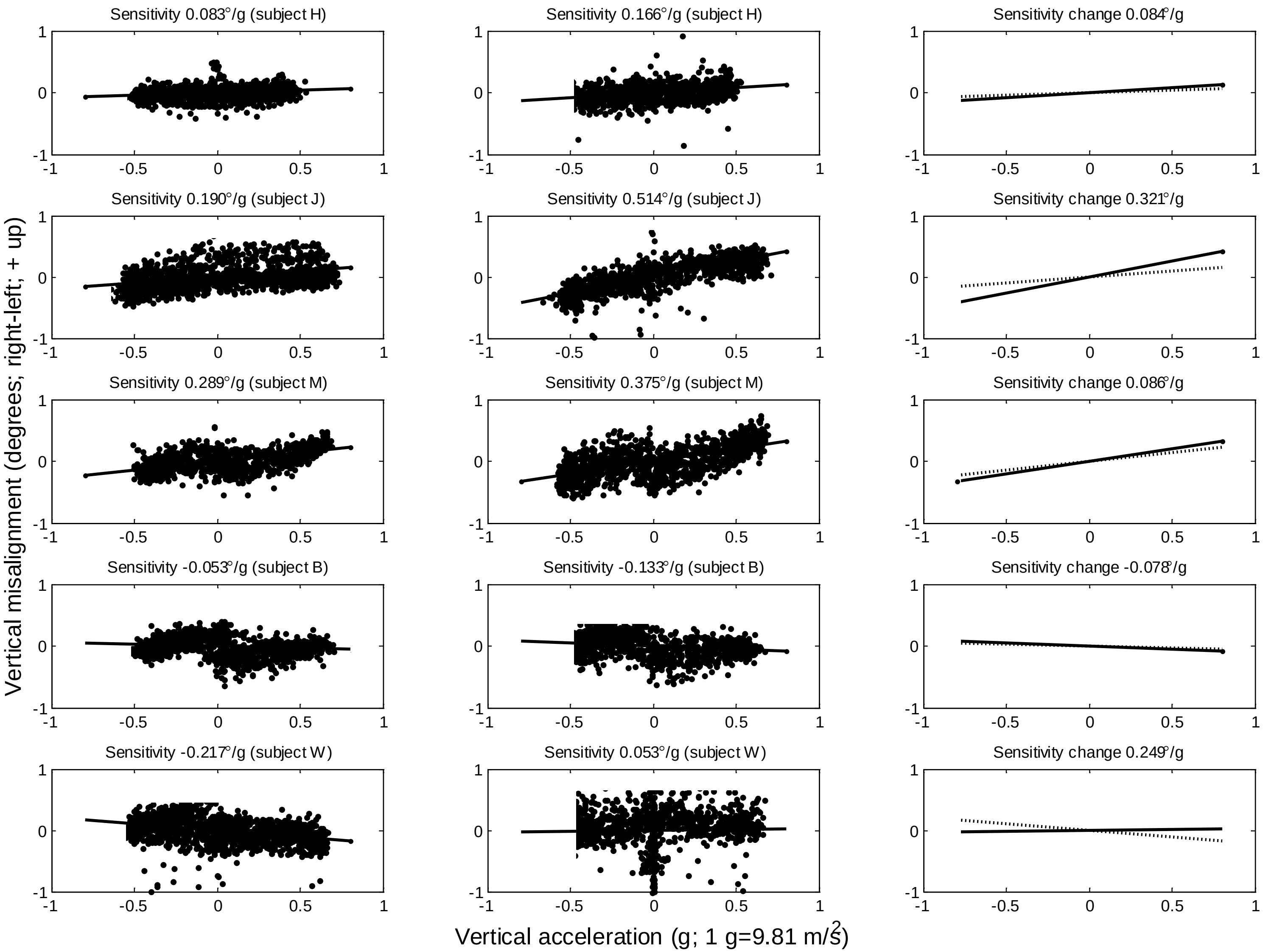


0.95 Hertz ±0.7 g peak acceleration

Response to vertical translation

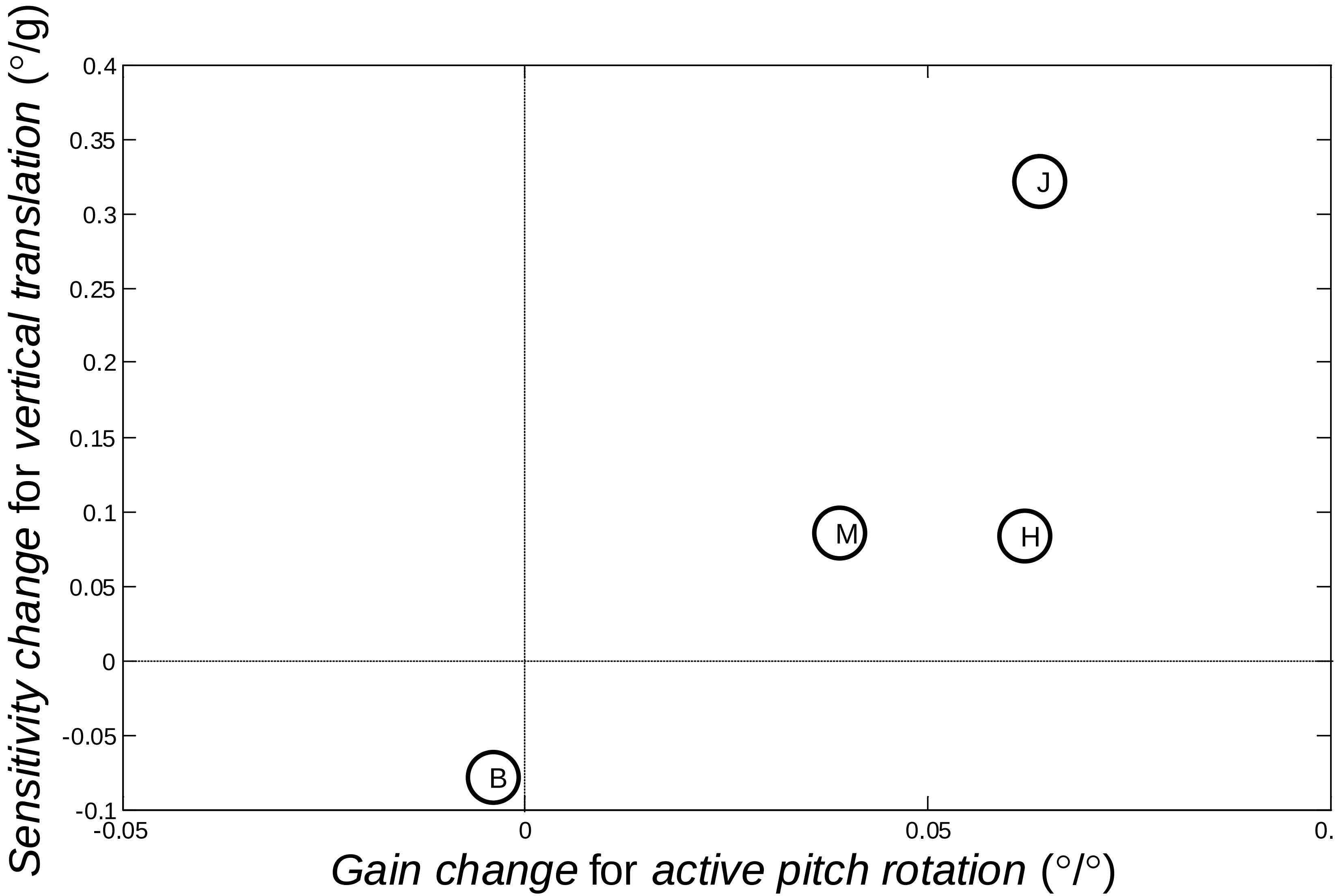


Sensitivity to vertical translation increases after adaptation of pitch response



- Increase in sensitivity increases for 4 of 5 subjects
- Change statistically significant in all subjects (GEE)

Sensitivity to vertical translation increases after adaptation of pitch response



Vertical translate study – summary

- Head-position-dependent adaptation of misalignment during pitch rotation was otolith organ dependent
- Adaptation transferred from otolith-dependent tilt response to otolith-dependent translation response
- Misalignment is a tool to study the otolith-ocular pathway: it allows questions to be asked about tilt/translation which are difficult to answer using conjugate eye movements

Modeling

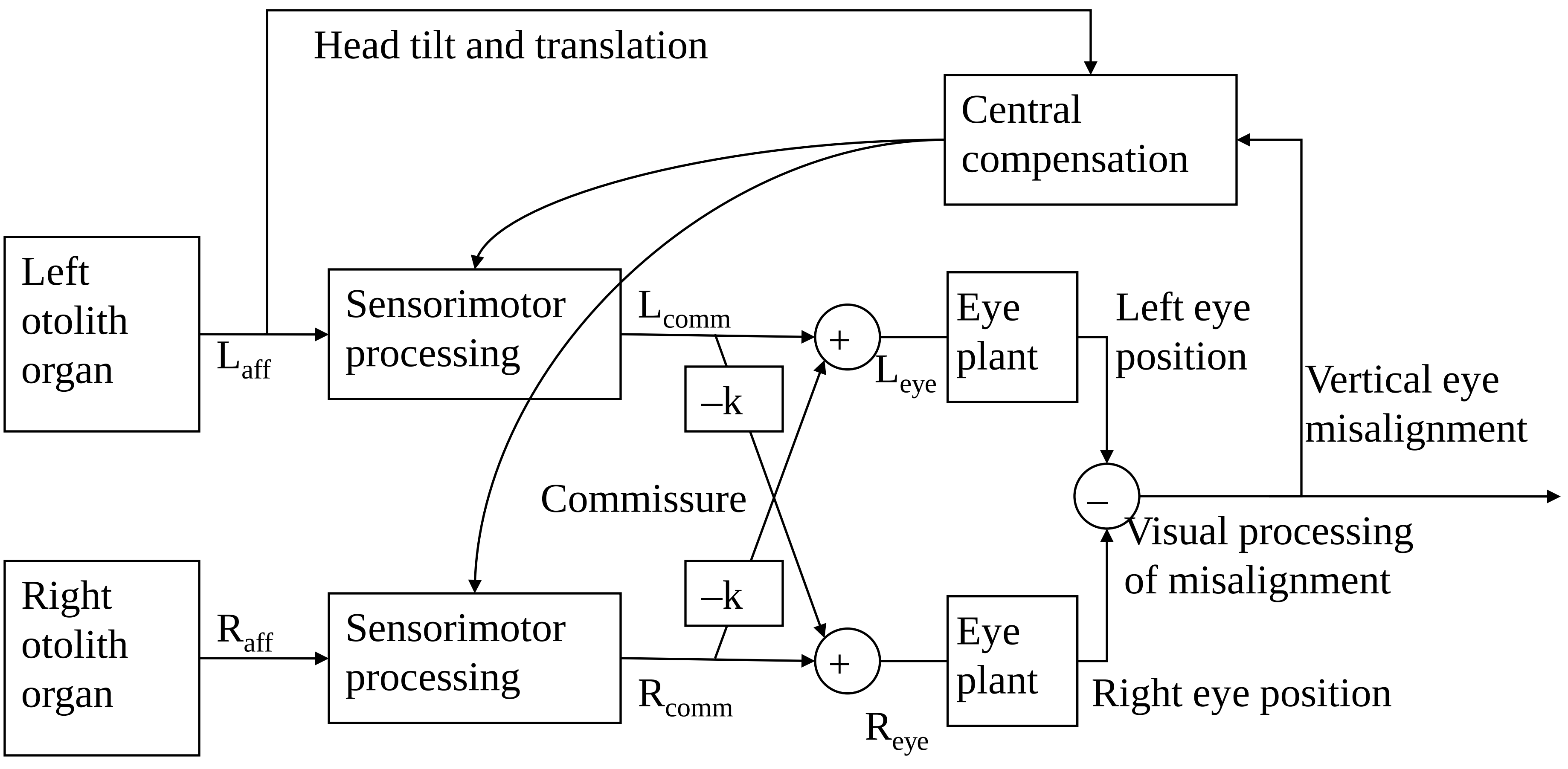
- What is the nature of the central compensation?
- What model of otolith organ information processing explains the transfer of adaptation from pitch rotation to vertical translation?

