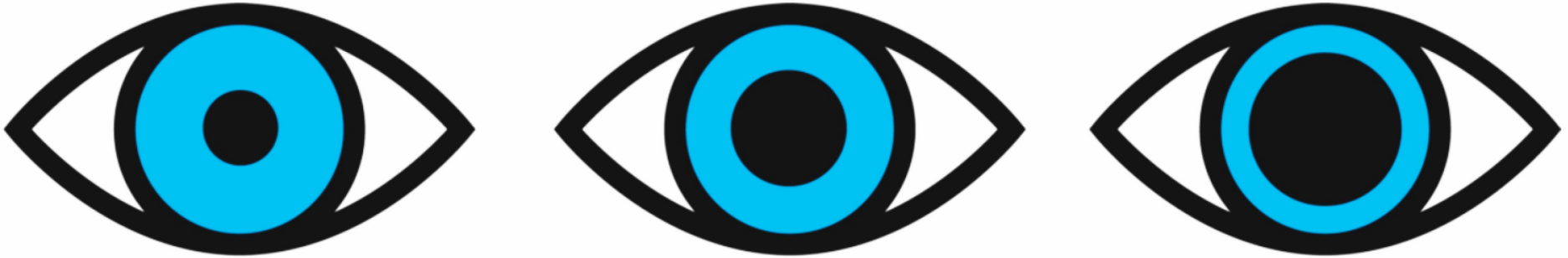
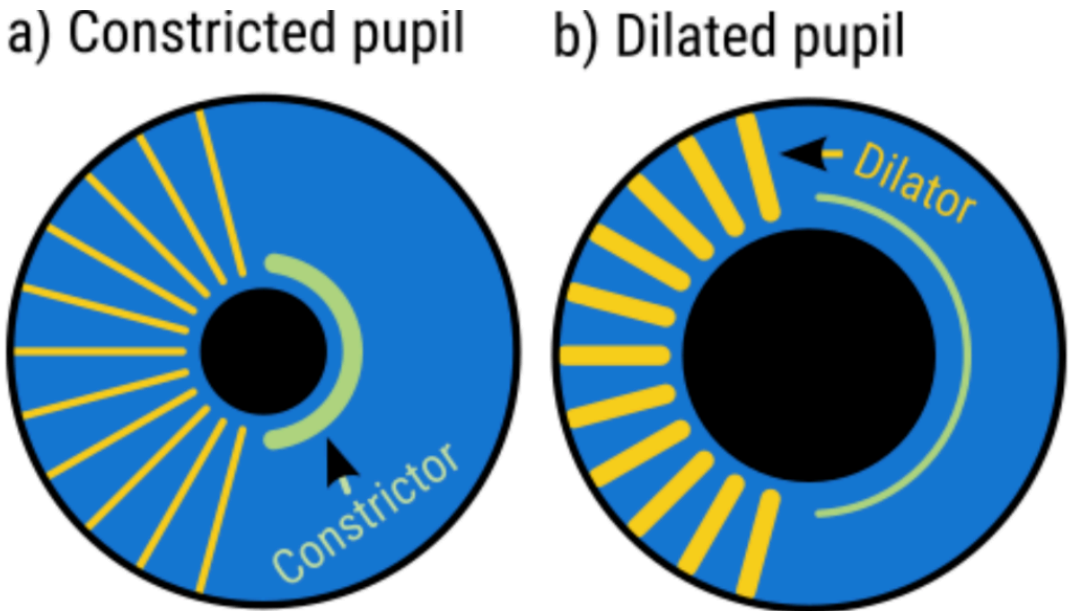
Pupillometry:
Psychology, Physiology, & Function



