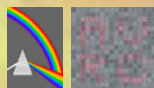


THE COLOUR GROUP (GB)
PALMER AWARD PRESENTATION



THE CONTRIBUTION OF THE ROD/MELANOPSIN DRIVEN GANGLION CELLS TO THE DYNAMIC PUPIL LIGHT REFLEX RESPONSE

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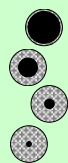
The National Hospital for Neurology and
Neurosurgery, Queen Square, London, UK



BACKGROUND



ipRGC (from Berson et al., 2002)

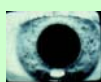


› The discovery of intrinsically photosensitive retinal ganglion cells (*ipRGCs*) led to a fundamental reassessment of non-image forming, light-derived signals from the retina that contribute to circadian responses, amongst other functions (Berson et al., 2002; Gooley et al., 2003; Hattar et al., 2003; Lucas et al., 2003; Panda et al., 2003; Dacey et al., 2005).

› Other studies examined the extent to which melanopsin (via *ipRGCs*) also contributes to the control of the pupil pathway, in addition to rod and cone mediated signals (Guprit et al., Neuron, 2010)

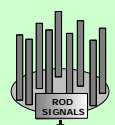
› Convincing evidence exists to suggest that in humans *ipRGCs* contribute to the steady-state size of the pupil, often beyond the offset of the light stimulus (Gamlin et al., 2007; Kawasaki & Kardon, 2007; Tsujimura et al., 2010).

› In spite of these observations, the contribution *ipRGCs* make to the dynamic pupil light reflex response remains controversial



In central vision rod signals do not contribute to visual perception at higher retinal illuminance. It remains unclear as to whether this is due to interaction of rod and cone signals or simply because of rod saturation

PURPOSE OF CURRENT STUDY



a. To establish whether rod signals can drive the pupil response at levels of light adaptation that are conventionally described as photopic



ipRGC

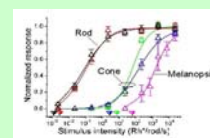
b. To examine the extent to which the dynamic light reflex response relies on melanopsin signals via *ipRGCs* in the absence of other photoreceptor inputs



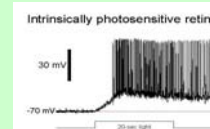
EARLIER FINDINGS

In general, it would be reasonable to expect that the following properties of melanopsin driven *ipRGCs* should be reflected in the pupil response:

(1) Melanopsin driven *ipRGCs* respond best only at very high light levels, usually orders of magnitude above rod threshold (Data from David Berson)



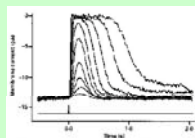
(2) Melanopsin signals are very sluggish. This would be consistent with unusually slow pupil response latencies (Data from David Berson)



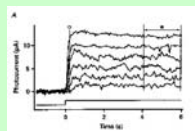
EARLIER FINDINGS

What are the spatial and temporal responses of rod photoreceptors?

1. Isolated rod photoreceptor signals increase in amplitude and exhibit shorter latencies with increasing flash intensities. Long decay times and a decreased sustained component can be observed for several seconds when rods are exposed to brief (11ms) bright flashes (Nunn & Baylor, 1984).



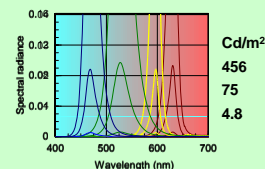
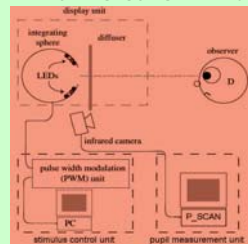
2. Rods generate more sustained responses that are proportional to the log of retinal irradiance. The effectiveness of rod signals is complicated by very extensive spatial summation and known rod-cone interactions.