Model overview

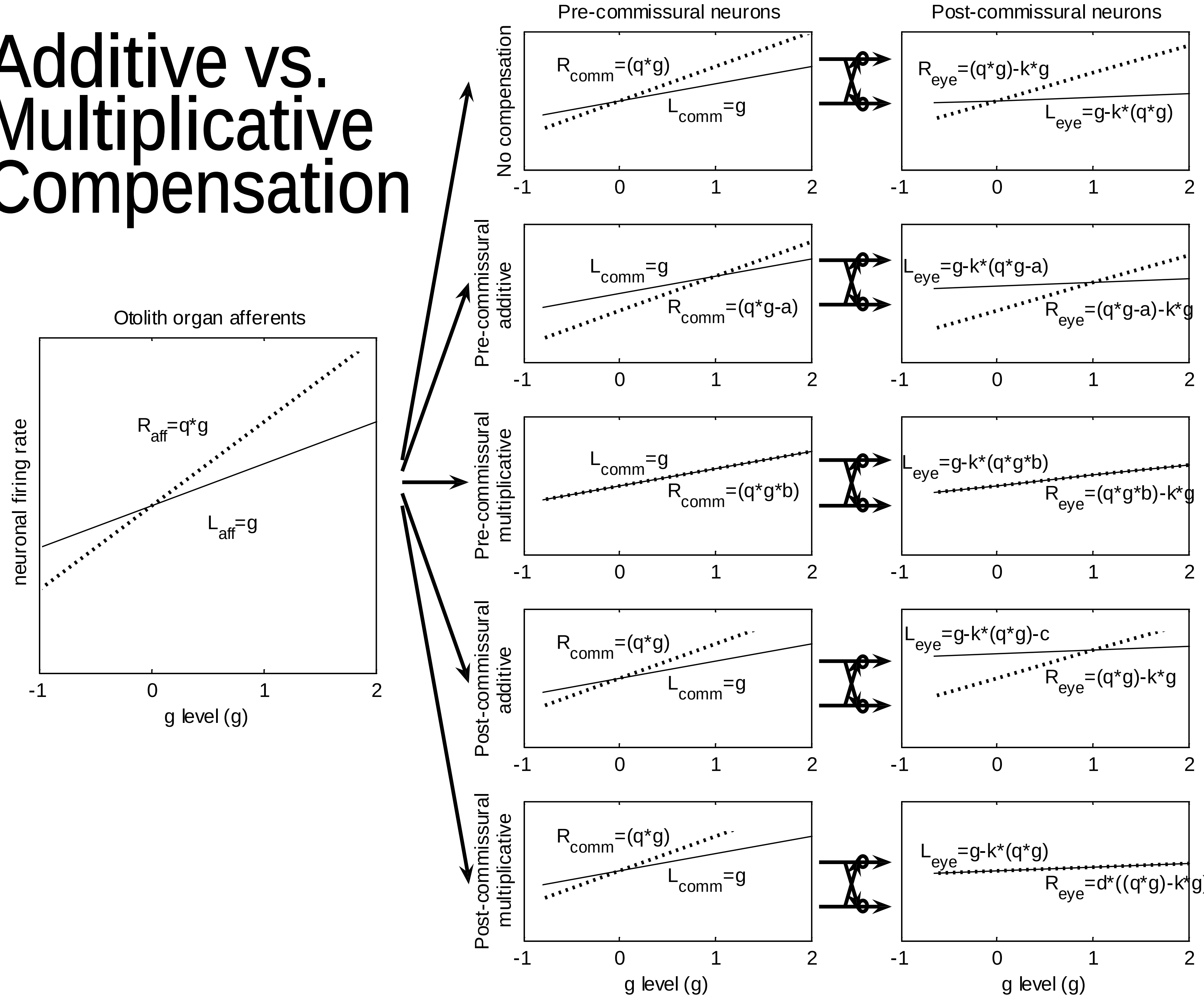
Additive

Multiplicative

Context-specific adaptation



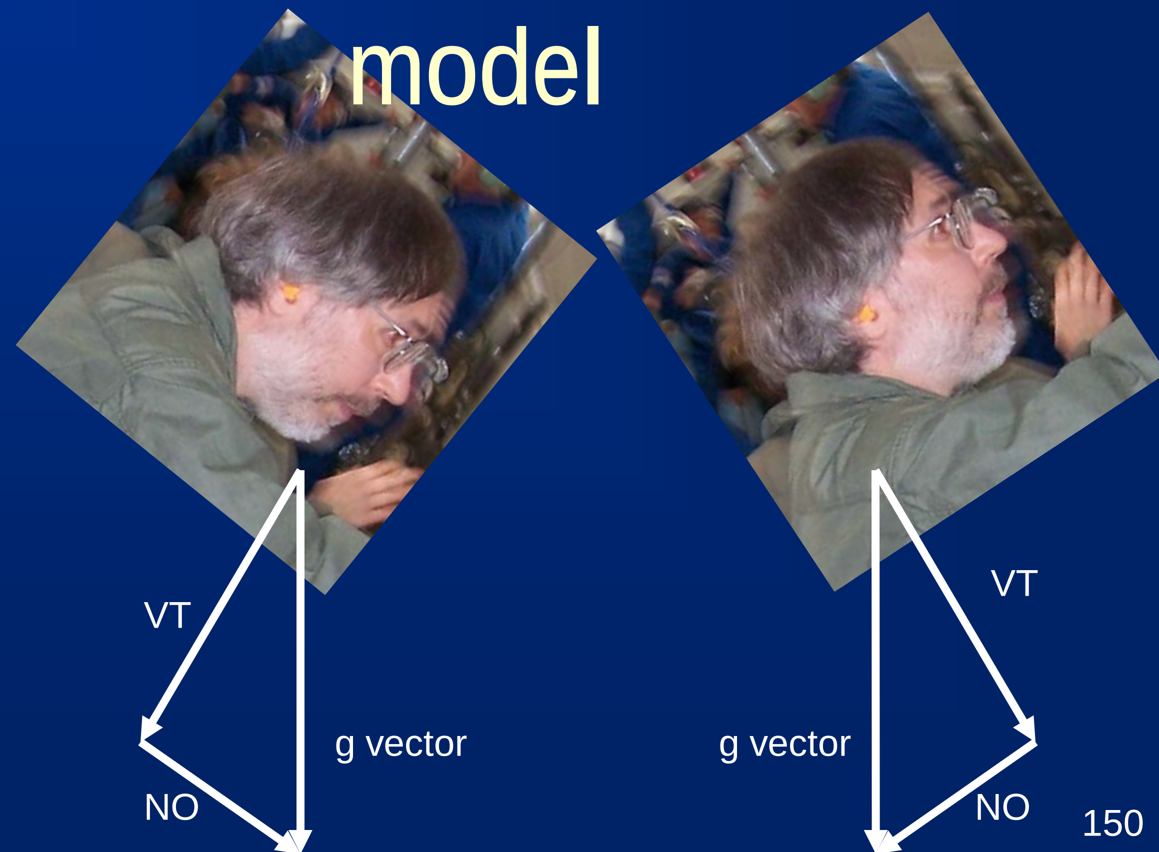
Additive vs. Multiplicative Compensation

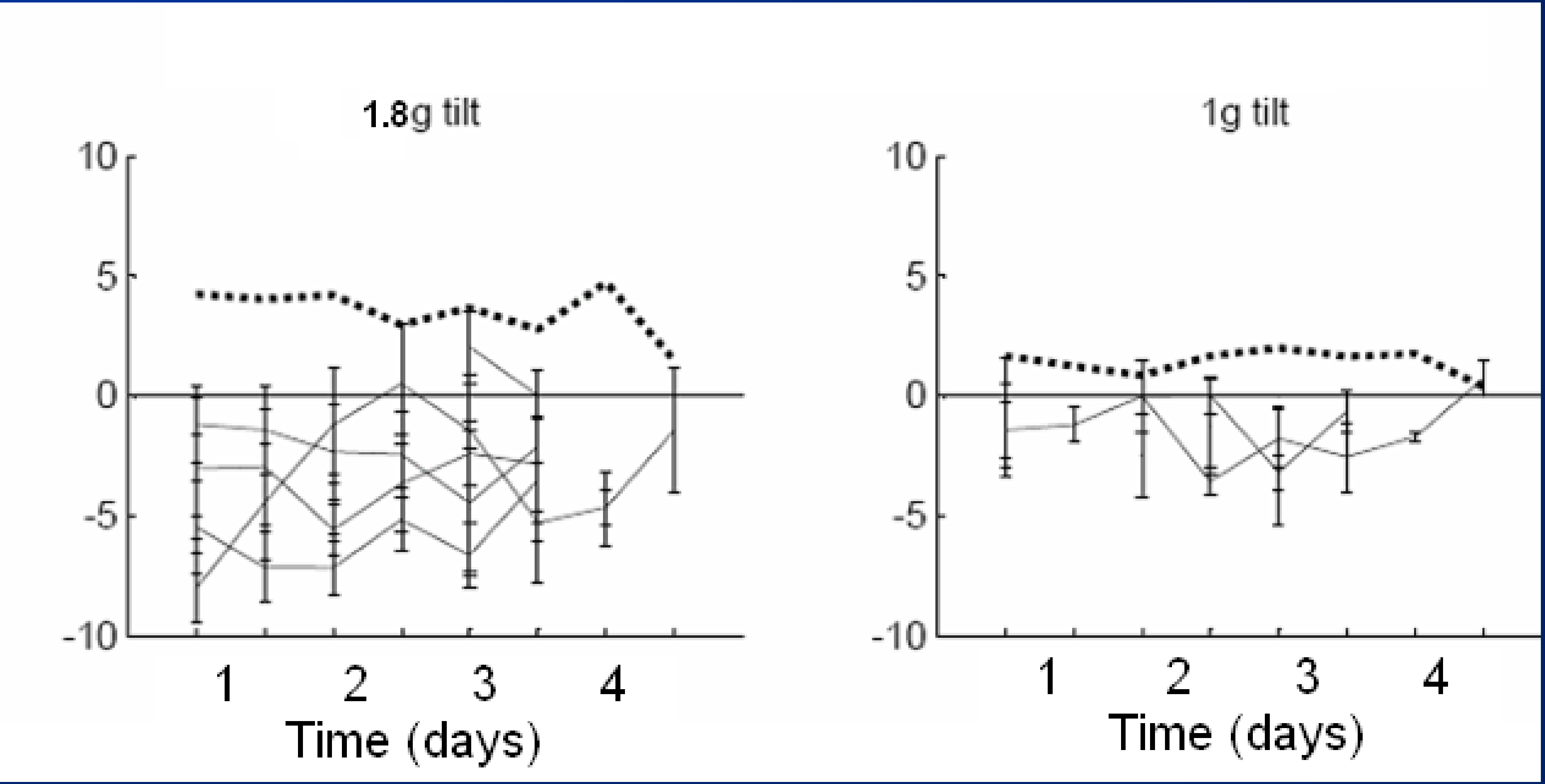


What model of otolith organ information processing explains the transfer of adaptation from *pitch* to *vertical translation?*