Gorina Elena

♡ **Vision Modeling Lab** ♡ HSE

Anatomy and neural pathways

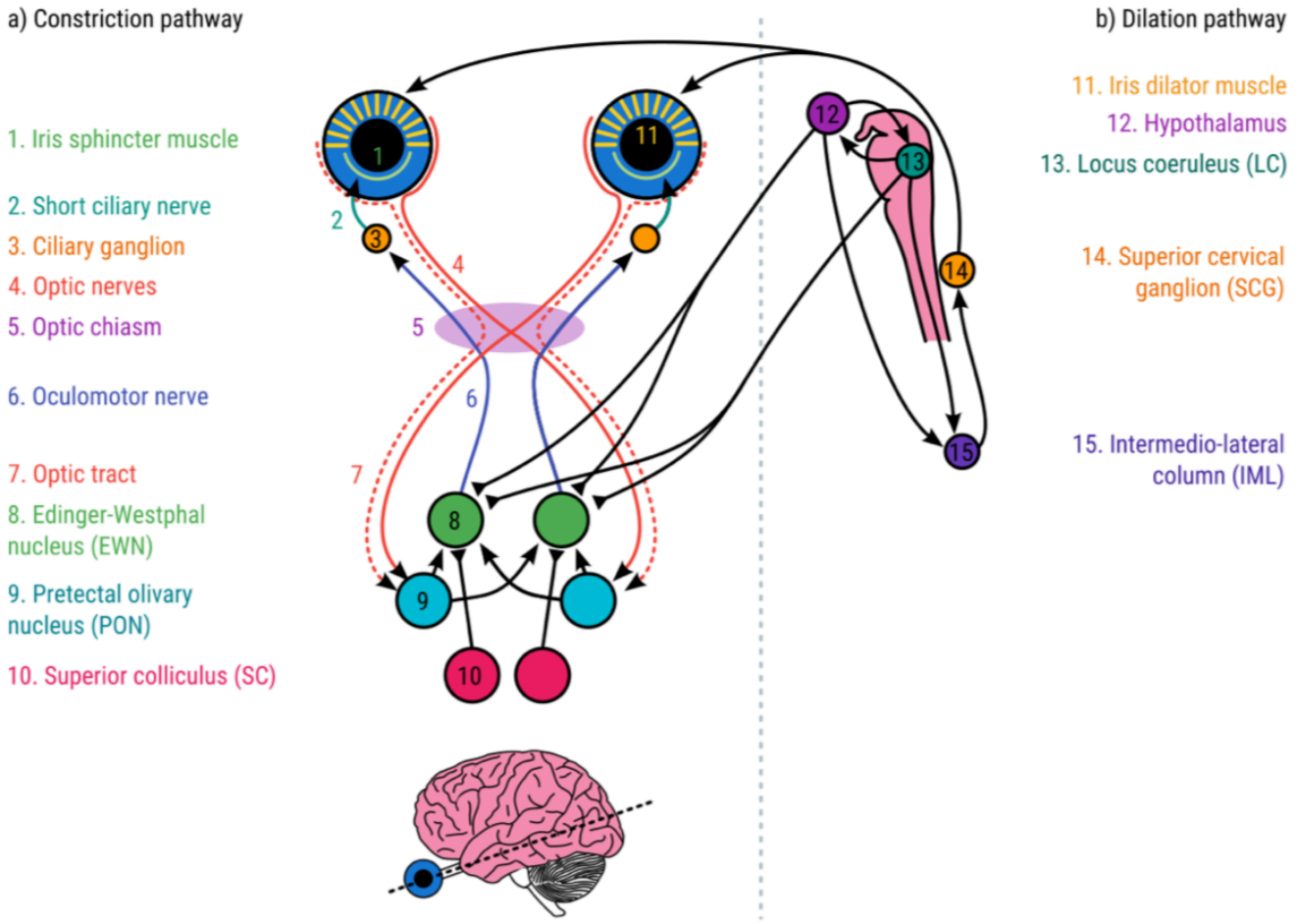


Parasympathetic constriction pathway
iris sphincter muscle (green) **constricts**

Sympathetic dilation pathway
iris dilator muscle (yellow) **constricts**

**pupils are relatively small at rest*

Anatomy and neural pathways



Anatomy and neural pathways

Pathways interaction:

- LC inhibits the EWN
  - arousal & mental effort
- SC inhibits the EWN
  - orienting response

- Eye
  - Blinks
  - Saccades
  - Anatomy (rods, cones)
- Visual
  - Orienting response (salient, sudden)
  - Light (PLR)
  - Color (blue)
  - Depth (PNR)
- Emotional
  - Fear
  - Stress
  - Arousal
  - Subjective attitude & meaning
  - Emotional stimuli (sounds etc.)
- Vegetative
  - Para/Symp balance
  - Cardiovascular
  - Hormonal state
  - Aging
  - Hippus
  - Before REM
  - Circadian
- Cognitive
  - Memory (LTM, WM)
  - Attention
  - Load / Overload
  - Difficulty
  - Novelty
  - Feedback
  - Errors (risk, uncertainty)
  - Uncertainty
  - Expectation
  - Mental imaginary
  - Anticipation of movement
  - Lying
  - Exploration / Exploitation
- Brain
  - Neurotransmitters
  - Myelination
- Disorders
  - Changed pattern
  - Traumas
- Doping
  - Meds / Drugs / Alco / Coffee etc.

Intro

Response to three distinct kinds of stimuli *(Mathôt, 2018)*:

- Constriction
  - pupil light response (PLR)
  - pupil near response (PNR)
- Dilation
  - psycho-sensory pupil response (PPR)

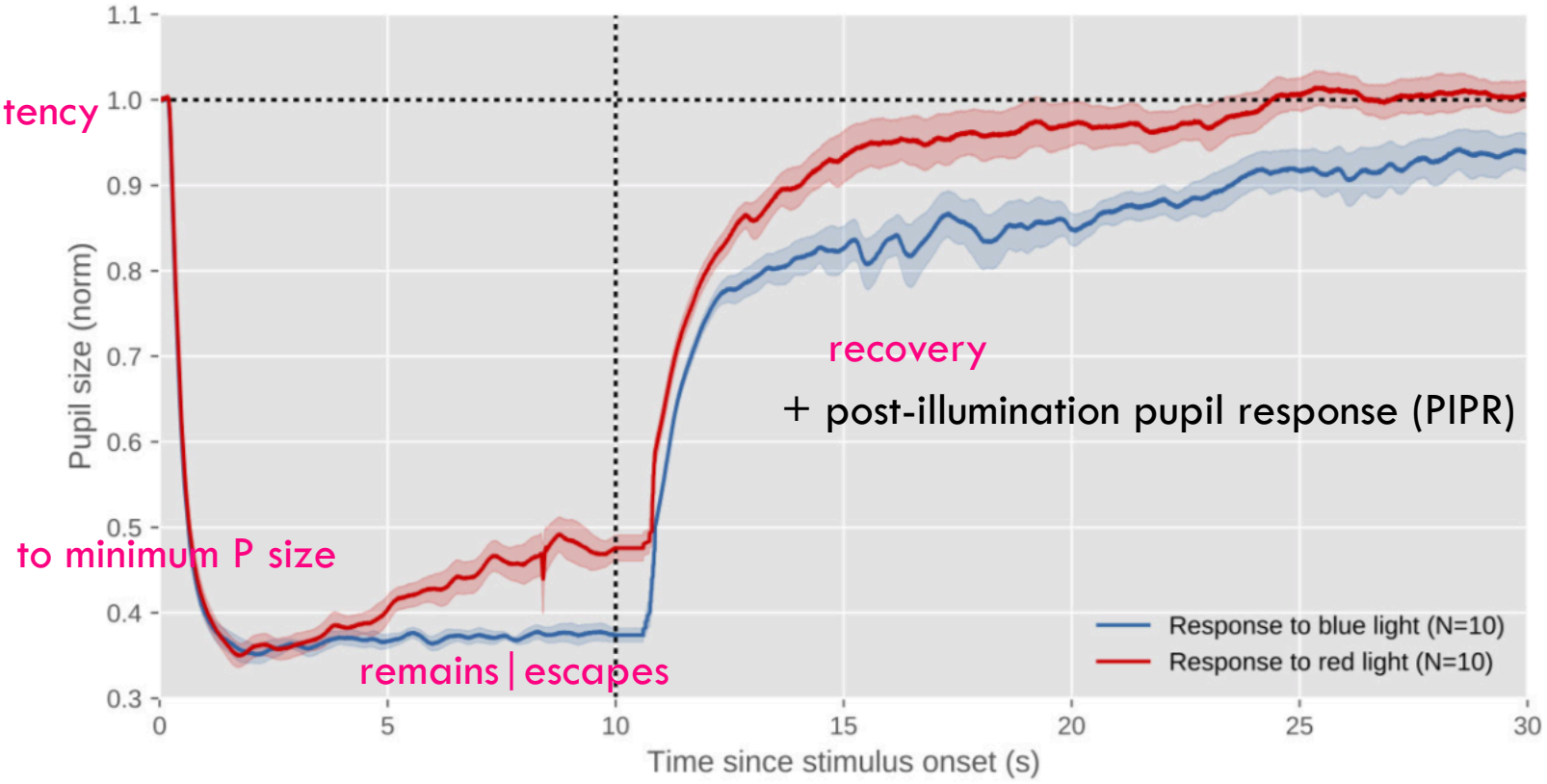
- Partly voluntary
  - ignore peripheral light = P constrict more &vv *(Binda & Murray, 2015)*

