Electrophysiology of Eye

Team Members

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1. Introduction and Background

Problems Revolving around in India[Reference used]:

- Currently health budget thats allocated is just 2% and non existing health insurances
- Challenge is to provide quality healthcare to everyone
- More than 10 million Indians blind
- India currently has 10000 **ophthalmologists ,** so that's just 1 **ophthalmologist for 100,000 people**
- Past year over **3.5 million surgical procedures** were performed for cataracts
- Two major barriers: Unequal distribution of **ophthalmologists(70% of them practise in urban areas while that just counts for 23% of the affected people,** nearly half of them have negligible surgical experience**)** and gross underutilization of those available
- Most of the **ophthalmologists** are self employed working in their clinics and don't have those heavy and expensive equipments required, and only 5% of them have subspecialities of **ophthalmology** but mostly target just refraction services and cataract surgery.

Current Available services in India

- Top five hospitals in India are :
- ❖ Sankara Netralaya, Chennai (1000 employees, treats 1200 patients a day)
- ❖ LV Prasad Eye Institute, Hyd (Reaches out to both rural(covers 1000villages(primary and secondary care) and urban areas since 1987 served 15 million people)
- ❖ Dr. R P Center of ophthalmic Sciences, AIIMS, New Delhi (Supports major part of North India)
- ❖ Aravind Eye Hospital, Madurai
- ❖ Apollo Hospitals, Chennai

Costs Involved in Treatments/Equipments:

- **Laser Treatment -** Rs 25,000 - Rs 100,000
- **Corneal Cross Linking**: Rs. 20000/- per eye. Rs. 35000/- per eye with topolinked PRK
- **Cost per test for adults for ERG - Rs 3000** per test and for **children - Rs 6000** (inclusive of anaesthetics)
- **ERG machine - Rs 1,200,000**

Different kinds of cases that come to the ophthalmologists: 25% neurological, 25% optic nerve related, 25% retinal cases and 25% others

Cases: are not always involved with both rods-cones & multi focal
Time spent per patient: 35mins per patient and double in children

Current Issues

- Devices are bulky, expensive and still very less accessible
- Children don't feel comfortable and they feel claustrophobic(because of darkness and isolation)
- The procedure currently in use for ERG is invasive.

2. Electrophysical signals related to the ERG

The flash ERG is the mass response of neural and non-neural retinal cells to full-field luminance stimulation. The initial action of light on the retina is to cause the photoisomerisation of rhodopsin. This sets up a chain of biochemical reactions within the photoreceptor, the phototransduction cascade, the result of which is hyperpolarisation of the retinal photoreceptors. The photoreceptors then signal to the bipolar cells, with rods and short wavelength cones (s-cones) being directly coupled to ON- (depolarising) bipolar cells (DBCs) and medium and long wavelength cones connecting both to cone ON cells (DBCs) and also OFF – bipolar cells (hyperpolarising). Different ERG components arise in relation to different structures and processes.
From a clinical point of view there are many proteins involved either directly in the process of or in the recovery from phototransduction. Retinal degenerations can arise as a consequence of mutations in these proteins.
The hyperpolarisation of the retinal photoreceptors creates an electric potential across the retina and its influence can be picked up by using conducting electrodes that may be in contact with the cornea, bulbular conjunctiva or the skin on the lower eyelid.

3. Signal Acquisition Methodology

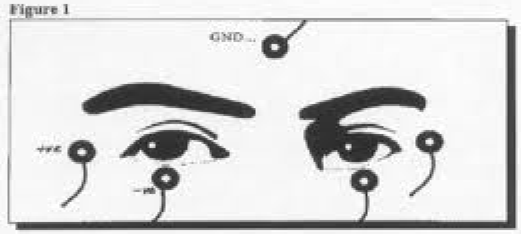
Human body is a connectom of signals. Eye being the medium of visual perception communicates to brain via optic nerve. There are different electric signals
generated in and around the eye due to physiological activities along with the visually evoked potential. The document talks about different electrophysiological movements leading to EOG, ERG, Nystagmography etc. It talks about the corneal analysis of different parameters wherein the measurement is done by placing electrodes directly on cornea. Here it was specified that the signal magnitude is around 0.4-1mV. A single wave generated propagates as a,b and c wave towards the retinal end to evoked light stimulus. Different cells responsible for this electric signal:

1. c-wave : Pigment Epithelium
2. b-wave : Bipolar, Ganglion cells
3. a-wave : Rods and cones.