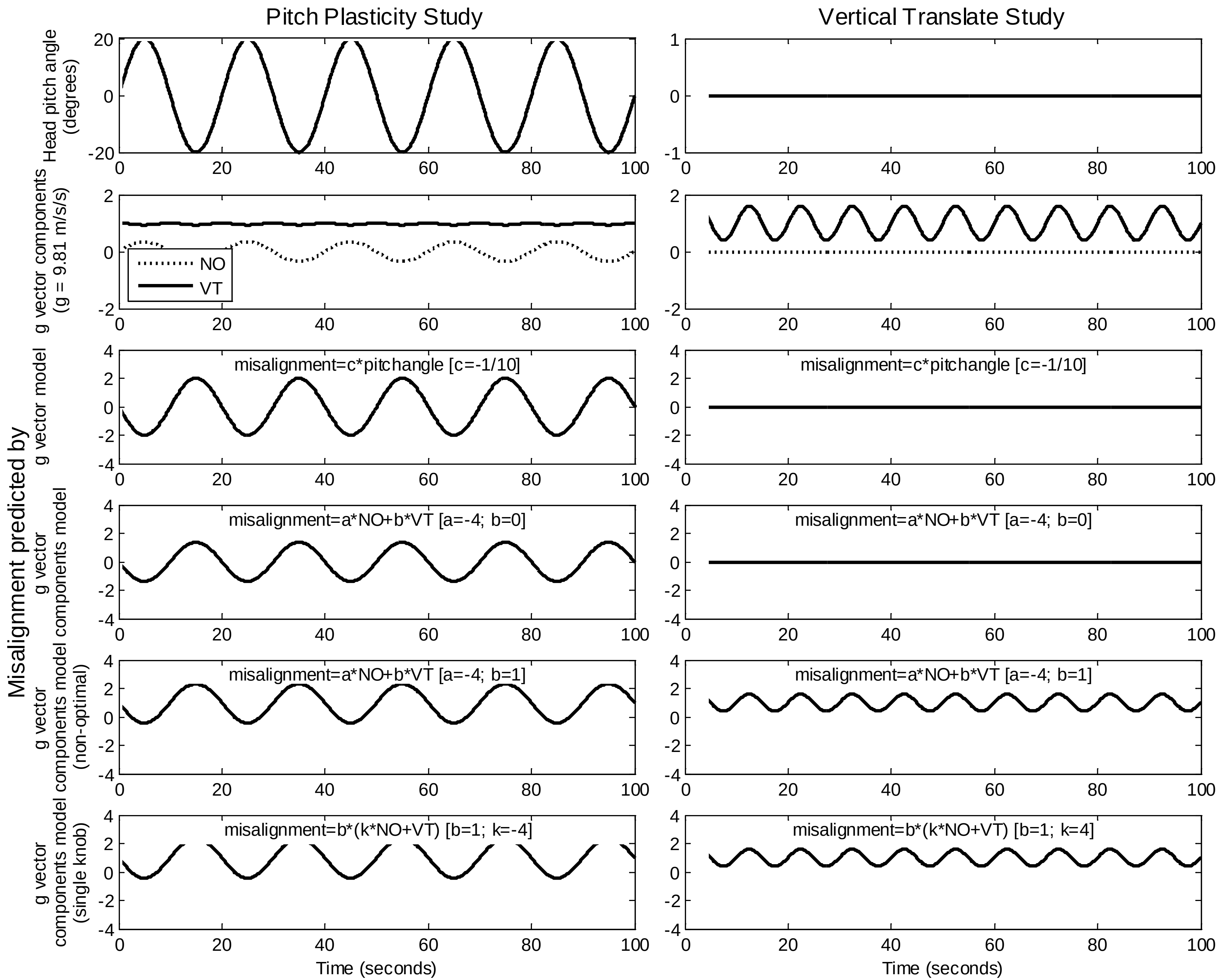
g vector model

g vector components model





- Eye torsion with head tilted during change g level
- Torsion changes even though g vector direction does not change
- Suggests the g vector component determines torsion



Pitch Plasticity Study
Vertical Translate Study
Head pitch angle (degrees)
g vector components (g = 9.81 m/s/s)
NO
VT
Misalignment predicted by
g vector model
misalignment=c*pitchangle [c=-1/10]
g vector components model
misalignment=a*NO+b*VT [a=-4; b=0]
g vector components model (non-optimal)
misalignment=a*NO+b*VT [a=-4; b=1]
g vector components model (single knob)
misalignment=b*(k*NO+VT) [b=1; k=-4]
misalignment=b*(k*NO+VT) [b=1; k=4]
Time (seconds)

Modeling – summary

- Context-specific adaptation is a likely candidate for central compensation
- Otolith organ information is processed in g vector components
- Adaptation affects all g vector components equally

Conclusions

- Vertical eye misalignments that are dependent on the otolith organs occur during pitch rotation
- Vertical eye misalignments that are dependent on the SCC occur during *fast* pitch rotation
- Otolith-dependent misalignments can be adaptively created during dynamic pitch rotation using a visual-vestibular mismatch
- Context-specific adaptation is a likely candidate for central compensation
- Components of the g vector are used to determine the ocular response; adaptation affects all components equally

Implications

- Understanding central compensation in the otolith-ocular pathway can improve the design of adaptation regiments for both astronauts and patients
- Understanding how otolith information is used by the brain can guide the selection of motion profiles used for adaptation paradigms
- The ability to measure innate misalignments using pitch rotation may help in assessing risks during spaceflight

Future work

- Model a SCC asymmetry by having canal planes that are slightly different in the left and right ear
- The relationship between head position and misalignment in the adaptive paradigm was linear – a parabolic relationship would help to separate otolith and SCC contributions
- In *fast* rotation, SCC-dependent misalignments were implicated – further investigation is required
- Transfer of adaptation from *vertical translation* to *pitch rotation*
- Transfer of adaptation between otolith-dependent tilt and translation with conjugate eye movements

Future work

Head orientation during adaptation		during first test		during second test	
rotation axis	g vector components stimulated	rotation axis	g vector components stimulated	rotation axis	g vector components stimulated
Pitch upright	VT & NO	Roll onside	VT (&IA)	Yaw onside	NO (&IA)
Roll upright	VT & IA	Pitch supine	VT (&NO)	Yaw supine	IA (&NO)
Yaw supine	NO & IA	Pitch upright	NO (&VT)	Roll upright	IA (&VT)

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- Scientific advise: Dr. Mark Walker, Dr. Howard Ying, SPH Biostats Clinic
- Undergraduate researchers: Ondrej Juhasz, Anton Aboukhalil, Tiffany Chen, Michelle Zwernemann
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- Funding: NSBRI, NIH, NSERC

Control of motion and posture

(AP Photo/Misha Japaridze)

The Vestibular System

- “Sixth sense” that keeps us balanced
- Stops us from falling when we stumble
- Helps move eyes (“gaze stabilization”)

Patients with Vestibular Disease or stroke	Astronauts affected by microgravity
Vertigo Difficulty walking Eyes move incorrectly	Vertigo and motion sickness Difficulty walking upon return Eyes move incorrectly

- Studying astronauts will help us cure people on the ground

Background & Significance

- Astronauts and others exposed to unusual acceleration environments get sick
- Torsional misalignment found in parabolic flight and may be due to otolith asymmetry
- Motion sickness correlated with torsional misalignment
- Motion sickness correlated with an otolith mass asymmetry in fish
- In pitch head movements, the otoliths detect a changing g vector and contribute to eye movements

Vestibular-Ocular Reflexes

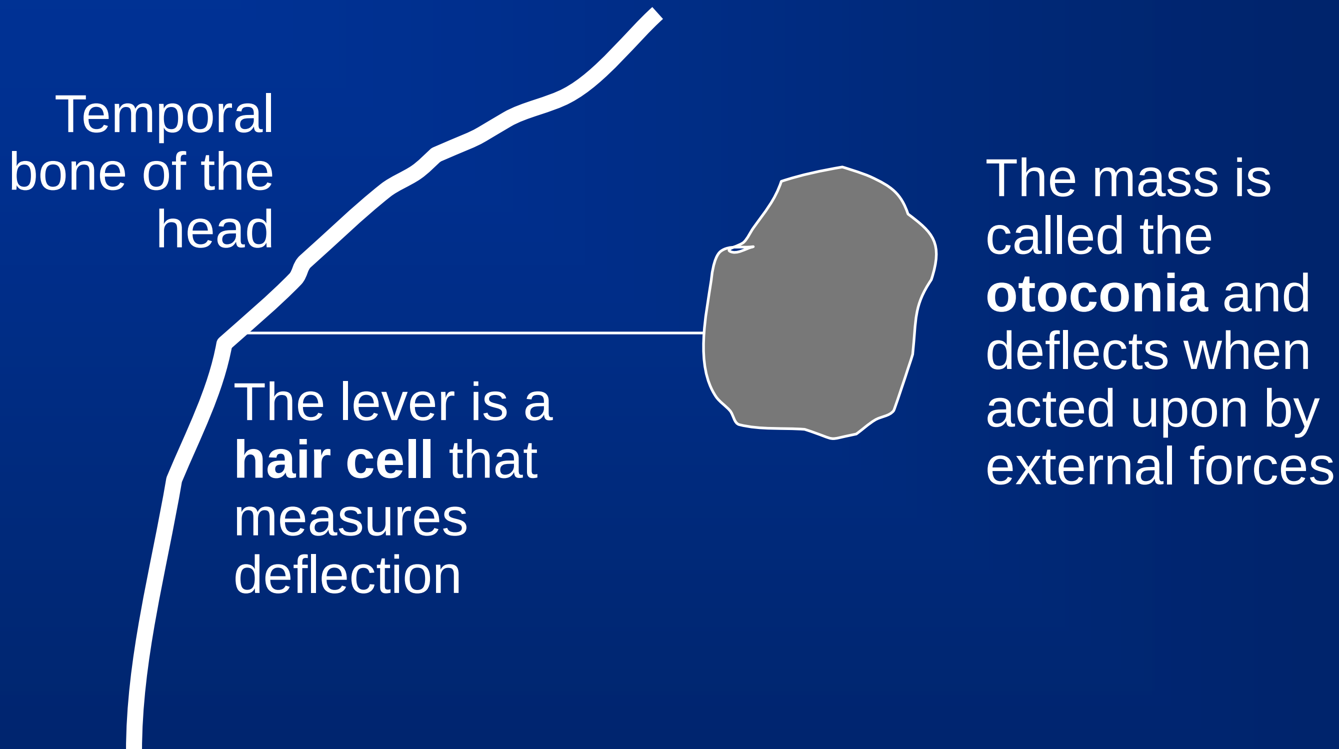
- **Otoliths** measure linear acceleration and gravity (contains **utricle** and **saccule)**
- **Semicircular canals (SCC)** measure angular velocity

- Eye movements opposite of head movements
- **Torsion** is rotation of eye about the line of sight
- **Conjugate:** eyes move together
- **Disconjugate**: difference between left and right eyes

Eye misalignment between L and R eye position

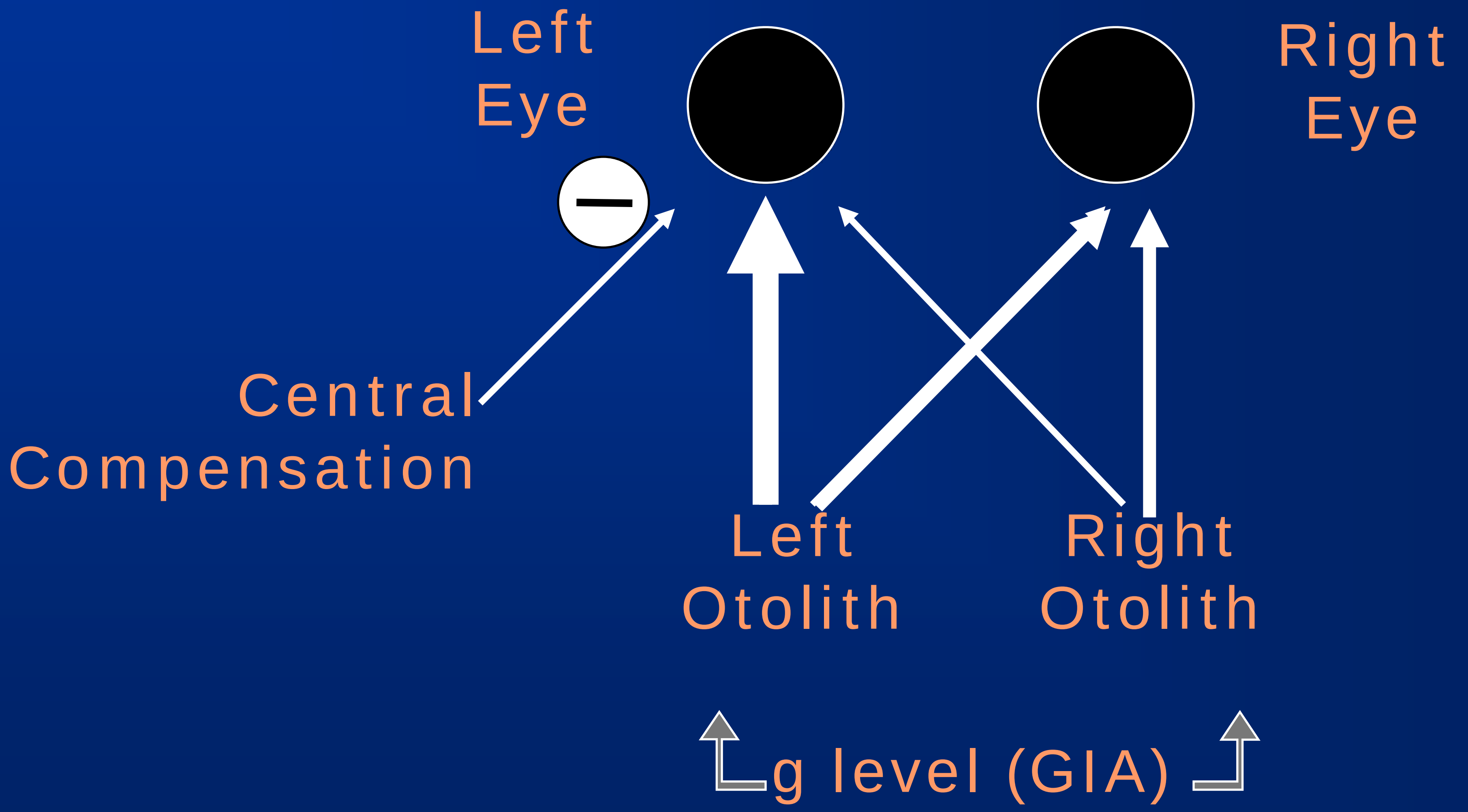
Visual disparity between what is seen by L and R eye

