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Light response differences in the superior colliculus of albino and pigmented rats

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Abstract

Multi-unit visual responses to light intensities ranging from −6.46 to 0.81 log cd/m^2 were recorded from the surface of the superior colliculus of dark-adapted normal pigmented and normal albino rats. Light sensitivity was significantly higher in albinos. The response onset latency was inversely proportional to the stimulus intensity. The progression of the stimulus intensity versus response onset latency curve showed a considerable difference between pigmented and albino rats. At low light levels, longer response onset latencies were recorded in pigmented rats than in albinos. This can be attributed to the transmission of rod-driven responses. The differences observed in the light response characteristics of albino rats may be indicative of their visual abnormalities.

Keywords: Superior colliculus; Electrophysiology; Albino rats; Pigmented rats; Visual threshold

Anatomical and physiological differences exist in the visual sensory system of pigmented and albino (hypopigmented) mammals. Albinos show a reduced number of rod photoreceptors and chiasmal misrouting (uncrossed pathway is reduced relative to the crossed pathway) [5,11,17]. These abnormalities may be explained in terms of disturbed neurogenesis consequent to the melanin deficiency. Albino rodents are reported to lack optokinetic responses due to their abnormal visual sensory system [18].

The light sensitivity in albino and pigmented rodents has been studied using behavioral and electrophysiological techniques [1–3,7,8,10,14–16,19]. There are differences in opinion regarding the visual sensitivity of albino rodents. Based on single unit recording from the superior colliculus, the dark adapted visual threshold was reported to be higher in albino than in pigmented animals [1,2]. However, behavioral and electrophysiological studies conducted later by other investigators could not find significant differences in the visual sensitivity between albino and pigmented animals [9,10,14].

The visual sensory processing in the inner retina is under the control of various neurotransmitters. These include inhibitory as well as excitatory transmitters and their receptors are localized in specific retinal neurons. Recent reports indicate differences between albino and pigmented rats in the level of these neurotransmitters [4]. Characterization of the visual responses from a visual center of the brain may elucidate the possible neurotransmitter-mediated difference in the transmission of light-driven visual responses between albino and pigmented rats.

The time for the light response to reach the visual centers of the brain (response onset latency) can be a reliable indicator of the visual sensory processing taking place inside the retina. Because of the structural and functional differences in the rod and cone visual processing pathways, the time comparison of the visual signals recorded from a central visual structure like superior colliculus can characterize these responses. This study gives further insight into the visual abnormalities reported for albino rodents.

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Animals were maintained in accordance with the Association for Research in Vision and Ophthalmology statement for the Use of animals in Ophthalmologic and Vision Research, and institutional approval was obtained. Rats for testing were obtained from in-house breeding colonies, originally obtained from Harlan Sprague–Dawley, Indianapolis, IN. Normal pigmented (ACI rats, 41–105 days old, $n = 6$) and normal albino (Sprague–Dawley (SD) rats, 45–115 day old, $n = 7$) rats of either sex were used. The animals were maintained on a 12 h light:12 h dark schedule with food and water provided ad libitum.

Electrophysiological assessment of visual responses in the SC was performed after modifying the method described earlier [21]. Briefly, the rats were dark-adapted overnight (<-6.00 log cd/m^2) and eyes were covered with a custom-made eye-cap that prevented bleaching of the photoreceptors during surgery. The cap could be easily removed at the time of visual stimulation. Animals were initially anaesthetized by intraperitoneal injection of xylazine/ketamine (37.5 mg/kg ketamine and 5 mg/kg xylazine), followed by a gas inhalant anesthetic (1.0–2.0% halothane in 40% O_2/60% N_2O) administered via an anesthetic mask (Stoelting Company, Wood Dale, IL, USA). Multi-unit visual responses were recorded extracellularly from the superficial laminae of the exposed SC using nail polish coated tungsten microelectrodes. Recordings were made with a full-field light stimulus (controlled by a camera shutter) projected on the back of a white plexiglass screen (diameter 20 cm) placed 10 cm in front of the contralateral eye (duration 50 ms). Blank trials, in which no light stimulus was delivered, were recorded to establish the baseline activity level at each site. A significant visual response was defined as the point at which a clear, prolonged (>20 ms) increase (at least twice) in the activity could be measured above the average background activity, which was determined using the 100 ms of activity preceding the light flash. Spontaneous activity was apparent when higher stimulus intensity was used, however, the visual responses could be easily distinguished because of its consistency in amplitude and latency.