- P response can be conditioned 🤤

The pupil light response (PLR)

Constriction to brightness | **Dilation** to darkness

* *effect of light* ***is twofold:*** *activates both the dilation (alertness) & constriction (light) pathways*



PLR: Neural basis and photoreceptors

- Cones
  - fovea, color, medium-to-bright luminance
  - require intense light to become active
- Rods
  - bluish-green, weak light & darkness, peripherally
- Both:
  - 0.2-1.5 s
  - strongest for light presented in central vision
  - desensitize quickly

- Intrinsically photosensitive retinal ganglion cells (ipRGCs)
  - 1.5–10 s
  - max response to bluish light
  - drives PIPR
  - much slower then rods & cons
  - lasts as long as the light is on

=> PON => constriction pathway

PLR: cognitive influences

- Is affected by how visual input is selected, processed, interpreted
- Pupil changes = up to 5%

- Visual awareness
- Covert visual attention
- Eye-movement preparation
- Subjective interpretation
- Mental imagery and word meaning
- Working memory

PLR: cognitive influences

Visual awareness

- *Bárány & Halldén (1948)*
  - PLR was strongest for light sources that were **consciously** perceived

PLR: cognitive influences

Covert visual attention

- *Mathôt et al. (2013)*
  - P constricted due to **covert shift of attention** to the brighter side of the display (Joe approved ☺)
- *Ebitz & Moore (2017)*
  - stimulated neurons in the frontal eye field (FEF)
  - stronger PLR to stimuli flashed within the stimulated receptive field

PLR: cognitive influences

Eye-movement preparation

- Mathôt et al. (2015)
  - respond (weakly) to the brightness of the cued side already while the eyes were still in motion

PLR: cognitive influences

Subjective interpretation

- *Naber & Nakayama (2013)*
  - images that contained a sun triggered stronger pupil constriction
  - disappeared when images were **flipped** vertically

PLR: cognitive influences

Mental imagery and word meaning

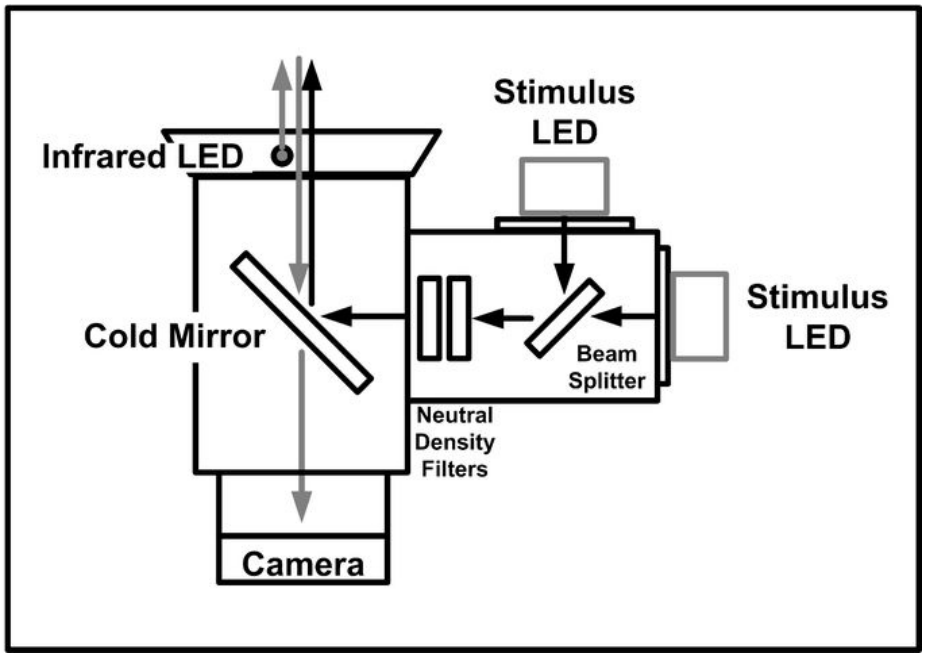
- *Laeng & Sulutvedt (2014)*
  - constricted for **mentally pictured** bright, compared to a dark, environment
- *Mathôt et al. (2017)*
  - P was smaller to **read or heard** words that conveyed a sense of brightness

PLR: cognitive influences

Working memory

= keeping smth bright or dark in working memory

- Fabius et al. (2017)
  - P was smaller for **memorizing** a location on a bright background
- Olmos-Solis et al. (2018)
  - when a stimulus **matches** the contents of visual working memory, it triggers a stronger PLR
- Blom et al. (2016)
  - found **no** evidence of working memory affected P size for the stimuli removed from the display


Stimulus
LED
Infrared LED
Stimulus
LED
Cold Mirror
Beam
Splitter
Neutral
Density
Filters
Camera

PLR: Function

- To protect the retina from damage due to overexposure
- Transitioning from brightness to darkness
- / depth of field (sharpness)
- / visual acuity
- Modulates visual sensitivity