The otoliths: a mass on a lever



Gravito-inertial acceleration (g level): the sum of linear acceleration and gravity. 1 g of downward gravity is indistinguishable from 1 g of upward acceleration of the head

Otolith Asymmetry Hypothesis



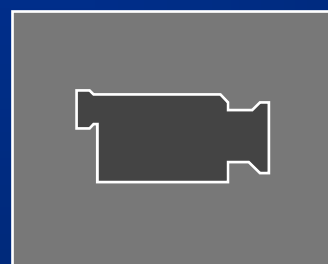
Implications of otolith asymmetry

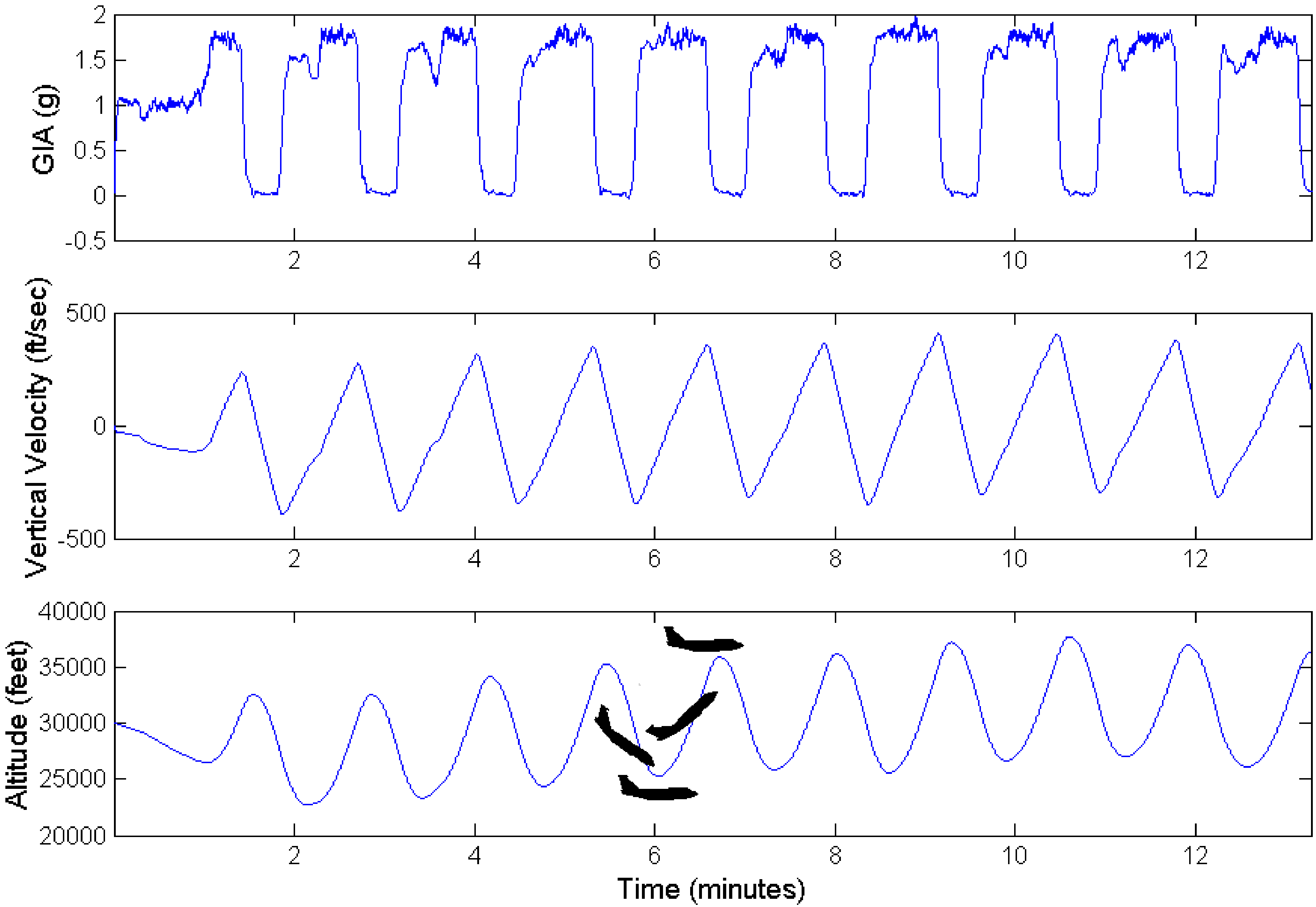
1. It can predict space sickness: a better understanding of the mechanisms may help to improve screening and produce simpler screening tests
2. It may reduce performance by misaligning the eyes
3. Understanding how it adapts may be useful in training including partial adaptation before flight

Hypotheses

- An otolith asymmetry will manifest as ocular misalignments when the magnitude and orientation of the g vector is unusual.
- An otolith asymmetry will imbalance the otolith contribution to the pitch VOR, resulting in ocular misalignment
- A reduction is misalignment will occur with experience in an environment, and this adaptation occurs within the central compensation mechanism

Experimental Methods: Parabolic Flight

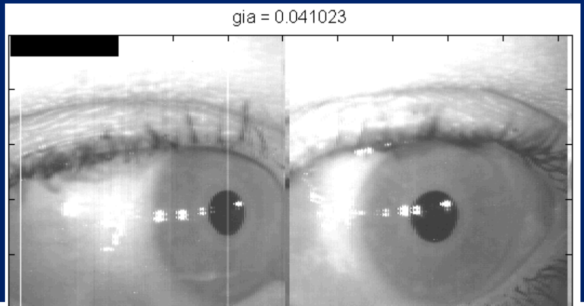


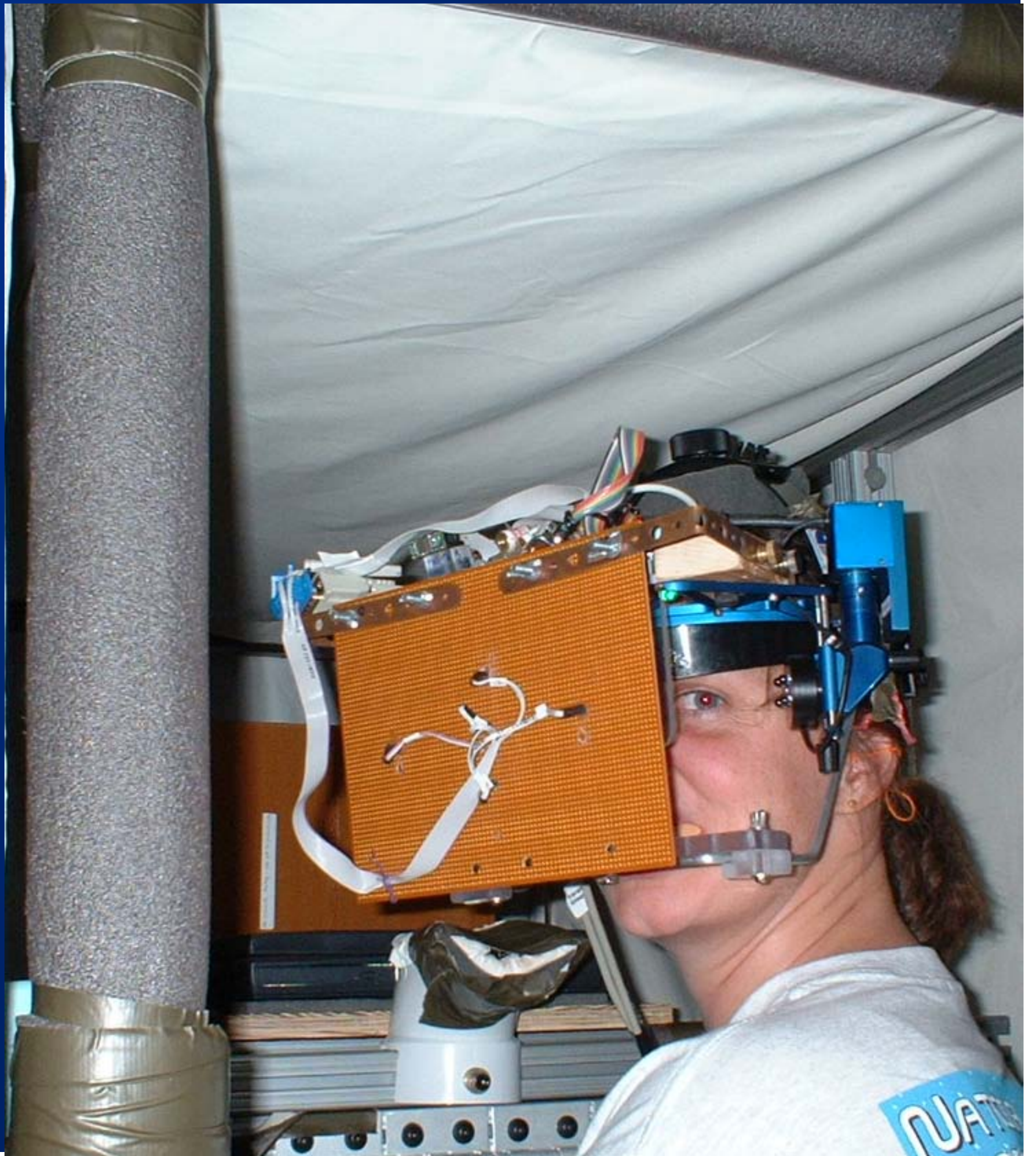


GIA (g)
Vertical Velocity (ft/sec)
Altitude (feet)
Time (minutes)

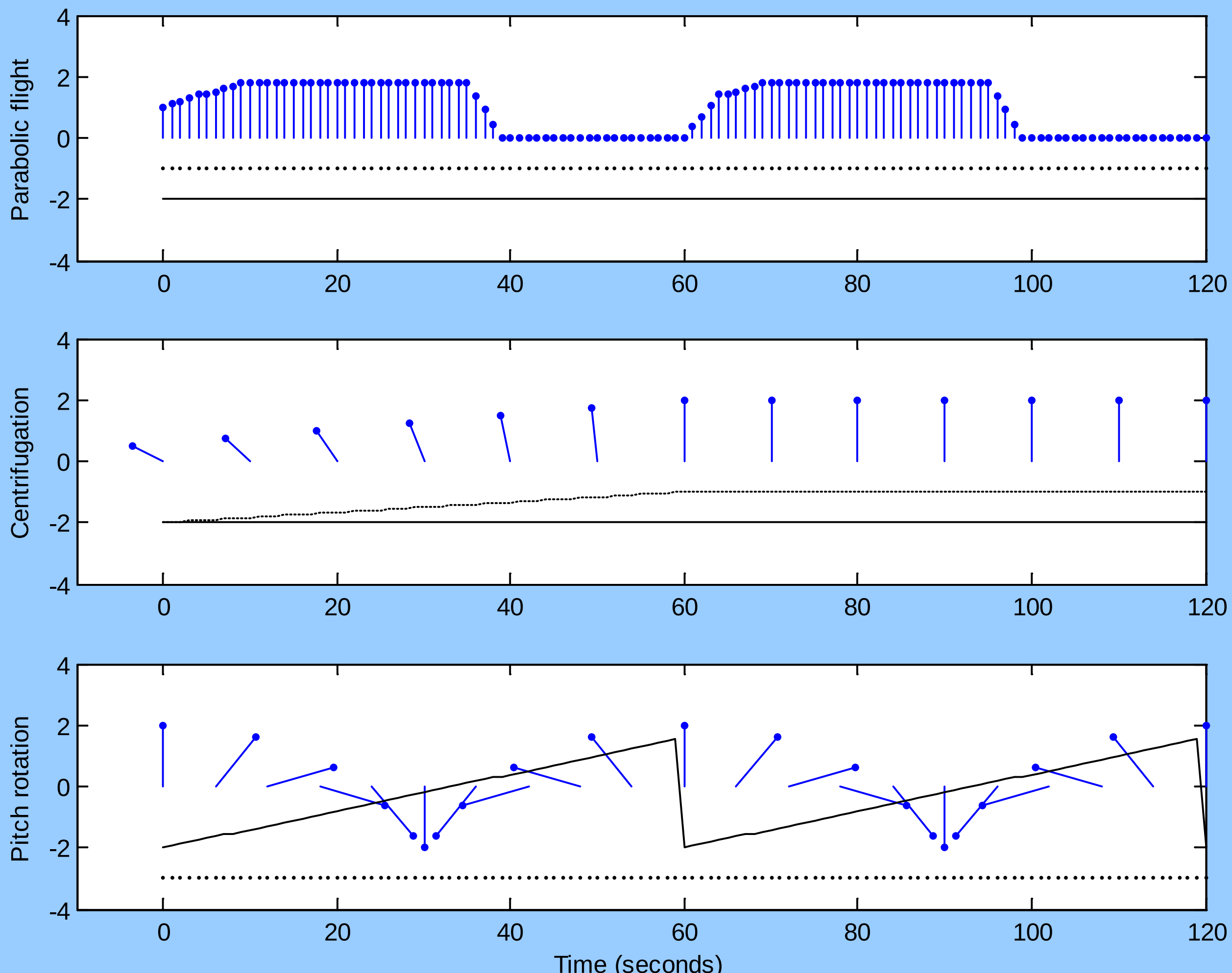
Experimental Methods: Video eye movement recording