Pilot studies conducted in albino and pigmented rats using very low intensity stimuli revealed that visual thresholds could be measured from most areas of the SC at the same light level. Very rarely, a difference in the threshold was found at a different SC location. This was later confirmed to be either due to brain tissue damage resulting from excess bleeding or when the electrode was not in perfect shape or due to variation in the level of anesthesia. Therefore, these data were not included.

Based on these preliminary results, the intensity of the light stimulus at the beginning of the recording was set at -6.46 log cd/m^2 and gradually increased (by steps of 0.25 log cd/m^2 controlled by neutral density filters) up to 0.81 log cd/m^2. In most of the rats, all recordings were made from a single site around the central SC from where the visual threshold was measured. In a few animals, the consistency of the visual response at different stimulus intensity steps was confirmed by recording from more than one electrode site (range 2–3). At each stimulus intensity step, the visual stimulus was presented at least six times with an interval of 10 s between the stimuli. All electrical activity was recorded using a digital data acquisition system (Powerlab; ADI Instruments, Mountain View, CA, USA). Blank trials, in which the illumination of the eye was blocked with an opaque filter, were also recorded.

For analyzing the visual responses properties, input from two channels were evaluated. One channel represents the external trigger from the camera and the second channel represents the signals from the SC cells. A pretrigger, 200 ms before the onset of the light stimulus, initiated each 1000 ms sweep. The latency of the response for each sweep was measured by positioning two cursors, one at the onset of stimulus artifact and the second at the onset of the visual response.

Properties of the visual responses used for detailed analysis include: (1) response onset latency and (2) visual threshold. Mean response onset latency and standard errors for each stimulus step was computed using data from the animals and SC locations in a group. Because the value remained similar for all the animals in a group, no standard error was calculated for the visual threshold.

Statistical comparisons were made using the Fisher exact probability test and one-way analysis of variance (ANOVA) with subsequent post hoc tests (statistics package of GraphPad Software, Inc., San Diego, CA, USA).

Multiunit recording from the SC demonstrated that light responsiveness of albino rats is higher than of pigmented rats ($p < 0.0006$, Fisher exact probability test). The dark-adapted visual threshold for the albino rat was -5.85 log cd/m^2 and that of the pigmented rat was -5.25 log cd/m^2.

The relationship between stimulus intensity and response onset latency is demonstrated by the light intensity–response onset latency curve (Fig. 1). In all the rats, the response onset latency became shorter with increasing stimulus intensity

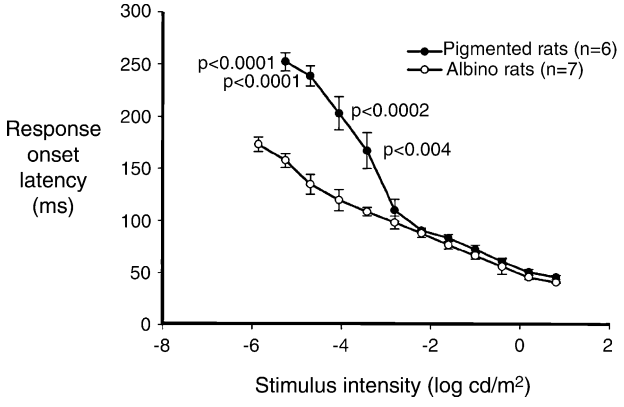

Fig. 1. Response onset latency vs. stimulus intensity plot of normal albino (open circles) and pigmented rats (filled circles) recorded from the superior colliculus. A deflection in the curve is observed in pigmented rats below -2.8 log cd/m^2, which may reflect the transition between photopic and scotopic responses. In contrast, the albino rats showed a more linear relationship between stimulus intensity and response onset latency.

