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LETTER
Visual responses in a transplanted eye: reality or chimera?

Key words
- eye diseases
- transplants
- retinal neurons

Dear Editor,

We read with interest the recent paper on JAMA by Ceradini *et al*. [1], reporting the clinical ophthalmological findings in a patient who received, for the first time, a whole-eye transplant. This patient underwent a detailed and state-of-the-art reconstruction of the hemiface and orbit with an excellent and important aesthetic postop result. The procedure was performed with great care also with respect to ethical issues [2] and, prospectively, could be an important step towards a therapeutic resource to treat patients with no viable alternatives. However, the transplanted eye resulted completely blind throughout the follow-up. Interestingly, the Authors evaluated both the structure and function of the retina and optic nerve in the transplanted eye, showing signs of atrophy at both retinal and optic nerve level; on the functional side, the Authors claimed some evidence of postop photoreceptor/bipolar cell function assessed by flicker electroretinograms. The Authors also claimed the presence of some electric signals of neural activity originating at the level of visual cortex, in response to flash stimulation (flash visual evoked potentials, VEPs) of the blind, transplanted eye. The recorded flash VEPs waveforms reportedly were blunted and delayed but within the range of International Society for Clinical Electrophysiology of Vision (ISCEV) standards for VEPs. This surprising finding raises several questions about the most effective VEP recording and analysis methodology to use, when recording VEP responses from severely visually impaired eyes. Transient VEP responses have the limitation of ambiguity of interpretation, or significance, when the amplitude response is reduced close to noise level, as in severely impaired eyes. Noise estimates should be considered in such contexts given their potential influence on the recorded signal. This can be done in different ways. The simplest way is to record the same VEPs with the stimulus completely occluded. Another useful way would be to digitally subtract odd from even (or *vice versa*) events in the averaging procedure. The difference may provide a signal reflecting the background noise-independent activity. Additional methods which proved to be efficient and well exploited in detecting very low-amplitude VEP signals are based on steady-state VEP recordings and application of sub microvolt methods based on the Fourier analysis and estimate of noise and signal-to-noise ratio [3, 4]. These methodologies, which are more advanced and sophisticated compared to the ISCEV standard clinically recommended procedures, increase the precision and confidence of measurements in blind or severely visually impaired eyes. The VEP signals reported in the study by Ceradini *et al*. [1], suffer from ambiguity and uncertainty, limiting an adequate interpretation of a finding (presence of a visual signal to visual cortex from the transplanted eye, presence of real, noise-free retinal signal) of the utmost importance when evaluating the results of whole eye transplantation. Digital methods of signal-to-noise ratio estimates may certainly improve the accuracy of functional results unlocking the doors to a better understanding of optic nerve graft to host integration.

Francesco Martelli[1]*, Benedetto Falsini[2] and Andrea Cusumano[2]

[1]*Dipartimento di Malattie Cardiovascolari, Endocrino-Metaboliche e Invecchiamento, Istituto Superiore di Sanità, Rome, Italy*
[2]*Macula and Genoma Foundation, Rome, Italy*

**Corresponding author*: francesco.martelli@iss.it

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