- Binocular (both eyes)
- 50 Hz
- Accelerometers and rate sensors
- Subjects in darkness
- Software finds pupil in image and computes gaze direction





Experimental Methods: Summary



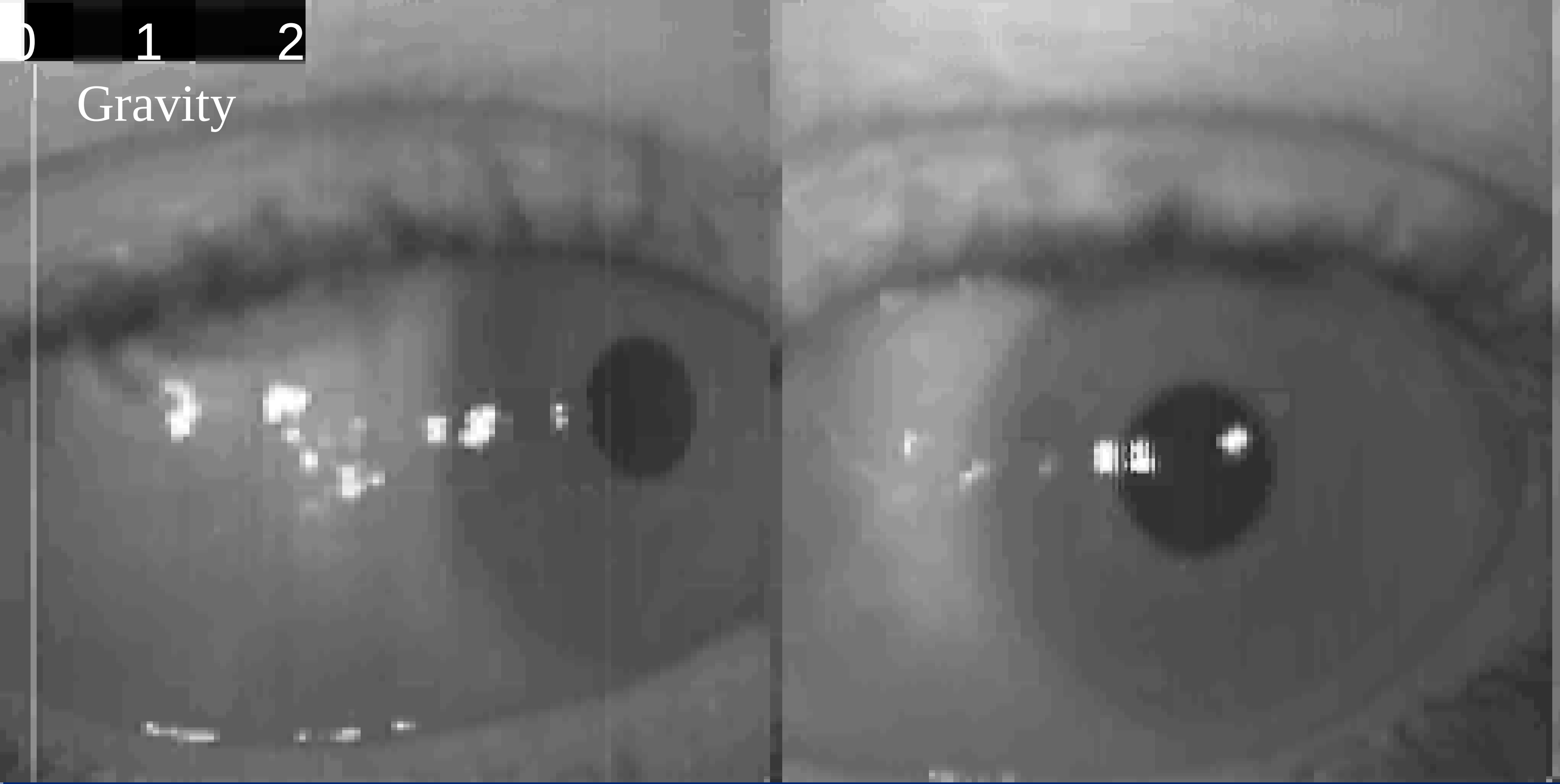
Parabolic flight
Otolith: vertical; change in magnitude (0-1.8 g) but not direction
Pitch rotation: 3 º/s
Roll rotation: 0 º/s
Yaw rotation: 0 º/s

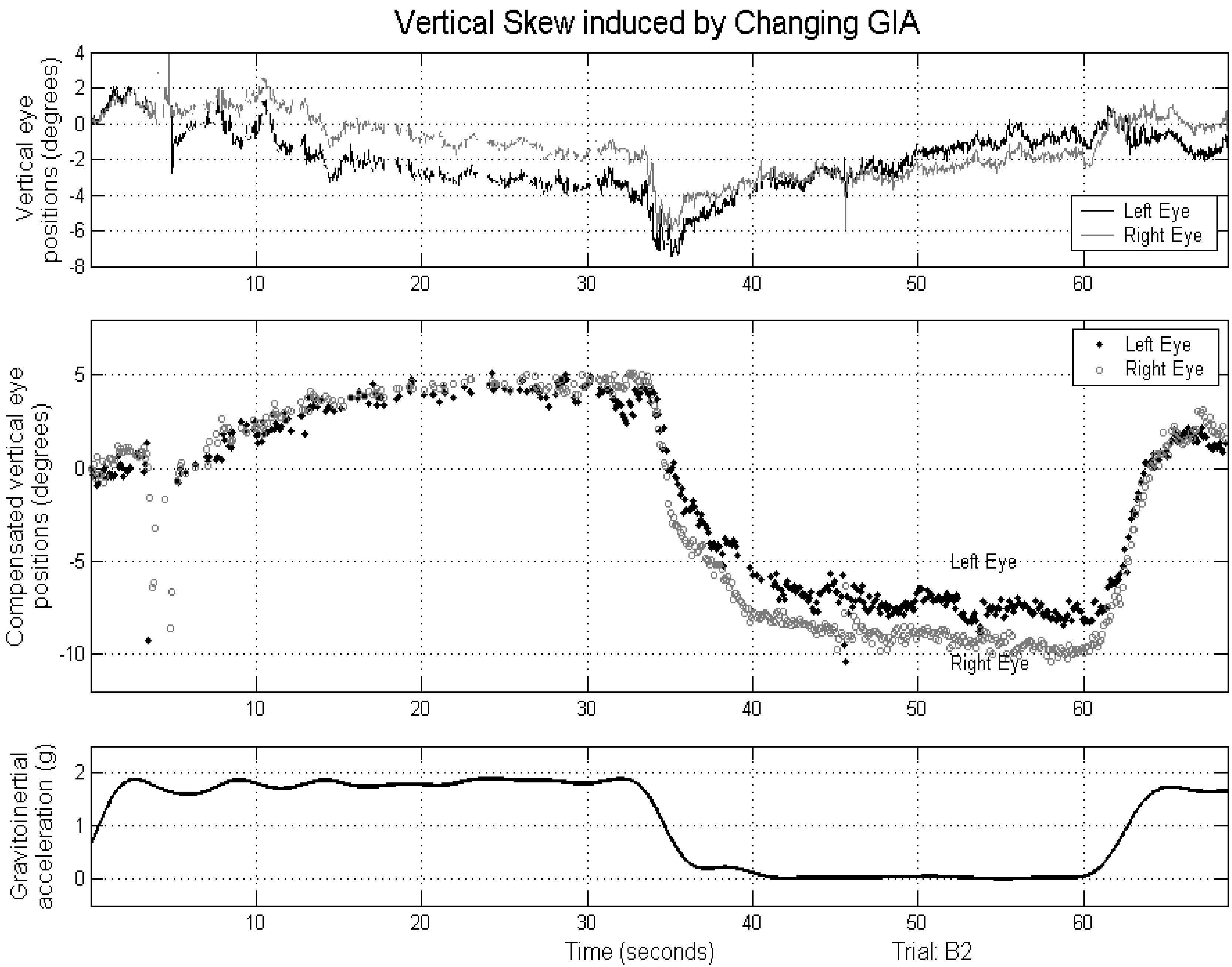
Centrifugation
Otolith: rotates in roll to vertical; change in magnitude 1-2 g and direction
Pitch rotation: 0 º/s
Roll rotation: 1 º/s
Yaw rotation: 0 º/s to 100 º/s

Pitch rotation
Otolith: continuously rotating in pitch; fixed magnitude g
Pitch rotation: up to 90 º/s
Roll rotation: 0 º/s
Yaw rotation: 0 º/s

Perceptual Observation

- Operator: "Did you notice the light diverging at all?"
- Subject: "**The little light… diverged, and I couldn't get it to come back together** again when I was looking off to the right. The two divergent red lights were not always in the same relation to each other."
- Operator: "Did they separate completely horizontally, completely vertically or something in between?"
- Subject: "…It was **mostly vertically**, but the bottom one would move across, moving horizontally more than the top one"
- Subject: "I tried to focus them back on top of each other. They were **always vertically separated but I tried to get them horizontally aligned**."
- Subject #2: "For right targets, one moved up and to the left. For left targets one moved down and to the right."
- Subject #2: "At the end I didn't notice it as much at all."

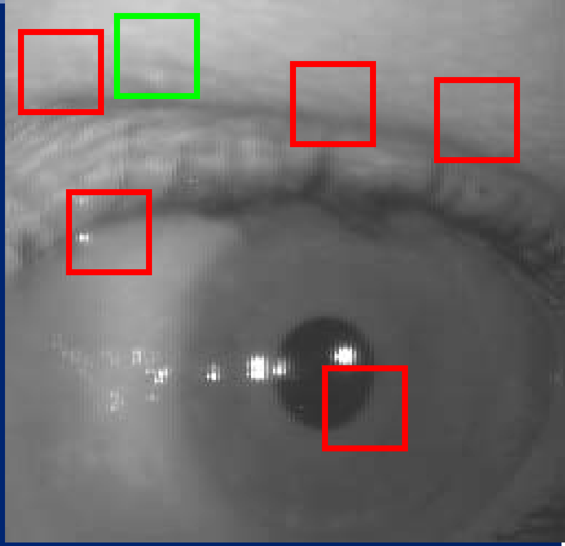

0 1 2
Gravity


Vertical Skew induced by Changing GIA
Vertical eye positions (degrees)
Left Eye
Right Eye
Compensated vertical eye positions (degrees)
Left Eye
Right Eye
Left Eye
Right Eye
Gravitoinertial acceleration (g)
Time (seconds)
Trial: B2

Goal

Develop a method to detect vertical translation of the camera relative to the eye using features in the video image