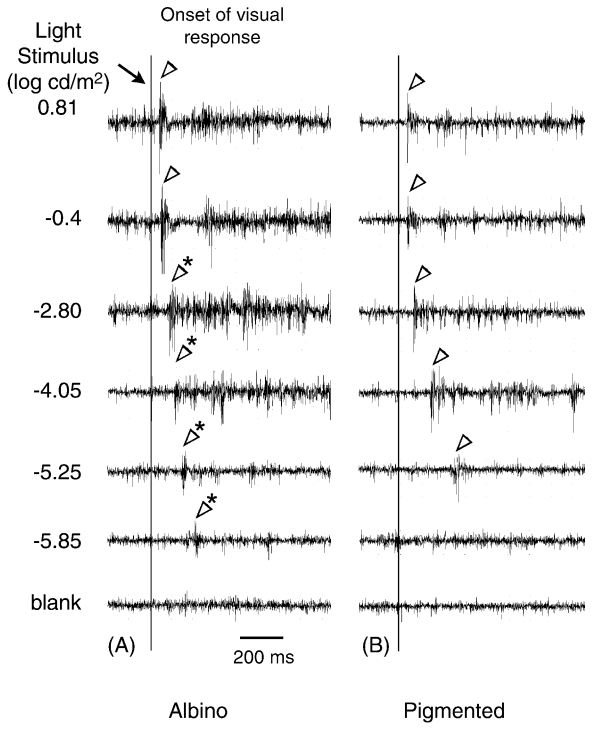

Fig. 2. Comparison of sample traces recorded at different light intensities from albino rats (A) and pigmented rats (B). The onset of the visual stimulus (duration 50 ms, −5.85 to +0.81 log cd/m^2) is indicated by a vertical line. The prestimulus recording shows the background activity. The onset of a visual response (at least twice the average background activity) is indicated by an open arrowhead. Significant differences in the onset response latencies between albino and pigmented rats are indicated by asterisks (see also Fig. 1A). In albino rats, responses with increasing latencies can be recorded starting with a threshold of −5.85 log cd/m^2. B. In pigmented rats, responses can only be recorded starting with a threshold of −5.25 log cd/m^2, and a significant increase in response onset latency is observed below—2.8 log cd/m^2.

(Figs. 1, 2a and b). The slope of the response onset latency curve in the pigmented rats in the stronger stimulus range (0.81 log cd/m^2 to −2.80 log cd/m^2) was mostly comparable to that of the albinos. However, an abrupt change in the slope of the curve was apparent in pigmented rats when the stimulus intensity was further reduced (<−2.80 log cd/m^2). In pigmented rats, the response onset latency became significantly longer with lower stimulus intensity; whereas the albino rats showed a more linear relationship between stimulus intensity and response onset latency (Fig. 1).

The present investigation demonstrates a significant difference in the visual sensitivity between albino and pigmented rats. Compared to the pigmented rats (−5.25 log cd/m^2), the albinos have a significantly lower visual threshold (−5.85 log cd/m^2) (higher light sensitivity). Previously, Balkema et al., based upon single unit recordings from the superior colliculus, reported that albino rats [1], mice and rabbits [2], has inferior visual sensitivity compared with pigmented. In reference [1], the author did not mention the number of animals used, the dark adaptation procedures and whether the eye was protected from stray light during surgery. In addition, the animals were maintained under long-term anesthesia (approximately 13 h, maintained by supplementary doses of ketamine/xylazine) that could influence the animal's physiological condition and thereby affect the visual sensitivity. The elevated dark-adapted threshold for rats in the Balkema study [1] was −2.92 log cd/m^2 for pigmented rat and −1.14 log cd/m^2 for albino rat; this may be due to one or more of the above-mentioned factors. A later investigation by Green and co-workers [9,10], also based on single unit recording from the SC, however, found no impairment in the visual sensitivity of albino rats. This study also reported a lower threshold level for albino (−5.84 log cd/m^2) than for pigmented rats (−5.54 log cd/m^2), similar to the results that are reported in this current investigation (albino −5.85 log cd/m^2 versus pigmented −5.25 log cd/m^2). However, the number of animals used in the Green study [9,10] ($n = 4$) was not large enough to yield a significant statistical difference.