METHODS

PUPILLOMETRY

STIMULUS LUMINANCE (cd/m^2): 456, 75 and 4.8

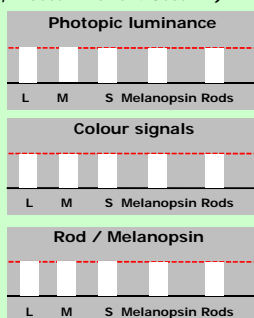
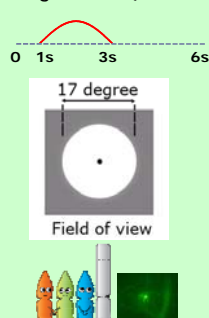


P_SCAN PUPILLOMETER fitted with TSUJIMURA four primary silent substitution stimulator (Tsujiura et al., 2010)

Contrast Measured from Spectral Scans		Photoreceptor Excitation (%)				
Condition	Modulation amplitude (%)	L	M	S	Melanopsin	Rods
L+M	25.70	25.4	25.8	-0.1	-0.6	3.1
Mel / Rods	56.4 & 47.4	-0.5	-0.9	3.7	56.4	47.4
L-M	-6.8 & 12.6	-6.8	12.6	0.2	-0.4	1.8

STIMULI EMPLOYED

- 3 stimuli (luminance, colour and rod / melanopsin)
- 3 light levels (456cd/m^2 , 75cd/m^2 and 4.8cd/m^2)

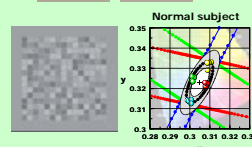
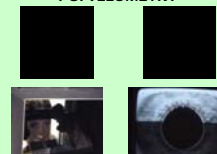


METHODS

Pupillometry, Colour Assessment & Contrast Acuity
Colour Assessment (CAD test)



PUPILLOMETRY

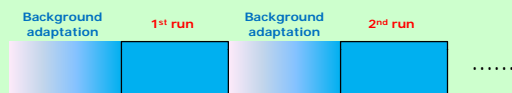


Visual Assessment (CAA test)



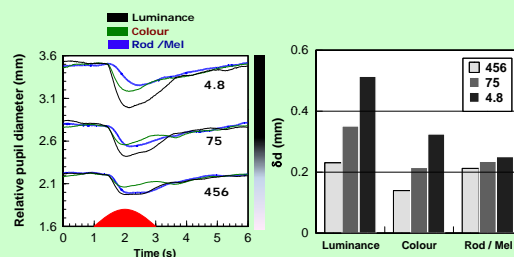
PROCEDURE

- ✓ Binocular viewing
- ✓ 5 minutes of light adaptation
- ✓ Pupil responses obtained by averaging 32 traces per stimulus

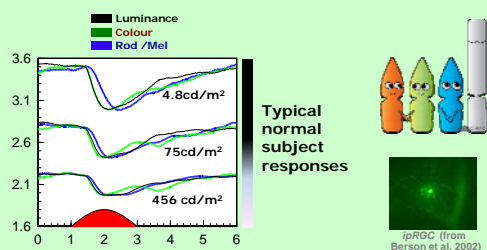


- ✓ 10 normal subjects (age: 23 to 65; males & females)
- ✓ 2 rod deficient subjects (age: 24 and 25; males)
- ✓ 1 rod monochromat (age: 55; male)
- ✓ 5 subjects with Optic Neuritis

RESULTS - Typical normal subject responses

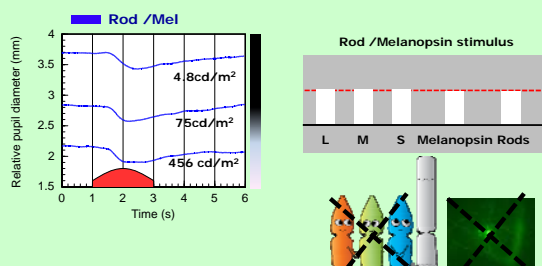


RESULTS – EQUALISED AMPLITUDES



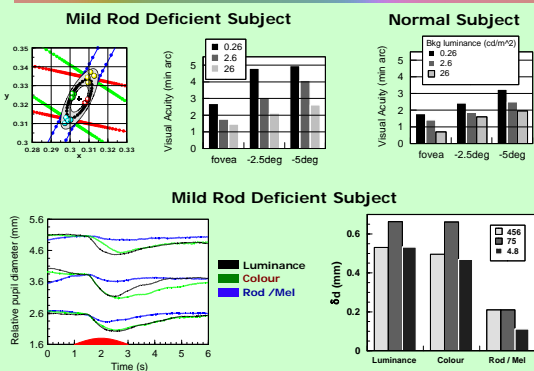
Contrary to expectations based on melanopsin stimulation, the largest response amplitudes correspond to the lowest light level. The response latency also decreases with light adaptation level.