… using an automatically selected landmark

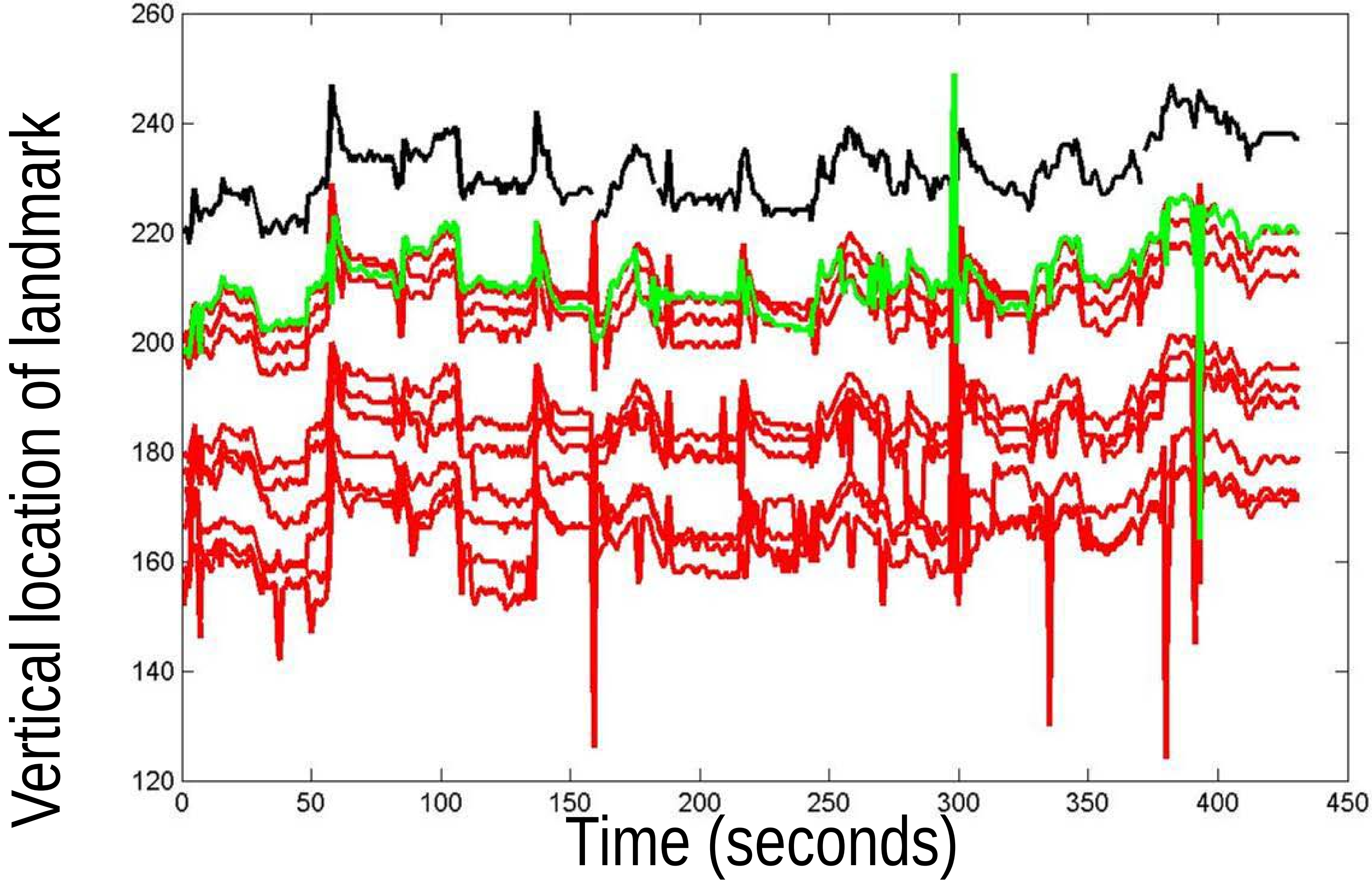


Algorithm

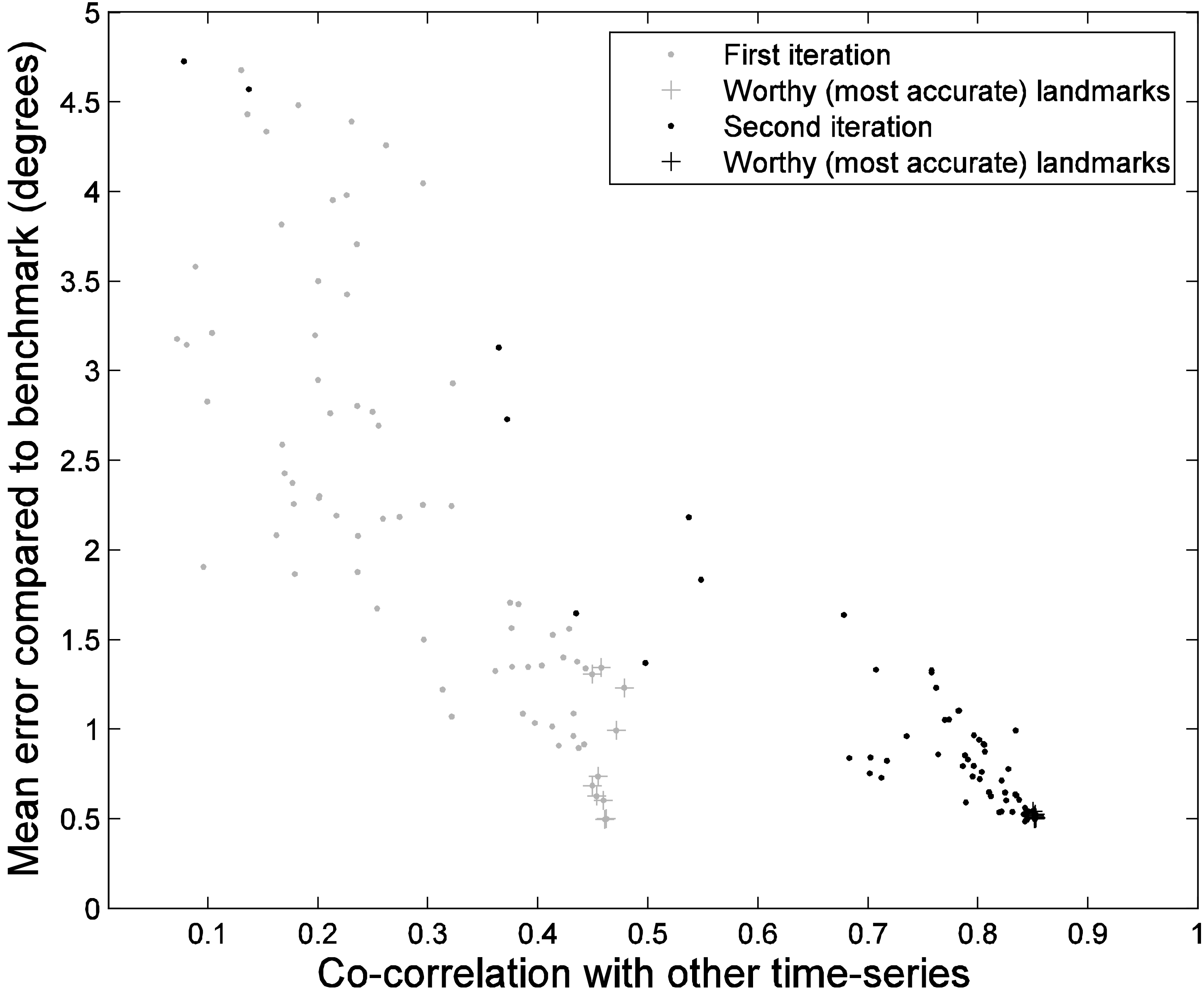
- Automatically select a smaller rectangular landmark
- Find in each video frame using cross-correlation
- “Temporal feature-selection”

Co-correlation

- Metric to estimate motion of a landmark relative to other landmarks



Co-correlation predicts landmark tracking accuracy

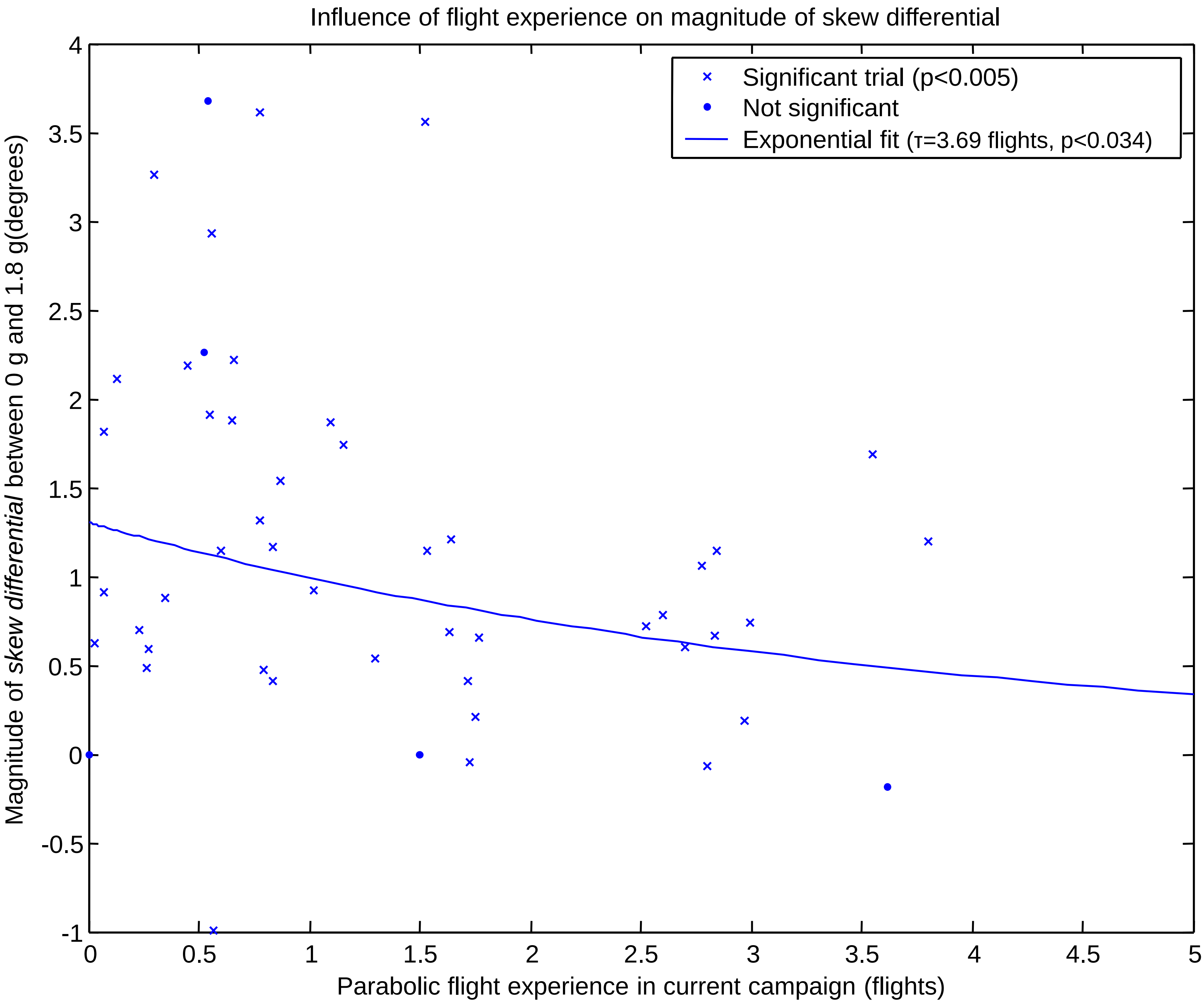


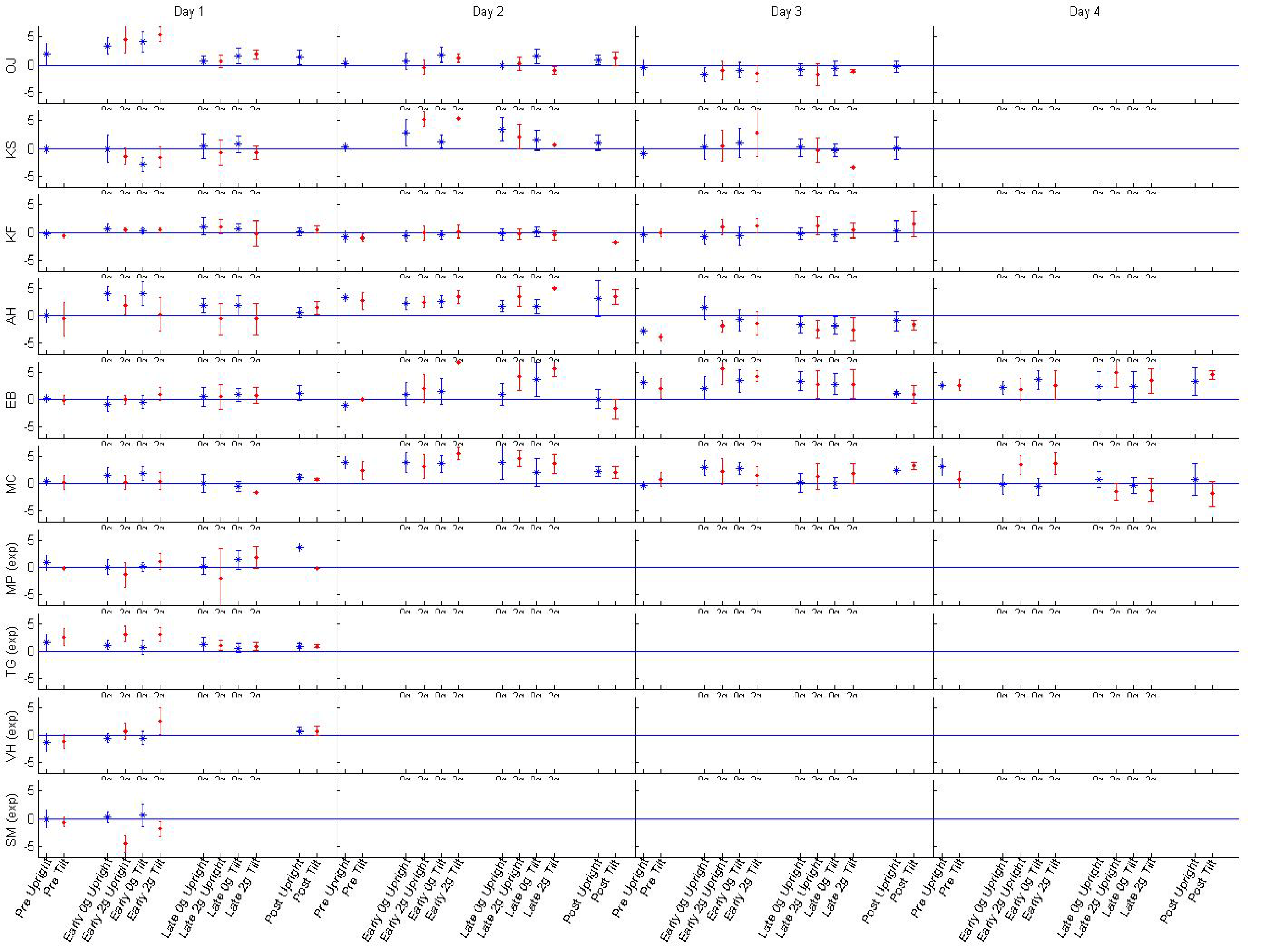
Aim 1: Parabolic flight vertical

3: How is disconjugacy influenced by target distance and position?