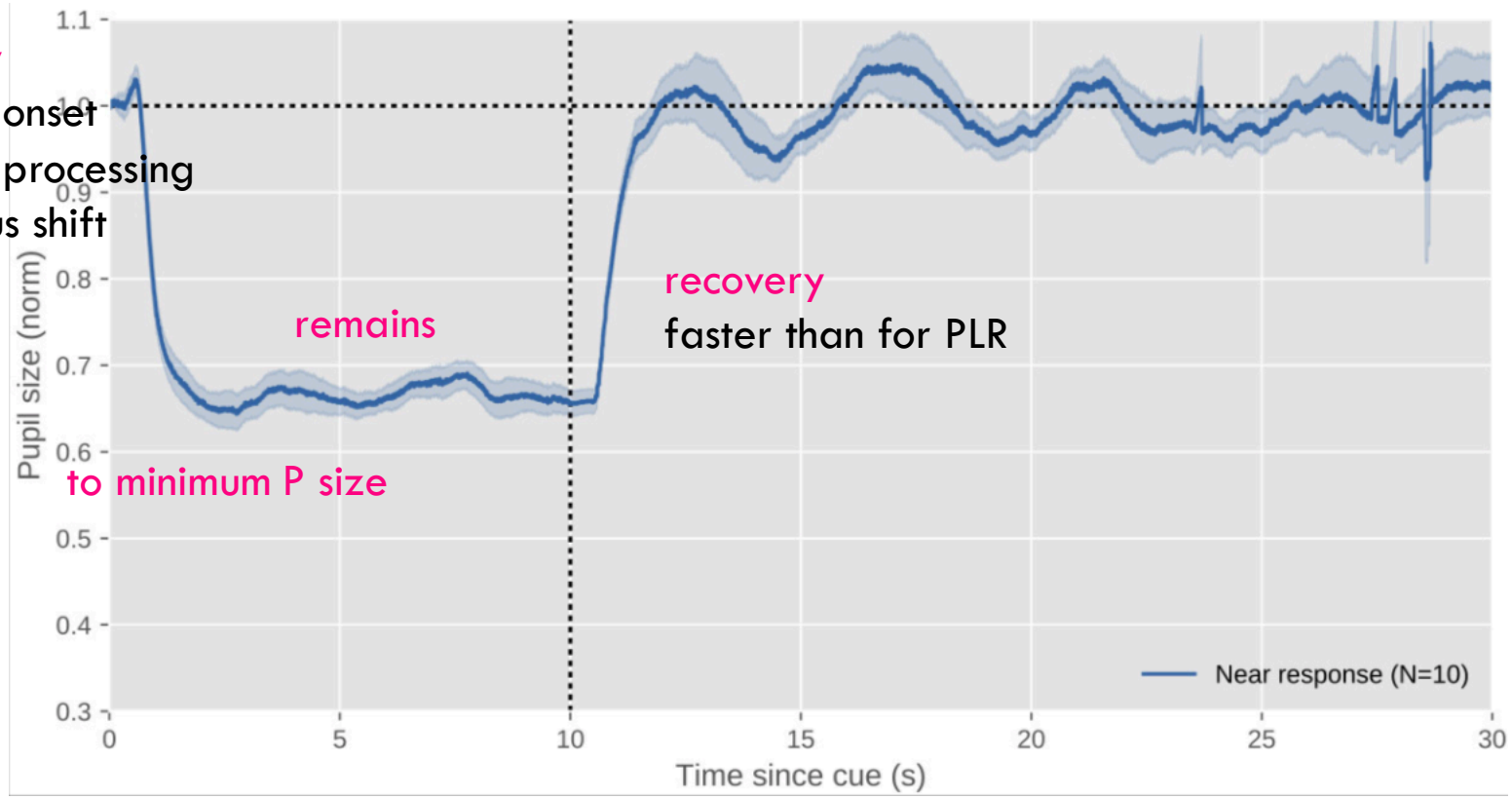
$$M(D) = \tanh^{-1}\left(\frac{D - 4.9}{3}\right)$$

$$\frac{\mathrm{d}M}{\mathrm{d}D}\frac{\mathrm{d}D}{\mathrm{d}t} + 2.3026\tanh^{-1}\left(\frac{D - 4.9}{3}\right) = 5.2 - 0.45\ln\left(\frac{\Phi[t-\tau]}{4.8118 \times 10^{-10}}\right)$$

The pupil near response (PNR)

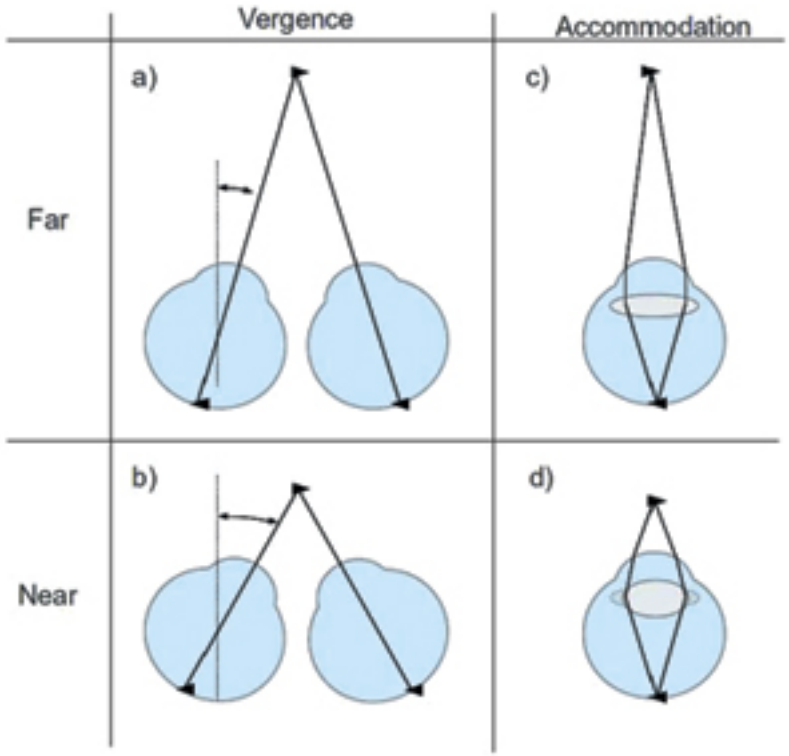
- **Constriction ~ nearby | Dilation ~ far-away**
- The **Near Triad:** PNR + *vergence* + *accomodation*

