

Case Report

Coexistence of fixation-off sensitivity and inverted fixation-off sensitivity in a female child with Panayiotopoulos syndrome: Video-electroencephalography documentation☆



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ABSTRACT

Fixation-off sensitivity (FOS) is a rare phenomenon elicited by elimination of central vision and fixation, which even in the presence of light induces occipital paroxysms or generalized paroxysmal discharges. It is most commonly encountered in patients with idiopathic childhood occipital epilepsies but may also be observed in cases of symptomatic focal and generalized epilepsies. We describe a female Emirati child with Panayiotopoulos syndrome who exhibited FOS in addition to the reverse phenomenon called “inverted fixation-off sensitivity,” in which the electroencephalographic discharges were suppressed by the absence of central vision or fixation and activated by central vision or fixation.

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1. Introduction

Fixation-off sensitivity (FOS) is an interesting electroencephalography (EEG) phenomenon elicited by the elimination of central vision and fixation [1]. Fixation-off sensitivity can act as a seizure trigger in patients with Panayiotopoulos syndrome (PS) and more frequently in patients with idiopathic childhood occipital epilepsy of Gastaut [2]. Rarely, it can be manifested in symptomatic occipital lobe epilepsy [2] or within the spectrum of benign childhood seizure susceptibility syndrome [3]. It can also be seen in eyelid myoclonia with absences [4], in atypical benign partial epilepsy (ABPE) [5], and even in asymptomatic children without epilepsy [6].

The reverse of FOS, inverted FOS (iFOS), in which the epileptiform activity is suppressed by the absence of central vision or fixation and activated by central vision or fixation, has been described in only two patients. In one patient with Lafora disease whose myoclonus was suppressed by passive eye closure, neurophysiologic studies disclosed that fixation was the most important enhancer of myoclonus [7]. Magnetoencephalographic studies of visual evoked fields revealed abnormal activation of the visual corticocortical pathway via the insular cortex not seen in controls. The authors hypothesize that abnormal

activation of the insular cortex may be involved in triggering the mechanism of fixation-sensitive myoclonus [7]. The second patient with iFOS was diagnosed with ABPE, in which a decrease of epileptiform activity was evident upon closure of the eyes and upon inhibition of fixation by the use of Frenzel goggles [8].

Here we describe the first reported case of coexistence of FOS and iFOS, documented in an Emirati girl with PS whose EEGs unexpectedly and repeatedly showed a combination of FOS and iFOS.

2. Case report

An Emirati girl with no significant pre- or postnatal history and normal motor and cognitive development presented to our pediatric neurology clinic at the age of 5 years and 3 months with a history of 4 attacks of screaming while asleep. The first seizure occurred at the age of 4 years and 4 months of age. At that time, she developed recurrent retching and vomiting, her eyes turned to one side, and she then became flaccid like a “rag doll,” with minimal motor activity for 2–3 min and following that was partially unresponsive for about 30 min. She was rushed to a local hospital where magnetic resonance imaging of the head was done and reported as normal. A standard wake EEG performed at that time showed bilateral occipital epileptiform discharges. The second and third attacks occurred 2 and 4 months later, respectively, with similar semiology and lasting for 1–2 min. The fourth attack occurred 2 weeks before the patient was presented to us, during which versive seizures with eye deviation to one side continued for about 30 min. She was treated in the hospital with rectal diazepam and parenteral fluids. All the attacks were associated with mild- to moderate-

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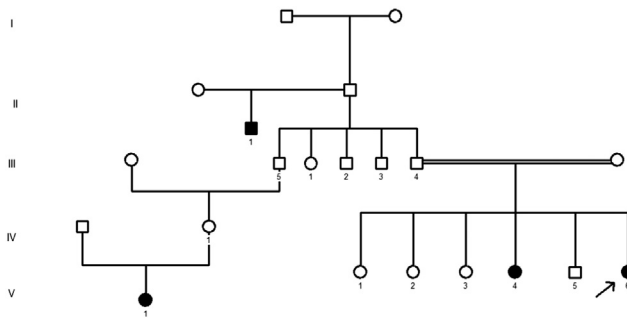


Fig. 1. Family pedigree illustrates family members with a history of epilepsy. Solid black symbols indicate individuals who demonstrated a history of seizures. Open symbols indicate healthy individuals.

grade fever. A diagnosis of PS was made, based on the symptomatology in addition to the EEG results, and the patient was started on oxcarbazepine orally. Ten days later, she developed a rash on the skin and mucous membranes associated with a mild fever and lethargy. Stevens–Johnson syndrome was suspected, and oxcarbazepine was discontinued and the patient was started on levetiracetam. The child has been seizure-free for the last 6 months.

2.1. Family history

The parents are first-degree cousins who have 5 other children, 3 girls and 2 sons. An older sister, the third sibling, an 8-year-old child, has a history of recurrent febrile seizures from the age of 5 months up to 4 years. Three near relatives on the father’s side have had epilepsy since early childhood. A male cousin to both parents who is now 12 years old had a history of frequent nocturnal seizures beginning at the age of 5 years. He was treated initially with traditional remedies with no improvement, then was treated abroad with levetiracetam and has been seizure-free since the age of 9. At the age of 7 years, it was determined that he has learning difficulties but is now in a regular

school with the help of a shadow teacher. Another paternal cousin, a girl, now 8 years of age, had a history of prolonged, most probably focal seizures associated with severe vomiting, 2 to 3 times per month, since the age of 5. She was put on oxcarbazepine and has been seizure-free for the last 18 months. The third relative with seizures is a distant paternal cousin, a 14-year-old boy, who had a history of seizures, usually during sleep, since the age of 11. He is now on levetiracetam and has been seizure-free for the last year. (For family pedigree see Fig. 1.)