- The magnitude of g-dependent vertical skew does not depend on the horizontal or vertical displacement of the fixation target (ANOVA; $p>0.4$)
- Vertical skew is significantly smaller for far targets compared to near targets (*t*-test; $p<0.1$)

Target	Near (12 cm)	Far (30 cm)	Overall
Right	+1.54°±1.13° (n=18)	+0.99°±1.04° (n=4)	+1.44°±1.16° (n=22)
Left	+0.99°±0.63° (n=9)	+0.70°±0.65° (n=3)	+0.92°±0.62° (n=12)
Center	+0.90°±0.67° (n=9)	+1.15°±0.00° (n=1)	+0.93°±0.63° (n=10)
Up	+1.20°±0.91° (n=4)	- (n=0)	+1.20°±0.91° (n=4)
Overall	+1.24°±0.93° (n=40)	+0.90°±0.79° (n=8)	**+1.18°±0.93°**


Influence of flight experience on magnitude of skew differential
Significant trial (p<0.005)
Not significant
Exponential fit (τ=3.69 flights, p<0.034)
Magnitude of *skew differential* between 0 g and 1.8 g(degrees)
Parabolic flight experience in current campaign (flights)
4
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
-1
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5



Day 1
Day 2
Day 3
Day 4
OJ
KS
KF
AH
EB
MC
MP (exp)
TG (exp)
VH (exp)
SM (exp)
5
0
-5
0g
2g
Pre Upright
Pre Tilt
Early 0g Upright
Early 2g Upright
Early 0g Tilt
Early 2g Tilt
Late 0g Upright
Late 2g Upright
Late 0g Tilt
Late 2g Tilt
Post Upright
Post Tilt

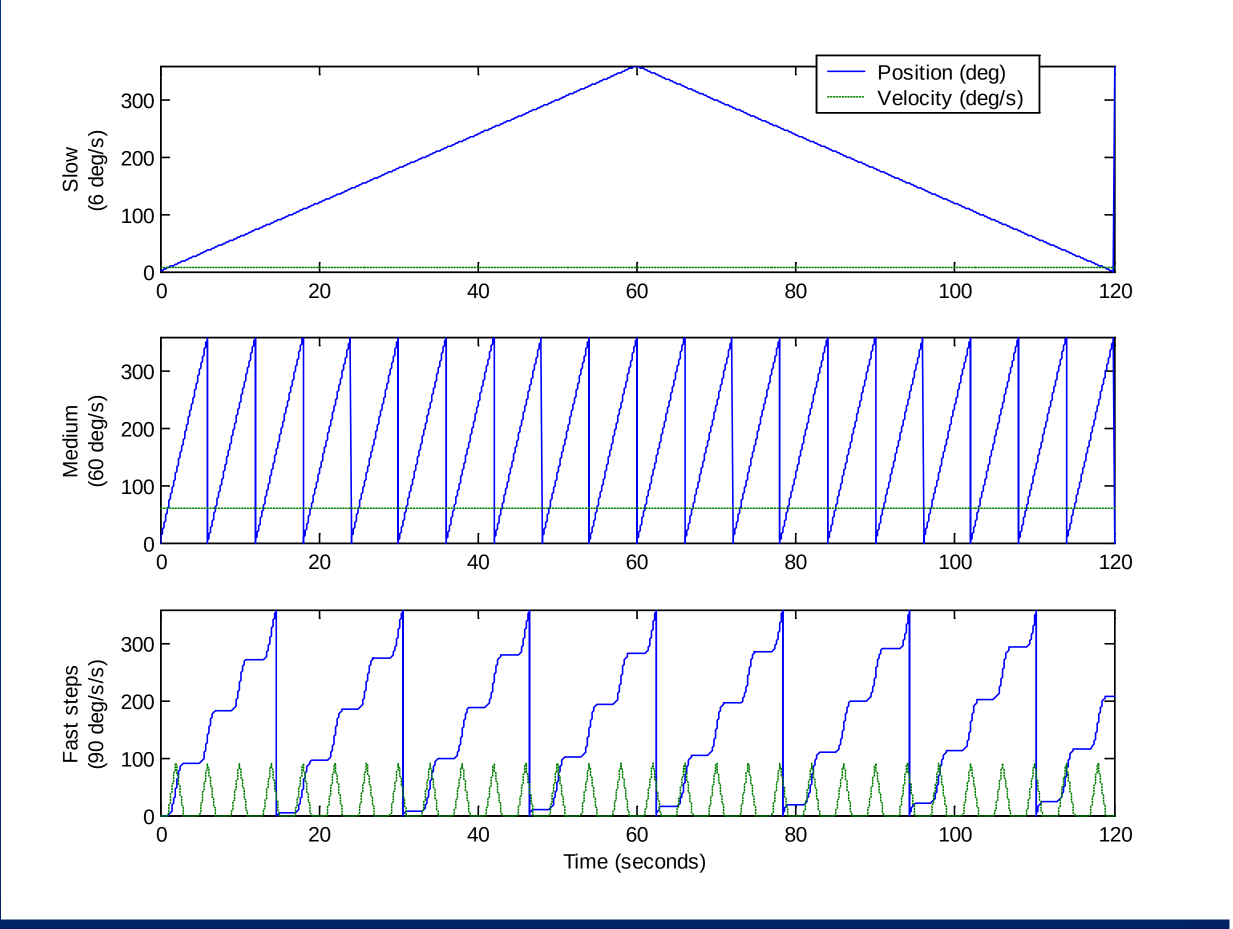
Summary Aim 1: Determine how binocular alignment is disrupted during linear acceleration

- The results provide evidence for vertical skew related to g level, possibly as a consequence of otolith asymmetry
- The skew is does not varies with target position (comitant) but reduces with target distance
- Vertical skew and torsional disconjugacy is reduced with exposure to parabolic flight
- The relationship between vertical and torsional disconjugacies will be studied

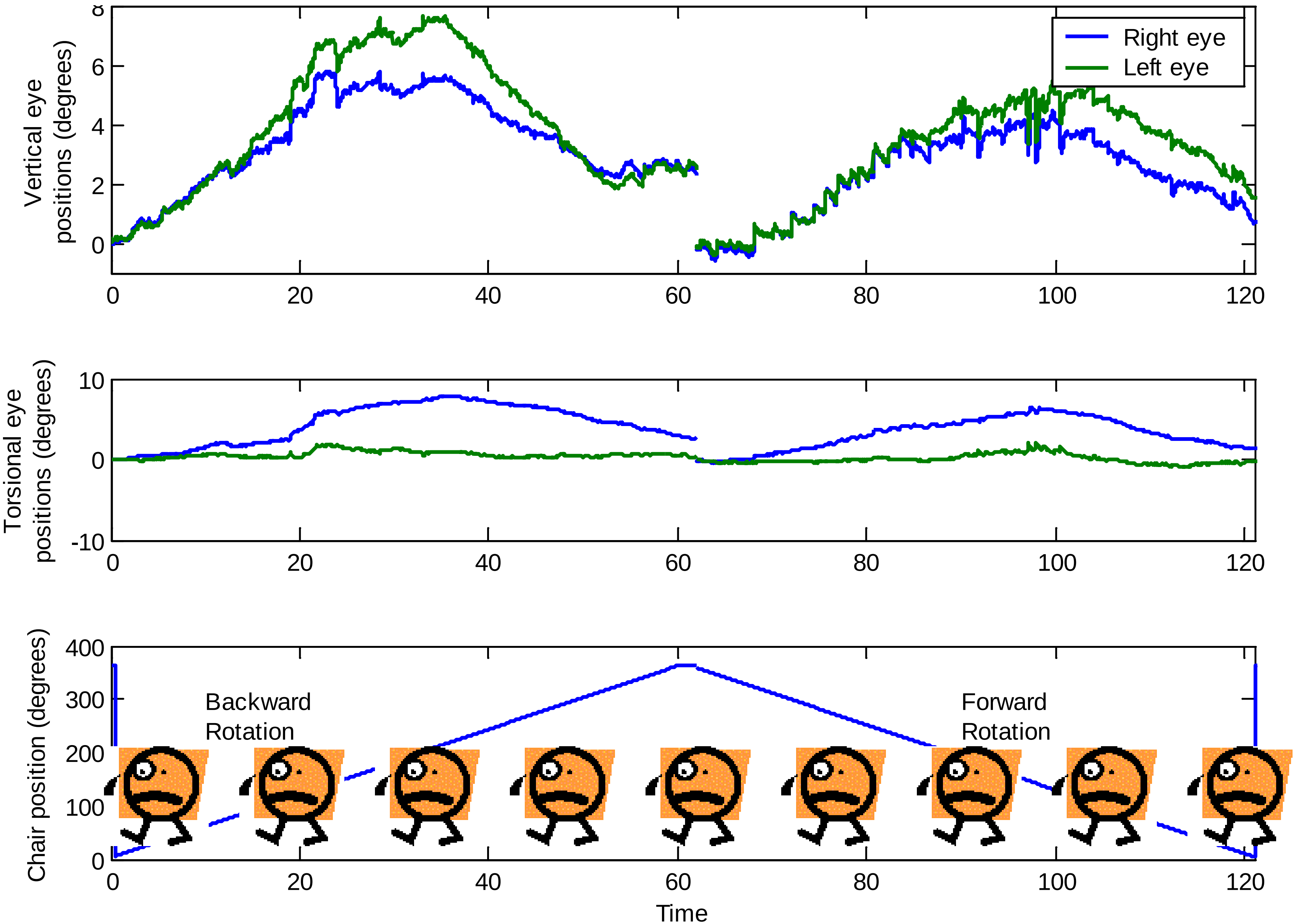
Aim 2: Pitch Rotations

Methods

- Rotate full body in the pitch direction
- Slow, medium, fast paradigms
- Eye movements recorded with scleral search coils