latency
- cue onset
- cue processing
- focus shift

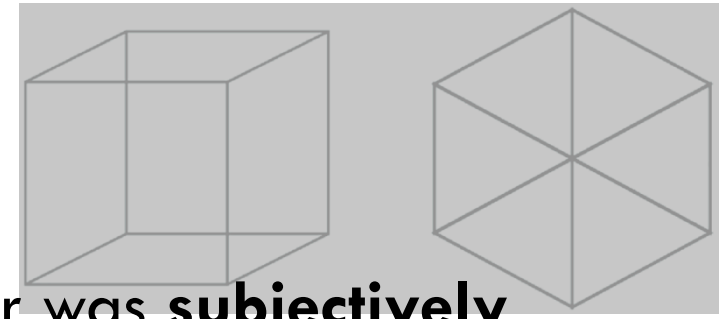


PNR: Neural basis

cortical projections (FEF, parietal cortex) => EWN => iris sphincter muscle



PNR: Cognitive influences



- *Enright (1987)*
  - Neckercubes
  - P was smaller when the corner was **subjectively nearby**, compared to far-away

- *Van der Mijn & Mathôt (2017)*
  - PNR is not modulated by covert shifts of attention, but **overt**
  - cognitive influences on PNR (if exist) are **smaller** than on PLR

PNR: Function

- Increase depth of field for near vision

The psycho-sensory pupil response (PPR)

= arousing stimulus | thought | emotion

= reflex dilation | arousal-related dilation | effort-related dilation

Types of PPR:

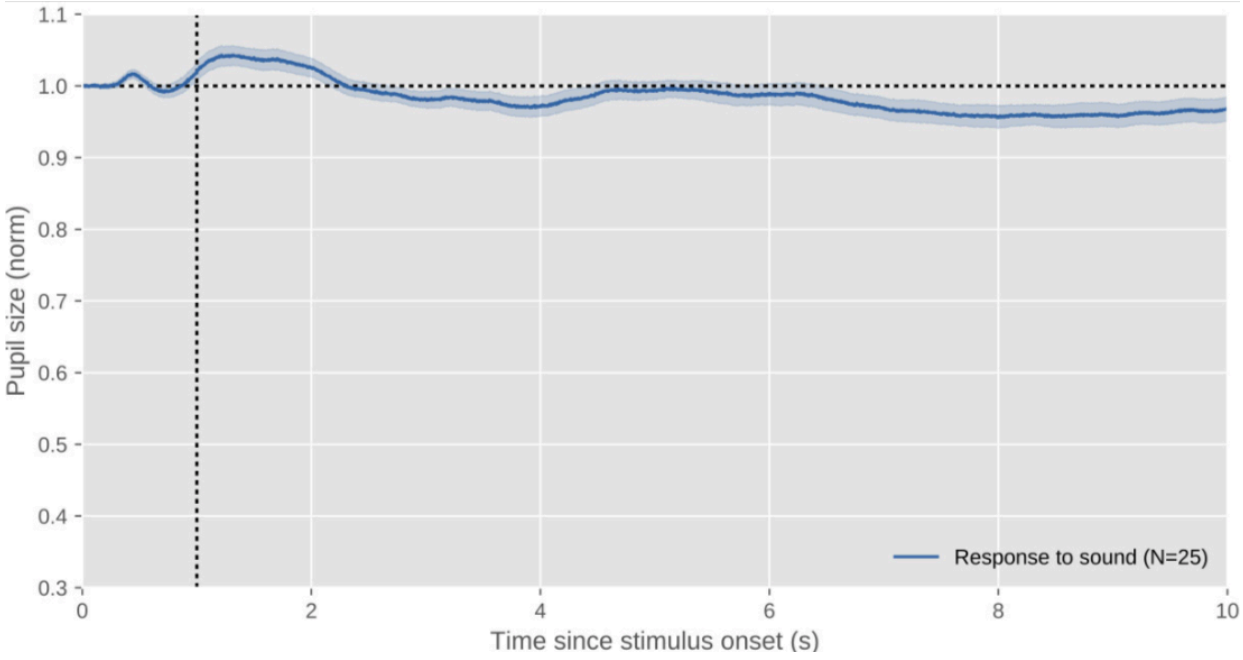
- Orienting response
- Mental effort and arousal
- The adaptive-gain theory

Types of PPR: Orienting response

Sudden events (sounds, movements, painful touch, etc.)