Present day technology uses corneal measurement for ERG, but we focussed towards doing the same with a non corneal approach. This was backed by the technical paper titled "Non-corneal

electroretinogram Parameters in normal children by ANN HARDEN".
4. For the non corneal approach, we use three electrodes , two for measuring the potential difference between two locations preferably just below eye, and the third for reference on the temple or forehead.

Figure 1



Electrode placement for recording cutaneous electro-retinograms.

Source:www.wch.sa.gov.au

4. ERG types and responses

The ISCEV defines 5 types of clinical ERG tests-

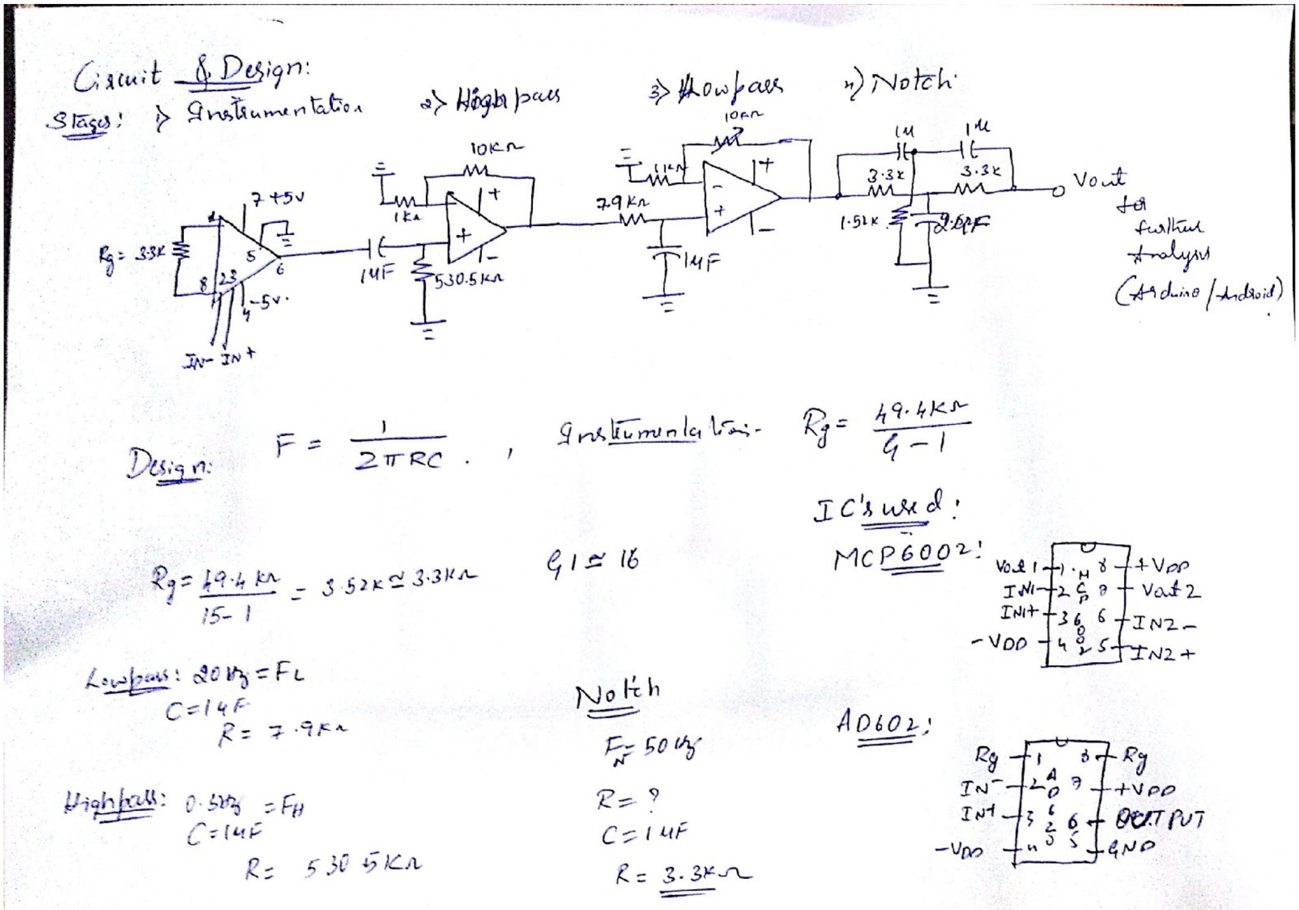
1. Rod receptor response in dark adapted eye.
2. Maximal response of dark adapted eye.
3. Oscillatory potentials (Dark adapted eye using 5 ms flash)
4. Cone receptor response in light adapted eye.
5. Flicker fusion response to periodic stimuli.