Slow pitch rotation



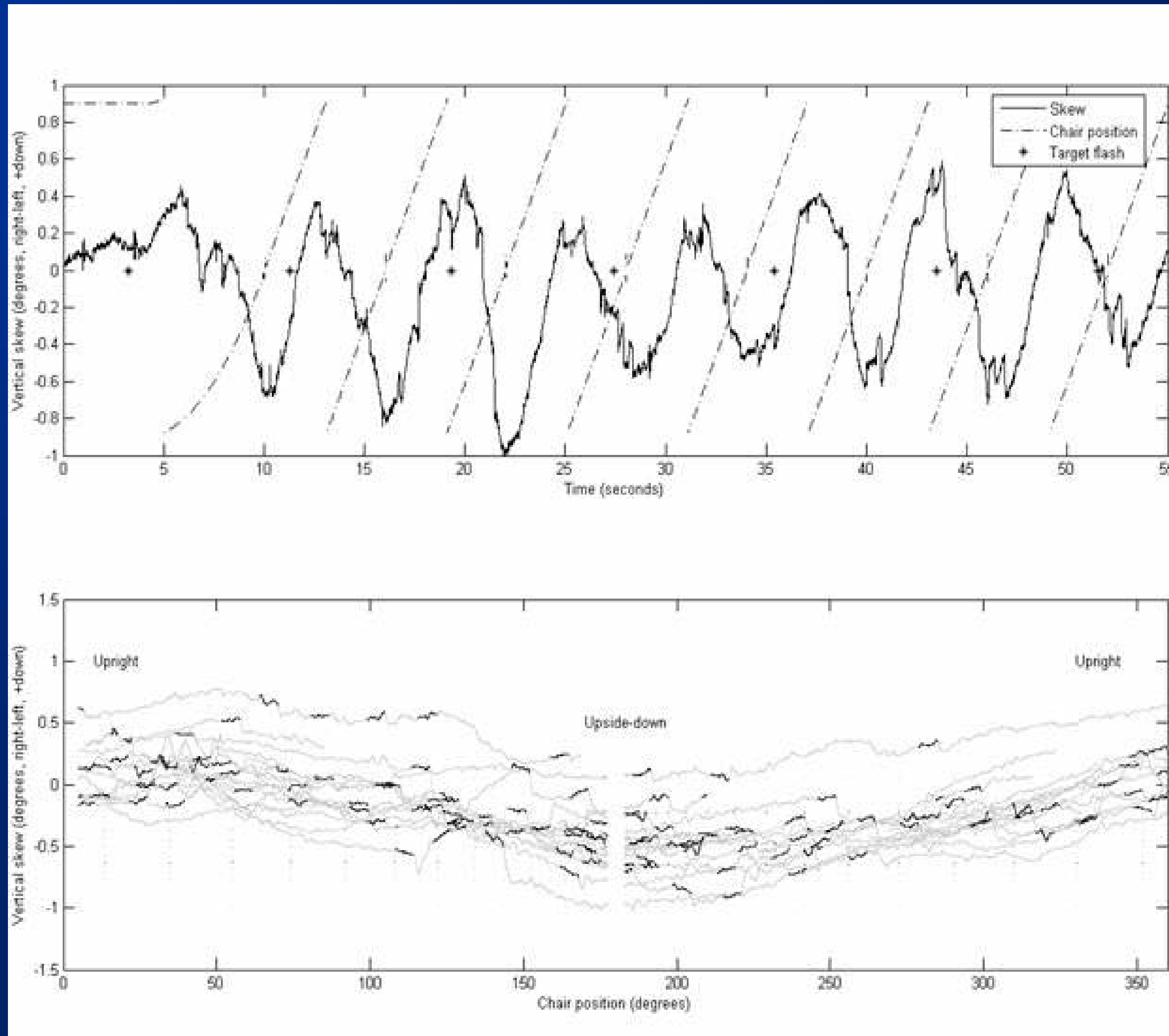
Medium pitch rotation

60 º/sec

Target flashes every 7 seconds resetting skew

Skew changes by 0.94º.

Will attempt to reduce noise by finding and removing fast phases



Summary of Aim 2: Determine how binocular alignment is disrupted during dynamic tilt (pitch VOR)

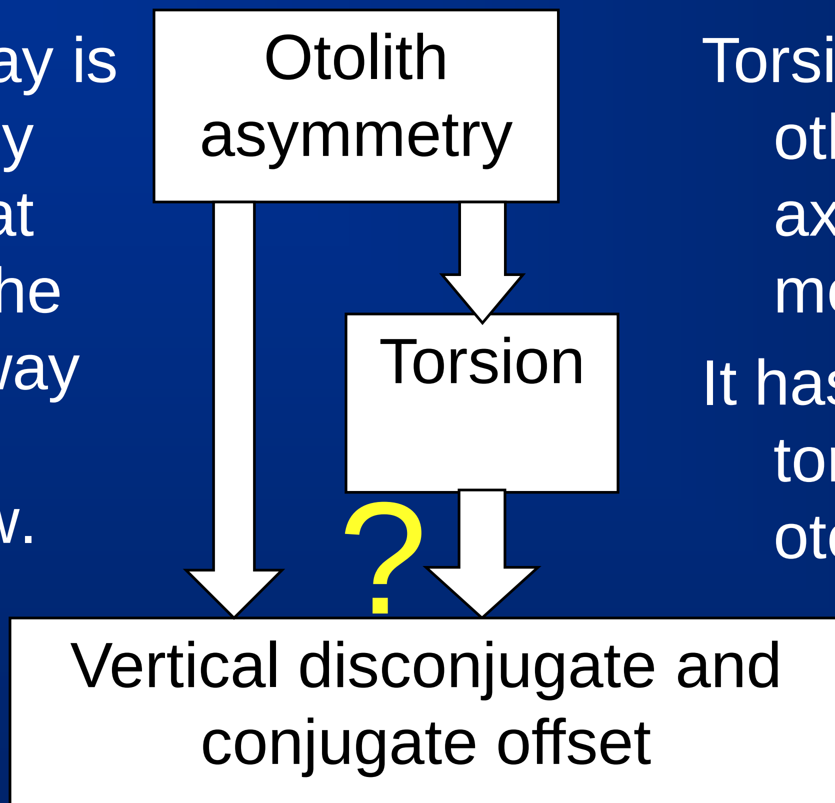
- Vertical skew occur in pitching with different motion profiles
- Torsional disconjugacy occurs in slow pitching; will look in medium, fast
- Will look for correlation between vertical/torsional
- Will perform regression of all experimental data to determine dependency on motion variables

Aim 4: Model how otolith asymmetry could contribute to disruption of binocular alignment under these different motion scenarios

- Can an anatomically-based otolith asymmetry model explain the vertical and torsional disconjugacies?
- Does a model suggest that the pathway is a direct otolith-vertical or that it is otolith-torsion-vertical?
- Does the model correctly predict changes in disconjugacy with different vestibular and visual inputs?
- Can the model predict adaptation? How are adaptation and central compensation related?

B: Does a model suggest that the pathway is: <u>direct otolith-vertical</u> *or* <u>otolith-torsion-vertical?</u>

A direct pathway is suggested by evidence that damage to the otolith pathway will result in vertical skew.

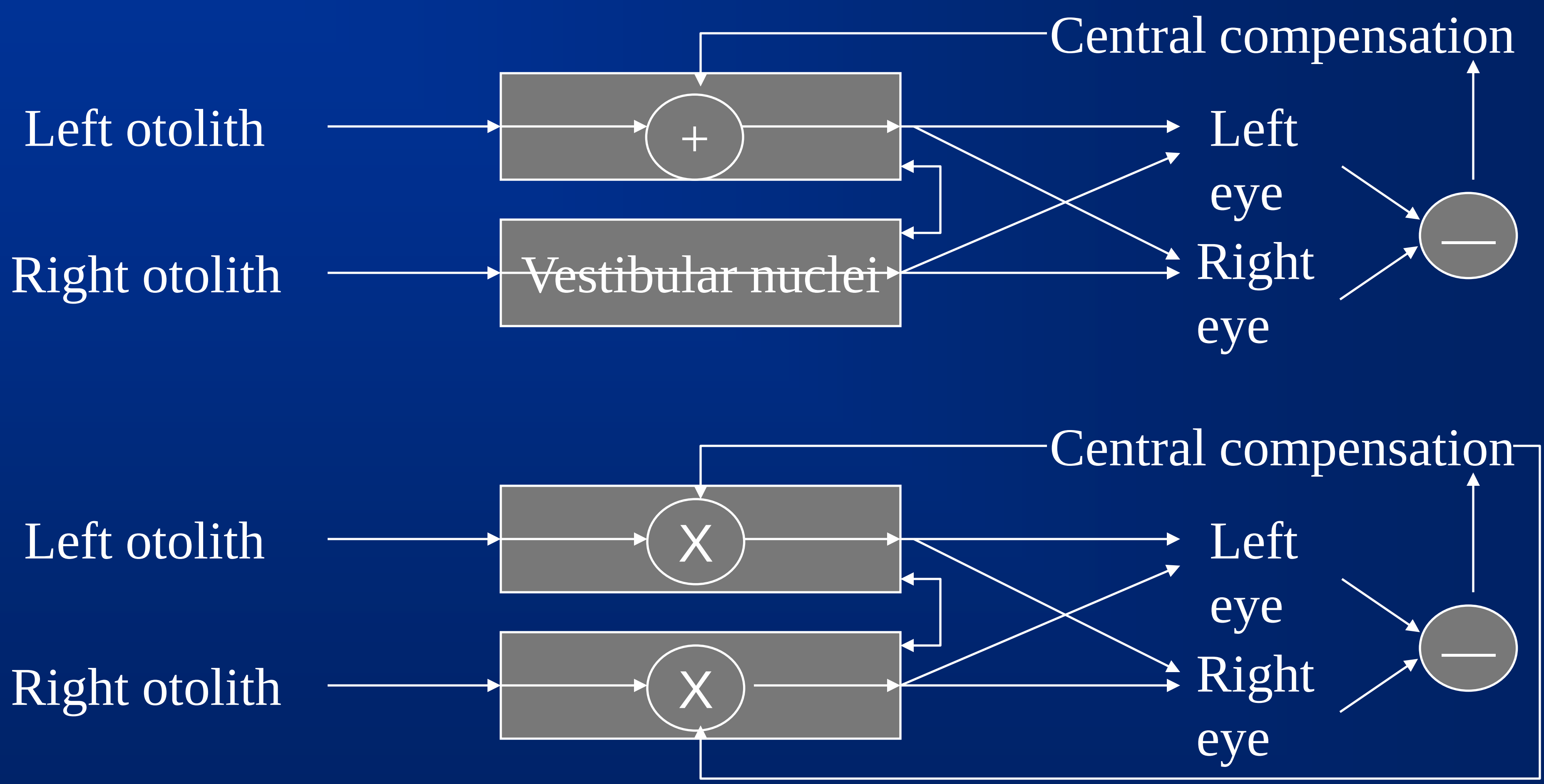


Torsion about an axis other than an optical axis will result in vertical movement.

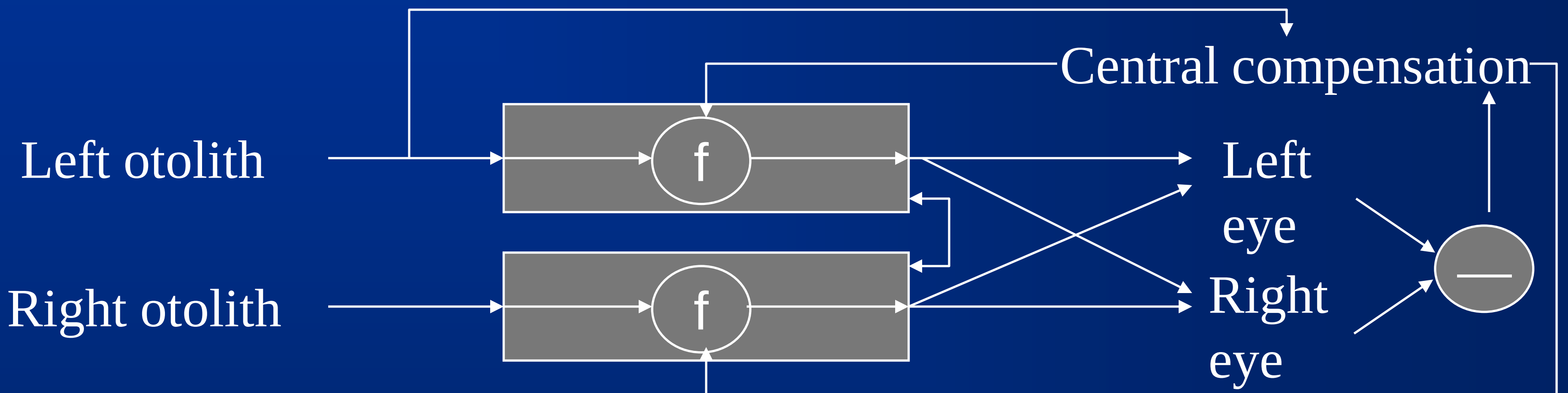
It has been shown that torsion results from otolith asymmetry.

The model incorporated the geometry of how torsion about different axes would cause vertical movements. We will use experimental data to determine which axis is consistent

D: How to model influence of central compensation on vestibular nuclei



D: How to model influence of central compensation on vestibular nuclei



- Context-specific adaptation

Acknowledgements

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- Pitch rotation: Dr. Dominik Straumann, Dr. Stefano Ramat, Zurich University Hospital staff
- Scientific insights / moral support: Dr. David Zee & the lab

Recruitment

- The lab is looking for new students – rotations, Masters, Ph.D.s
- Mark Shelhamer
  mjs@dizzy.med.jhu.edu

Otolith asymmetry: Implications for disruption of human binocular alignment in unnatural gravito-inertial environments

Faisal Karmali

October 11, 2006