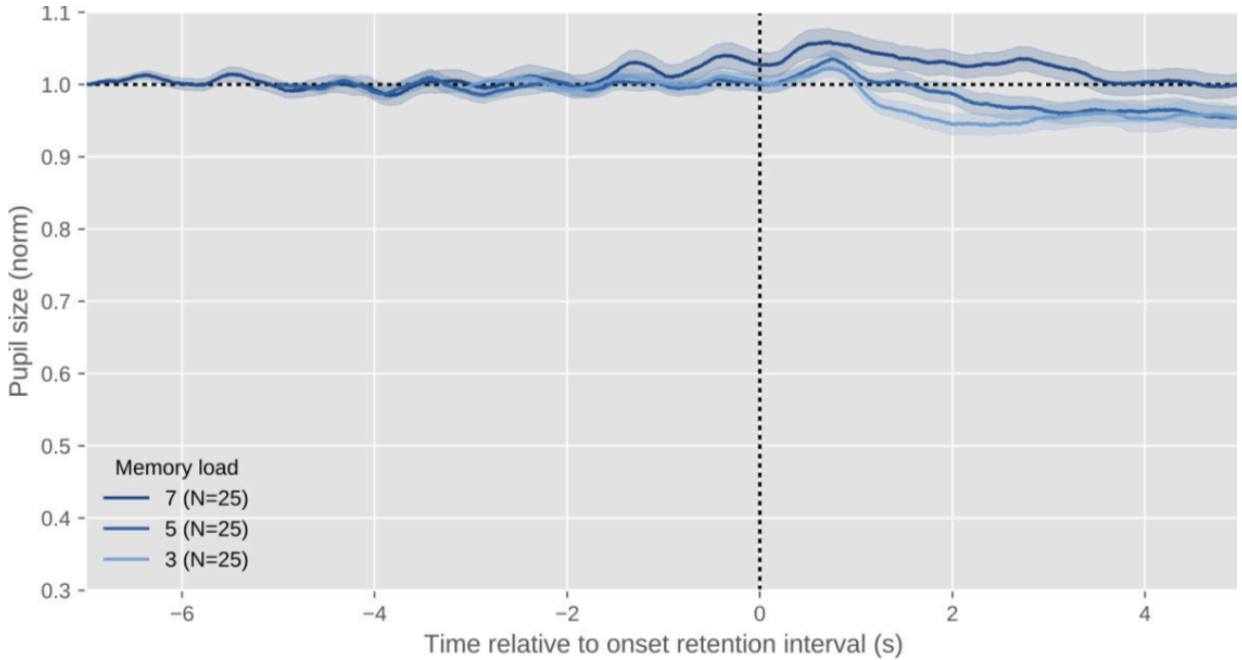
- **unexpected** *(Friedman et al., 1973)*
- **salient** *(Wang et al., 2014)*

- Fast: 0.5-1 s
- Smaller < PLR & PNR
- Second period of dilation: 1-2 s



Types of PPR: Mental effort & Arousal

- Endogenous
- Size and profile = highly **variable**
- Arousal *(Hess & Polt, 1964)*
  - the harder the calculation, the larger the P
  - doesn't depend on valence (positive v negative), but arousal itself *(Bradley et al., 2008)*
- Mental effort, cognitive load, cognitive intensity *(Kahneman & Beatty, 1966)*
  - P size reflected the number of digits memorized



Types of PPR: The adaptive-gain theory

Aston-Jones & Cohen (2005), Jepma & Nieuwenhuis (2011), Gilzenrat et al., (2010)

Locus Coeruleus (LC) **=>** behavior

- Exploitation intermediate phasic LC activity => **intermediate** pupil size
- Exploration high tonic LC activity, reduced phasic responses => **large** pupil size

PPR: Neural basis

- Orienting-response
  - intermediate layers of the SC
  - phasic activation of LC
- Arousal & Mental-effort
  - Hypothalamus
  - LC
- Adaptive-gain theory
  - LC

PPR: Function

- Optimal trade-off between visual sensitivity and visual acuity

* *how much P dilate under extreme conditions (non-Lab) is yet **unclear***

Spontaneous fluctuations in pupil size

= *hippus* = *pupillary unrest*

- reflects fluctuations in level of **arousal**
  - esp. for tired subjects (smaller & more restless)
  - ~ with changes in eye-movement behavior:
    - smaller P = attention to conspicuous parts (~low arousal)
  - during constriction, visual brain areas became less responsive *(Reimer et al., 2014)*
  - ~ with activity in NA projections to the cortex & other areas *(Joshi et al., 2016)*
- Cardiovascular
- Neurotransmitters
- Degenerative diseases & Psychiatric

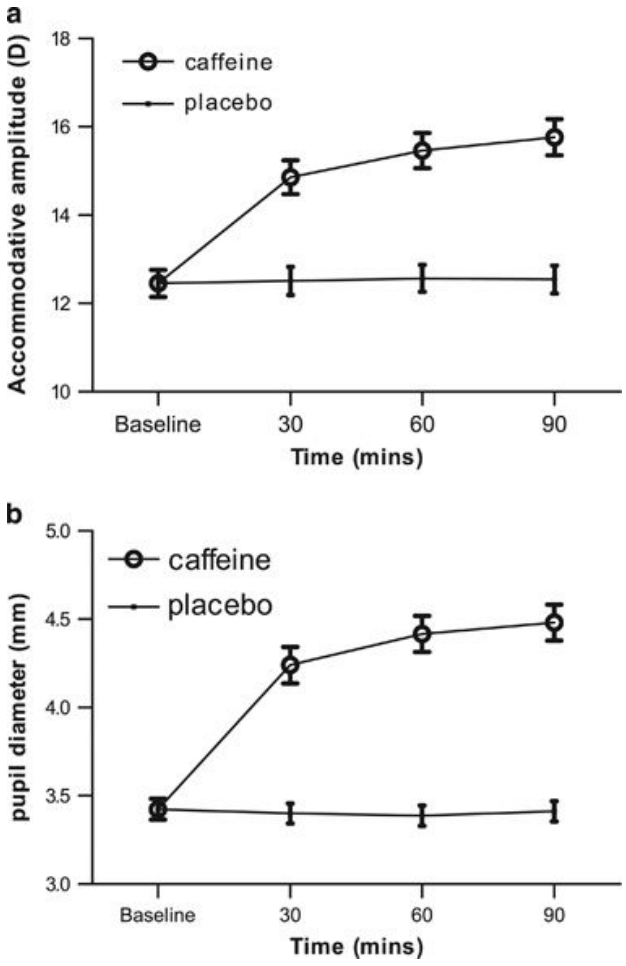
- Due to time of the day

Neurotransmitters effects

- LC-NA system
  - arousal, attention
- /Da – increases dilation (L-dopa)
  - errors, reward
- /S - increases dilation (SSRI)
- /Oxytocin - enhances stimulus-induced dilation
- Opioids
- etc.

		
Heroin Morphine Oxycodone Fentanyl Methadone Codeine	Marijuana Cocaine or Crack Benzodiazepines (i.e. Xanax) Depressants (i.e. Alcohol or Sedatives)	Amphetamines Methamphetamines Cocaine or Crack Hallucinogens (i.e. LSD or mushrooms) Opiates (prescription painkillers)

...coffeeee mmmmm...