The Flash ERG response gives a multitude of data responses but we are interested in a few important ones, these are-

- The a- wave
    - It is due to the mass hyperpolarisation of rods and cones to test flash. It is recorded from the baseline to the 1st negative peak of the ERG.
- The b-wave
    - It is due to the activity of 2^{nd} order retinal neurons in middle of retina and involves the ionic currents around the glial cells. The b wave amplitude is measured from the negative a-peak to the positive b-peak. The b wave time to peak is measured from the beginning of the flash to the b-peak.
    - Parameters to be studied are the a and b wave amplitudes and the b time to peak for diagnosis of various diseases.
- Oscillatory Potentials
    - Seen after the b wave these potentials arise from the amacrine cells for stimulus

conditions that reflect both rod and cone responses.

5. Instrumentation Design and Approach:



In corneal ERG the signal parameters are,
a. Frequency= 0.3Hz to 300 Hz
b. amplitude= 0.4 to 1mV

for our design approach we considered,
a. Frequency= 0.3Hz to 20Hz
b. amplitude= order of few microvolts(Typically 400-500 uV).

Reason: As we go higher in frequency the noise factor increases. To avoid that we scaled down the frequency. And due to the signal attenuation by skin muscles, the amplitude decreases by a lot.

Stages of Circuit:
1. Instrumentation stage: AD620

For taking the potential across to electrodes wrt the reference. Instrumentation amplifiers are very less susceptible to noise as CMRR is high and is very suitable for bio-electronics application.

Rg(Gain resistance)= 3.3K

Gain obtained G1= 15.9

2. High pass stage: MCP6002 op-amp

   To eliminate signals below 0.3Hz

   C=1uF, R=530.516K ohm (used 330+100+100K=530K)

   Gain factor G2= 10

3. Low pass stage: MCP6002 op-amp

   To eliminate signals above 20 Hz

   C=1uF, R=7.9K ohm(used 4.7K+3.3K)

   Gain factor : Variable (Used a potentiometer 10K) Maximum gain G3=10.

4. Notch stage:

   To take out the 50Hz AC frequency noise in supply

   C=1uF, R=3.3K.

Total Gain Factor: G=G1*G2*G3=16000(approx).

Design used F=1/(2*pi*R*C).

Specifications:

1. Supply voltage: -5V -- +5V(From SMPS, As Instrumentation stage requires dual supply)
2. Expected output voltage range <1V.

Calibration

A quick review of the ISCEV calibration guidelines 2003 has necessitated to implement the following calibration:

1. Calibration of intensity of Ganzfeld strobe flash and background illuminance
2. Calibration of amplifier scale against standard signal

The aforementioned calibrations will be implemented in the new design

6. Design Overview:

Existing portable devices: ephios; HMsERG (Handheld Multi species Electroretinography), reteval.

1. **ephios**: "The **ephios • eph-01** ERG/VEP device provides the ophthalmologist with the capability to a quick and effective test of the retinal function for screening or in cases of diffuse blindness." (http://www.ephios.com/products.htm)

2. **HMsERG**: All in one full fiedl flash ERG device. Can be used as a portable device and/or can be used on a stand. (http://www.ocuscience.us/sitebuildercontent/sitebuilderfiles/hmserg_full_brochure.pdf)

3. **reteval:** Handheld, Utilizes skin electrodes, Mydriatic- free, Ultra low-noise digital amplifier (http://www.excimed.com/products-a-services.html?page=shop.product_details&flypage=&product_id=1333&category_id=0)

Guidlines: ISCEV (2008) Guidance for flash and VEP

Existing methodology:

1.Dark adapt patient for a set time of 30 minutes.
2. Attach electrodes using dim red illumination. We use an indirect headlamp with several Wratten 26 red filters so that it simulates a mobile darkroom "safe" light.
3. Record ERG using single scotopically-balanced dim blue and red flashes, and bright white flashes as illustrated in sample ERGs of Figure 9b. Some laboratories average several responses.
4. Turn on moderately high background illumination of about 10 ftL for about 10 minutes and record ERGs using 30 Hertz flicker and bright white flashes. Responses recorded using moderately high background illumination accentuate the cone system by bleaching the rods and only cones can recover fast enough between flashes to accurately follow a flickering 30 Hertz light.