NORMAL SUBJECT: PUPIL TRACES EQUALISED FOR RESPONSE AMPLITUDE AT EACH LIGHT LEVEL

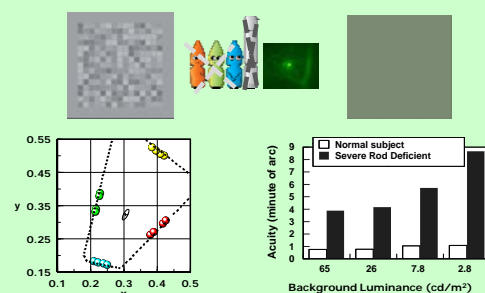


It is of interest to establish the extent to which the observed pupil constrictions in response to the rod / melanopsin stimulus in normal subjects reflect only rod signals?

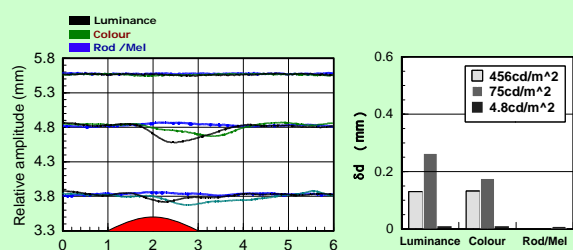
PUPIL RESPONSES IN SUBJECT WITH MILD ROD PHOTORECEPTOR DEFICIENCY (Mild manifestation of RP)



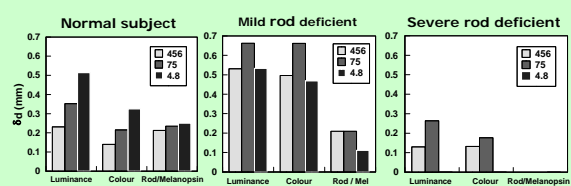
PUPIL RESPONSES IN A PATIENT WITH AUTOSOMAL DOMINANT RP (ALMOST ABSENT ROD FUNCTION AND REDUCED CONE SIGNALS)