Abokyi, 2016

Pupil dilation in disorders

- Depression
  - decreased P-dilation following stimuli
  - non-task related P dilation not in relation to the cognitive prompt time frame
- Parkinson's Disease
  - larger P diameter after light adaptation
  - reduced amplitude of contraction
  - prolonged contraction time at PLR
- Multiple System Atrophy
  - larger P after dark & light adaptation
  - higher anisocoria during light,
  - increase in latency, contraction time,
  - reduction in contraction amplitude.
- ASD
  - greater phasic P response & tonic dilation
  - increased latency
  - lower speed & magnitude
- Anxiety
  - smaller P dilation (pattern of emotional avoidance)
- etc…

- Eye
  - Blinks
  - Saccades
  - Anatomy (rods, cones)
- Visual
  - Orienting response (salient, sudden)
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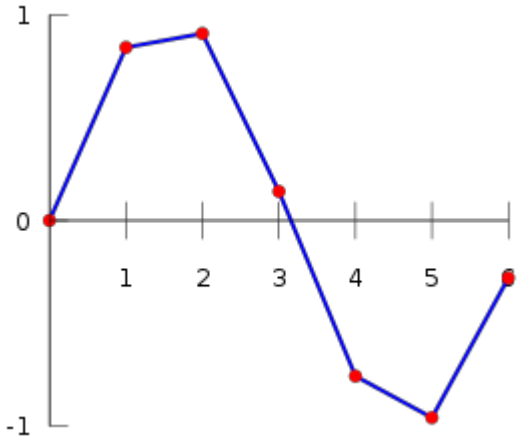
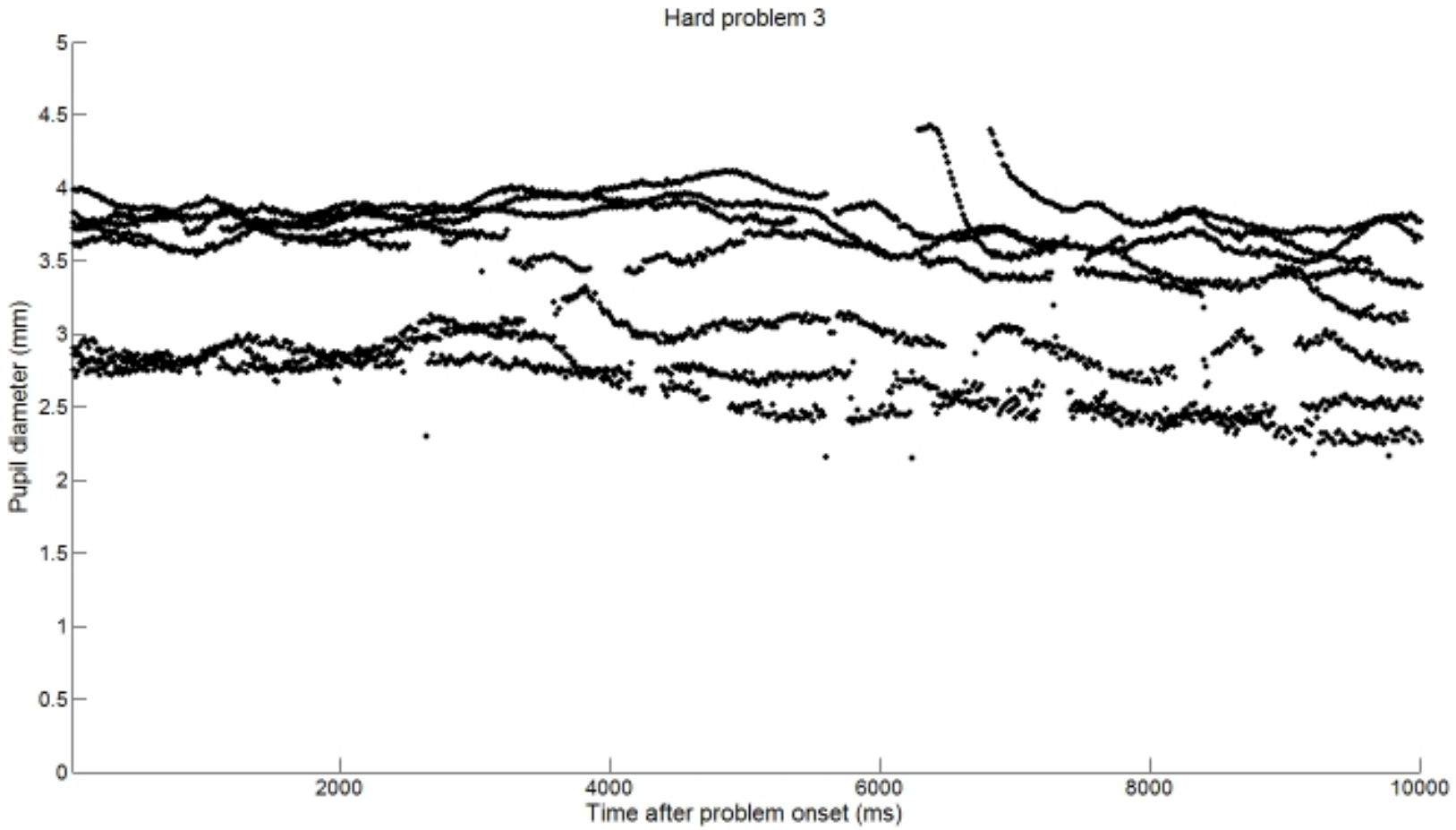
Methodology: Steps in pupil analysis