Requirements:

Reference electrode: Two electrodes below the eye lid and one as reference on forehead (signal contamination risk) or orbital rim.

Ground electrode: earlobe or forehead.

Stimulus: Flashes of max 5ms and a stable white background light.

Design constraints:

1. Non -corneal contact.
2. Portable.
3. Real time - display of results and diagnosis.
4. non invasive.
5. Easy to use and interpret.
6. Affordability.

Packaging Requirements:

- 3 electrode points
- external stimulus
- complete covering of eye. (minimum/no light loss)
- circuitory
- display screen.

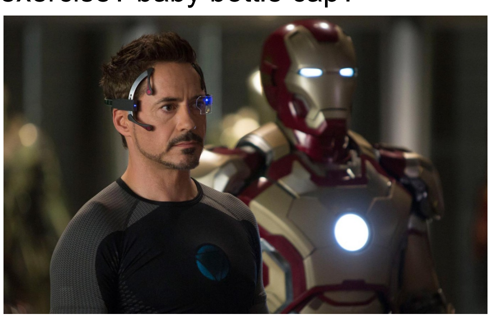
Additional Design points:

- Aesthetic considerations
- User friendly and comfort

Avoiding feature creep: Single eye diagnosis at one particular time.

Possibilities for the electrode setup?

*A single eye covering (like in Avengers or iron man? awesome) with light stimulus. - transparent? plastics? routing of electrode wires? plexi glass? ABS? proper covering? eye cap used during eye exercise? baby bottle cap?



First Inspiration

Basic outline:

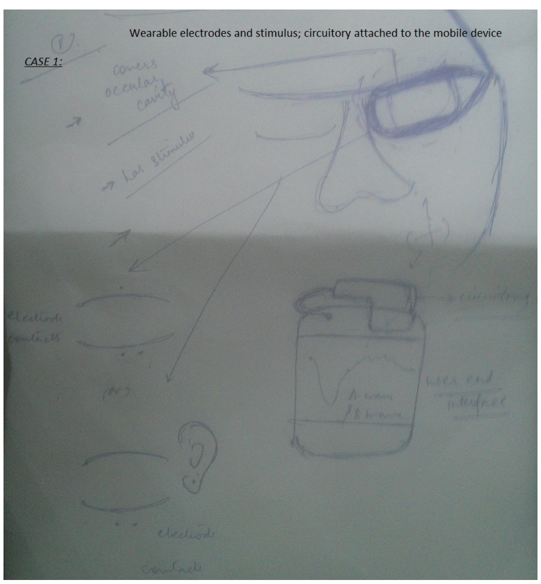
one power source

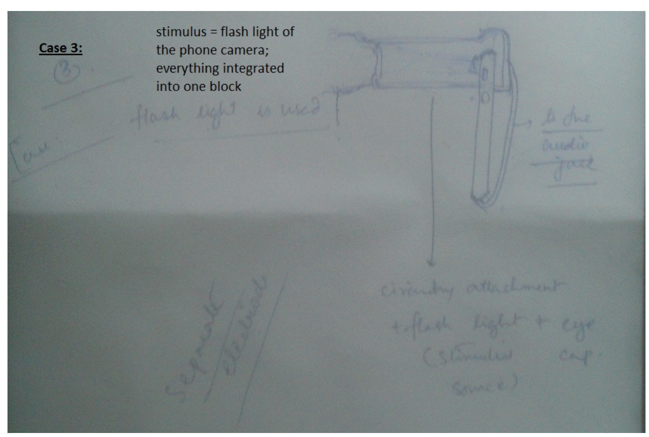
Electrode connections + external stimulus — circuitory — arduino interface and/or android