In addition, several other reasons could contribute to the discrepancies in the outcome of the various investigations. Our SC data is based on multi-unit recording from the SC whereas most of the other reports were based on single unit SC recording. The threshold level obtained by single unit recording may exhibit variations due to the functional differences in the rod pathways, as has been reported for mice [22]. Visual thresholds may be also affected by the type of anesthesia used and by variations in the surgical procedures. Other physiological parameters such as ambient light conditions and the dark adaptation procedures may also influence the outcome.

Looking into the intensity versus response onset latency curve, it is obvious that the response onset latency is inversely proportional to the stimulus intensity. A short response onset latency was detected in pigmented and albino rats when the stimulus intensity was high. At the highest level of stimulation (0.81 log cd/m^2), the albino rats had significantly shorter response onset latency than pigmented rats ($p < 0.05$), suggesting more rapid processing of the photic signals. Apart from this, both albino and pigmented rats had more or less similar response onset latencies until the stimulus intensity was reduced to −2.8 log cd/m^2. With further reduction in the stimulus intensity, the response onset latency was significantly prolonged in pigmented rats.

Physiological differences associated with the melanin production, such as different levels of dopamine and other neurotransmitters [4], may also influence the visual sensory system of albino and pigmented rats. The lower level of retinal pigmentation in albino retina can cause scattering of the light stimuli, which in turn may shorten the response onset latency. Developmental abnormalities due to melanin deficiency such as reduction in the uncrossed pathways (into the ipsilateral SC) [5,11,17] may also affect the response onset latency.

The delay in the visual signal transmission during very low light stimulation observed in pigmented rats can also be

the manifestation of the rod-driven responses. Generally, the rods acts slower to light stimuli [6] and their responses may be further delayed due to the presence of additional synapses through specific amacrine cell system [20]. Hence, the abrupt change in the progression of the intensity–response onset latency curve in pigmented rats can be the reflection of the transition between scotopic and photopic responses.

In albino rats, a more linear relationship was observed between stimulus intensity and response onset latency, suggesting considerable differences in the visual signaling pathways of albino and pigmented rats. Interestingly, this dichotomy in signal transmission pattern is mostly limited to the scotopic phase (level of the rods). A recent report by Blaszczyk [4] demonstrates quantitative differences in the retinal neurotransmitters between albino and pigmented retinae. In albino rats, the level of GABA is reduced by nearly 30% compared to pigmented rats retinae. Also, significant increase of the glutamate to GABA ratio by nearly 20% is reported in albino retinae [4]. It may be noted that, during retinal neural transmission, the activity of GABA is inhibitory whereas glutamate is excitatory. There are also reports suggesting contributions of GABA and glutamate in the specific transmission of rod-driven visual signals [12,13]. Hence it may be speculated that the longer response onset latency in the scotopic range of pigmented rats could be the manifestation of the inhibitory GABA system. The possible role of other neurotransmitters such as dopamine also cannot be ruled out in this regard.

In conclusion, the differences of cone and rod-driven visual signals in the superior colliculus are more obvious in pigmented rats. The albino rats have higher light sensitivity and more rapid signal transmission at lower light levels. This differential light perception pattern of albino and pigmented rats could be due to the differences in their visual sensory processing mechanism [5,11,17]. The acuity and contrast sensitivity related visual abnormalities reported for albino rodents could be attributed also to their “hyper sensitivity” to photic cues.

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