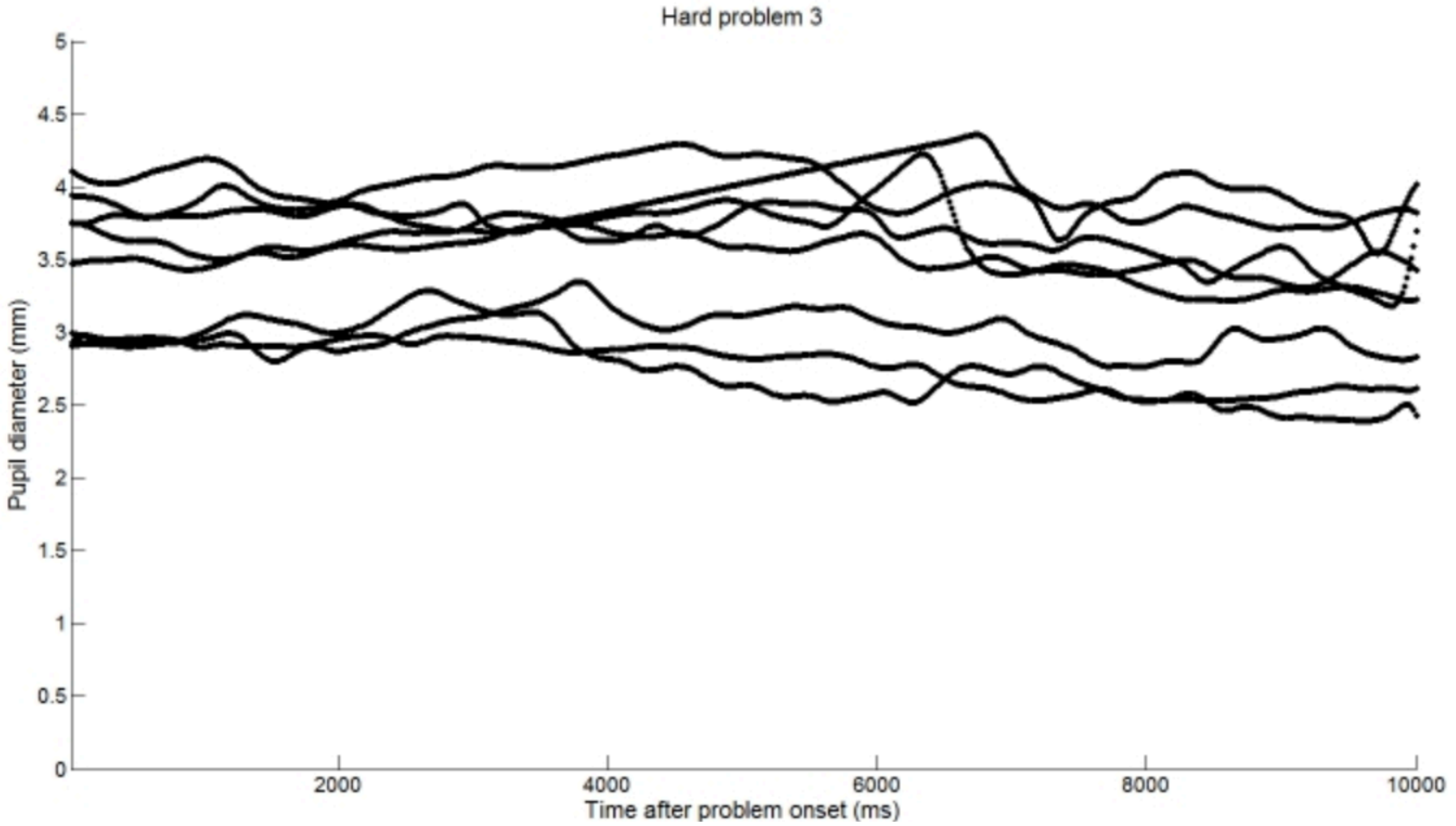
- Data inspection & artifacts rejection (e.g. Hampel filtering)
  - *thresholding* - remove data caused by eye blinking, loss of pupil tracking, and/ or headmovement
- Noise filtering
  - Low-pass with 10/15 Hz
- Replacement of missing data
  - Use of other eye (if available)
  - *Linear interpolation*
  - or discarding trials
- (Averaging both pupil size values)
- Baseline corrections
- Calculating baseline-adjusted measures
- (Normalizing)
    - Participant's pupil mean
    - Condition's pupil mean



Raw Data


Hard problem 3
Pupil diameter (mm)
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
2000
4000
6000
8000
10000
Time after problem onset (ms)

Cleaned Data



Methodology: Pupillometry parameters

- baseline diameter
  - 500 ms before critical stimulus
  - neutral stimulus
- minimum & maximum diameter
- mean diameter - average in an interval of interest

- response amplitude
- re-dilation amplitude

- response time
- re-dilation time

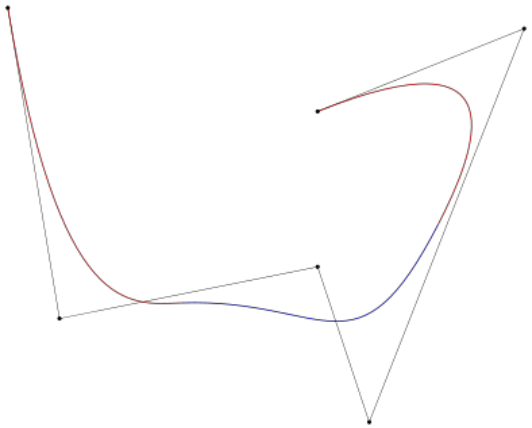
- average constriction velocity
- average re-dilation velocity
- maximum constriction velocity
- maximum re-dilation velocity

- onset latency
- peak latency - amount of time before peak size is reached

Task Evoked Pupillary Response (TEPR)

Methodology: Analysis techniques

- Means of time windows *(Laeng et al., 2007; Falk-Ytter, 2008)*
- Slope in a time window *(Engelhardt et al., 2010)*
- B-splines *(Jackson & Sirois, 2009)*
- Like EEG/ERP data
- PCA
- Fixation-based pupil measures



Summary

- Pupillometry is fun!

- Non-invasive marker
- Task design, set & setting – carefully
- Differentiate bw effectors
- Participants
- Data processing – carefully, improve
- Clinical: differential diagnostic (ASD vs. schizo)

- Most papers that report pupil size don't know anything of previously mentioned

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Thank you for your pupil dilation!