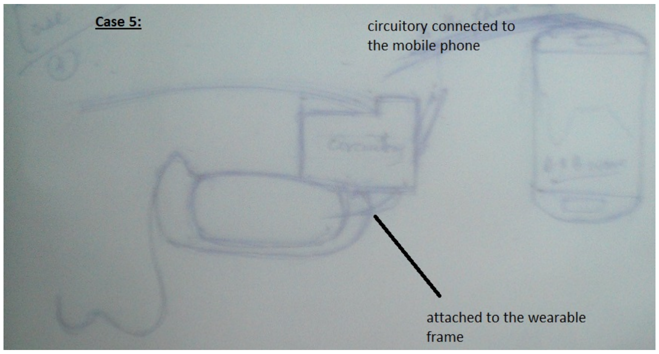
- LCD screens
- camera flash
- combination of LEDs

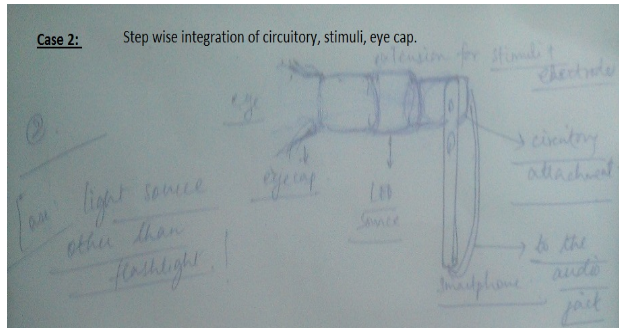
Design Process Pictures:

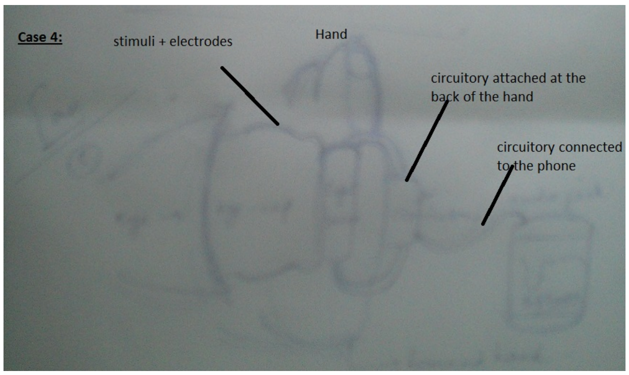
Day1:



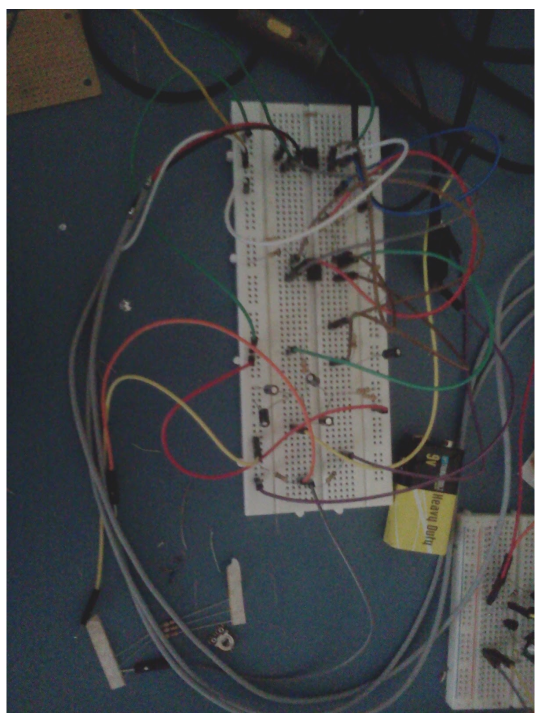


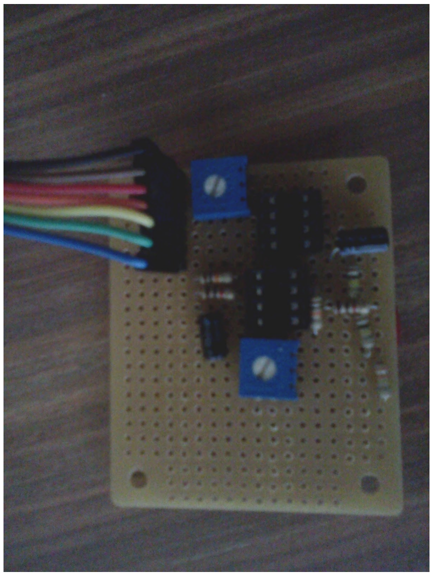




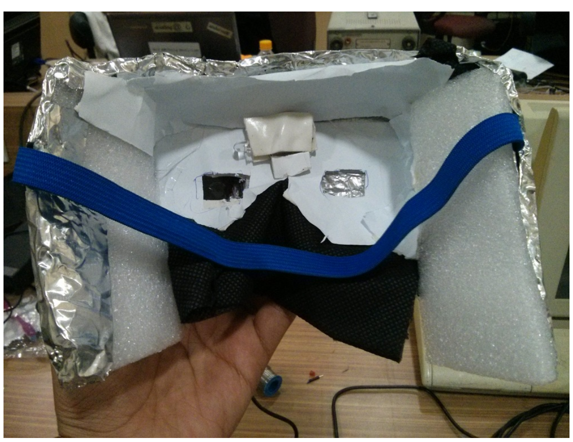


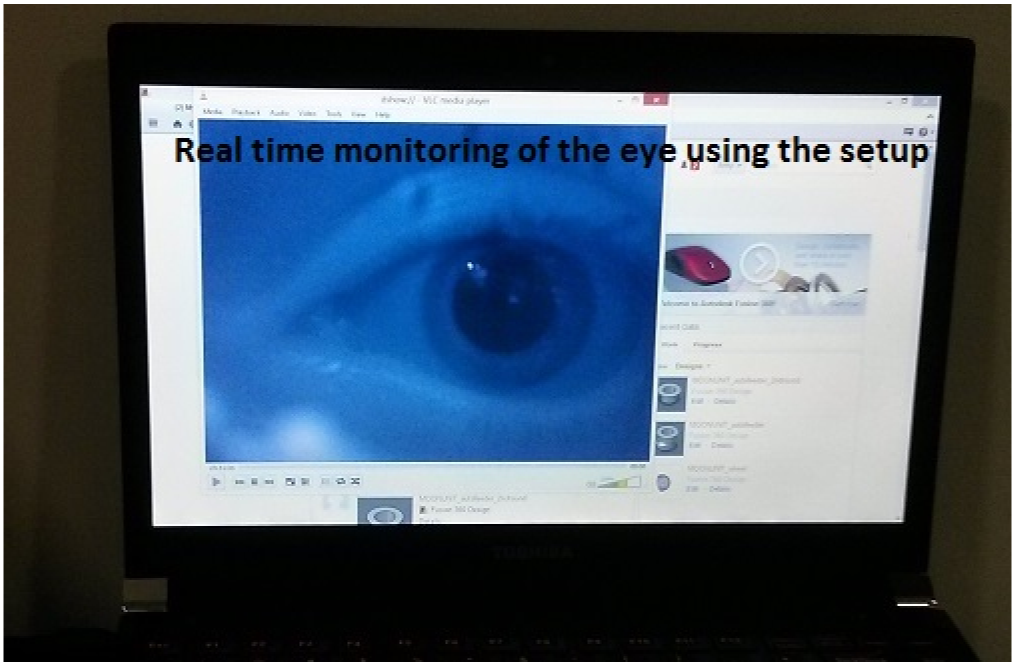
Designs of Day 2:





Progress till Day 3:





Scope of design improvements using modern platforms

The analog frontend is based on mature techniques while there is continuous improvement in the hardware and software platforms available for implementing logic. Cost of hardware has reduced making use of digital signal processing more attractive.

Currently, two platforms are being considered:
A portable and complete microcontroller based solution, where the ERG signal coming from analog frontend is digitized and processed by a microcontroller. The microcontroller also handles filtering for analysis, an integrated display for presentation of the signals and storage.
Pros:
A standalone device
Platforms are available to implement this easily

Cons:
Does not offer very interactive interface
Expensive compared to second option

A smartphone based solution that uses an add-on that connects to the smartphone and uses it's hardware and computational capabilities very efficiently

Pros:
Smartphone has better reachability
The additional hardware required is relatively less expensive
More dynamic and interactive data visualization

Cons:
Absence of required native interface in smartphones

Factors that may have effect the tests

1. Electrodes position
2. Pressure on the electrodes
3. Application of gel(Types, amount etc)
4. Type of skin (Oily)
5. Noises caused due to muscular signals and different other factors like blinking
6. Eye movement
7. Flash intensity
8. Pre testing conditions
9. Atmospheric factors
10. Setup of the erg
11. How much influence does ambient light source causes?
12. Intensity of the ambient light
13. Size of the electrode
14. Material of the electrode
15. Area of contact
16. Position of LEDs
17. Check oculogram