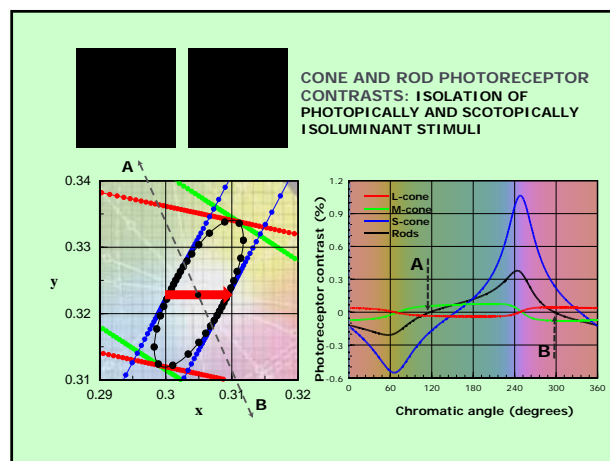
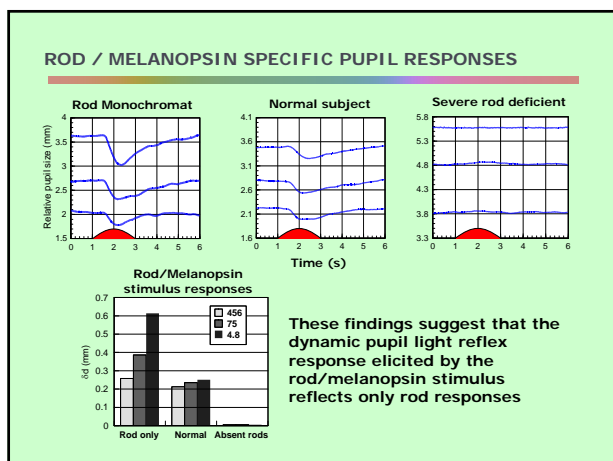
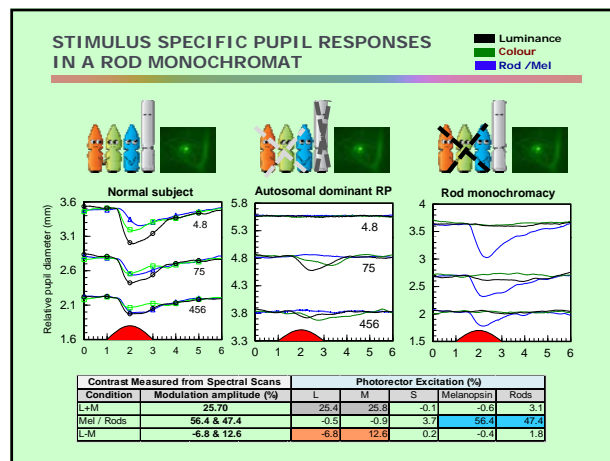
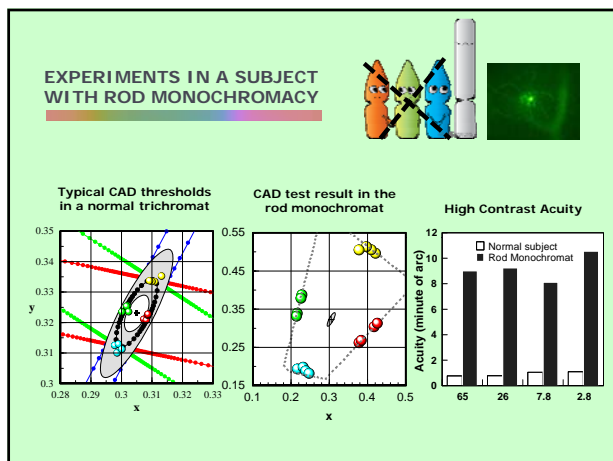
PUPIL RESPONSES IN A PATIENT WITH AUTOSOMAL DOMINANT RP (ALMOST ABSENT ROD FUNCTION AND REDUCED CONE SIGNALS)



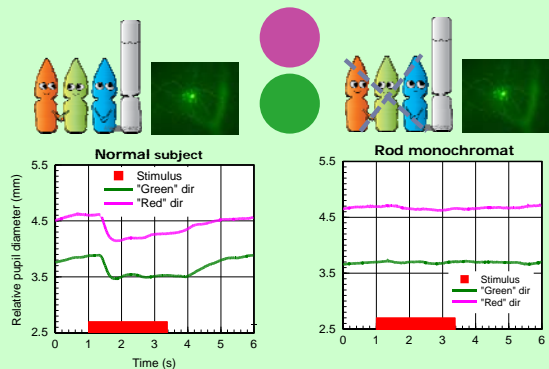
COMPARISON OF NORMAL AND ROD DEFICIENT SUBJECTS



The results suggest that the pupil responses to the Rod/Melanopsin stimulus are largely from rods and can be completely absent in cases of rod deficiency



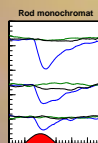
ROD-FREE RESPONSES FROM THE ROD MONOCHROMAT



CONCLUSIONS



- Pupil responses in normal subjects exhibit decreased latencies as the light level is increased. The rod/melanopsin stimulus tends to generate large response amplitudes, particularly at lower light levels when rods are more sensitive.



In response to the rod/melanopsin stimulus, the rod monochromat produced pupil responses of latency and amplitude similar those measured in normal subjects. Neither "photopic luminance", "colour" or "colour & melanopsin" stimulation produced any measurable response.

- These findings suggest that the dynamic pupil light reflex response in human vision involves mostly rods and cone signals, with little or no input from melanopsin

ACKNOWLEDGEMENTS



<http://www.city.ac.uk/avrc/>



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