2.2. Video-EEG recording

A 20-channel scalp video-EEG was recorded at our EEG laboratory over a 30-min period on 2 separate occasions. The first test was performed at the time of the patient’s initial presentation at the age of 5 years and 3 months. The second one was performed 1 month later. All recordings were performed according to the protocol suggested by Panayiotopoulos, which consisted of spontaneous eye opening and closing in a well-illuminated room, with and without the use of dark underwater goggles covered with opaque tape, underwater goggles covered with semitransparent tape, and Frenzel lenses to eliminate central fixation and vision. The patient was asked to open and close her eyes every 6 s for a total of 6 times. She was instructed to look at a fixed point to ensure fixation. Hyperventilation and intermittent photic stimulation were performed in all records, and a natural-sleep EEG was also obtained.

Both EEGs revealed a normal background, and iFOS was suspected when continuous right-sided, moderate-voltage occipital paroxysms appeared when the patient opened her eyes in a lit room and disappeared immediately when she closed her eyes (Fig. 2). During the same recordings, high-voltage, continuous bilateral occipital epileptiform discharges were seen when the patient closed her eyes, and this persisted for as long as her eyes were closed, which suggested FOS (Fig. 3). The diagnosis of FOS was unequivocally established by demonstrating that these occipital discharges are activated by impeding central vision using the Panayiotopoulos protocol mentioned earlier (Fig. 4A and B).

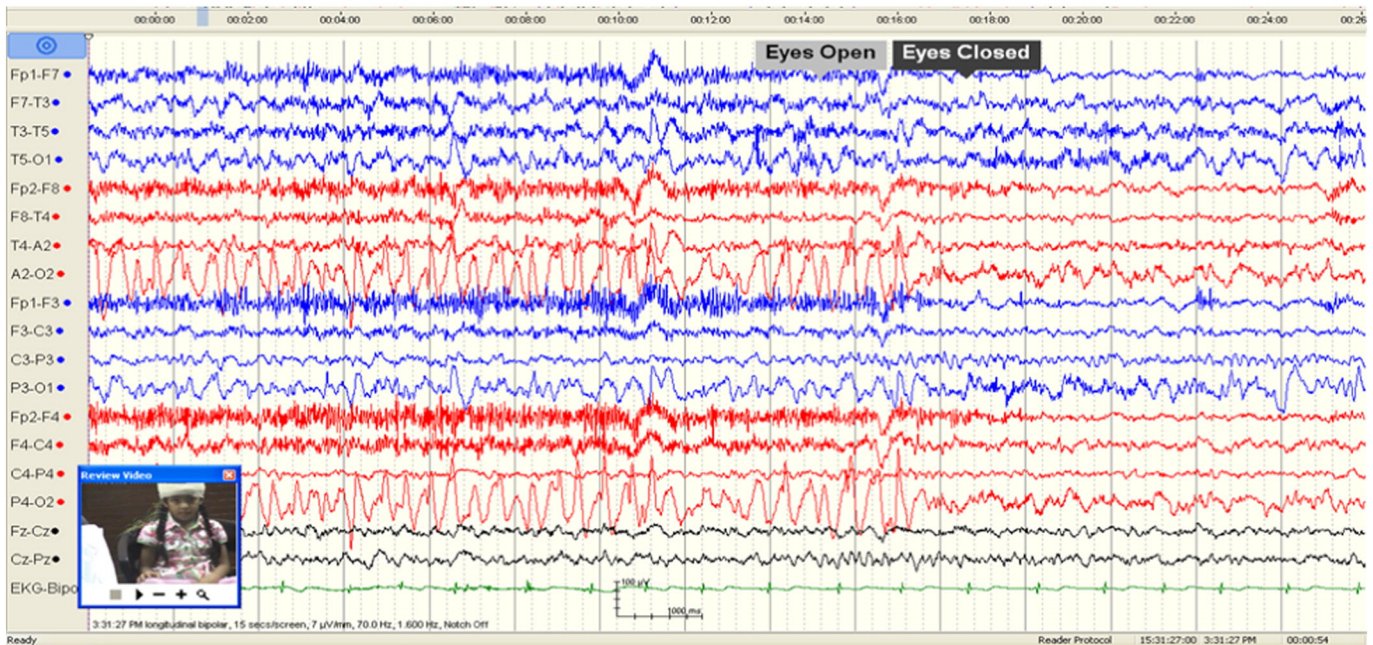


Fig. 2. Inverted fixation-off sensitivity. EEG recording with lights on. Right-side occipital epileptiform discharges appeared when the patient opened her eyes, which persisted as long as she kept her eyes open and disappeared immediately whenever the child closed her eyes. Low-cut filter, 1 Hz; high-cut filter, 70 Hz.

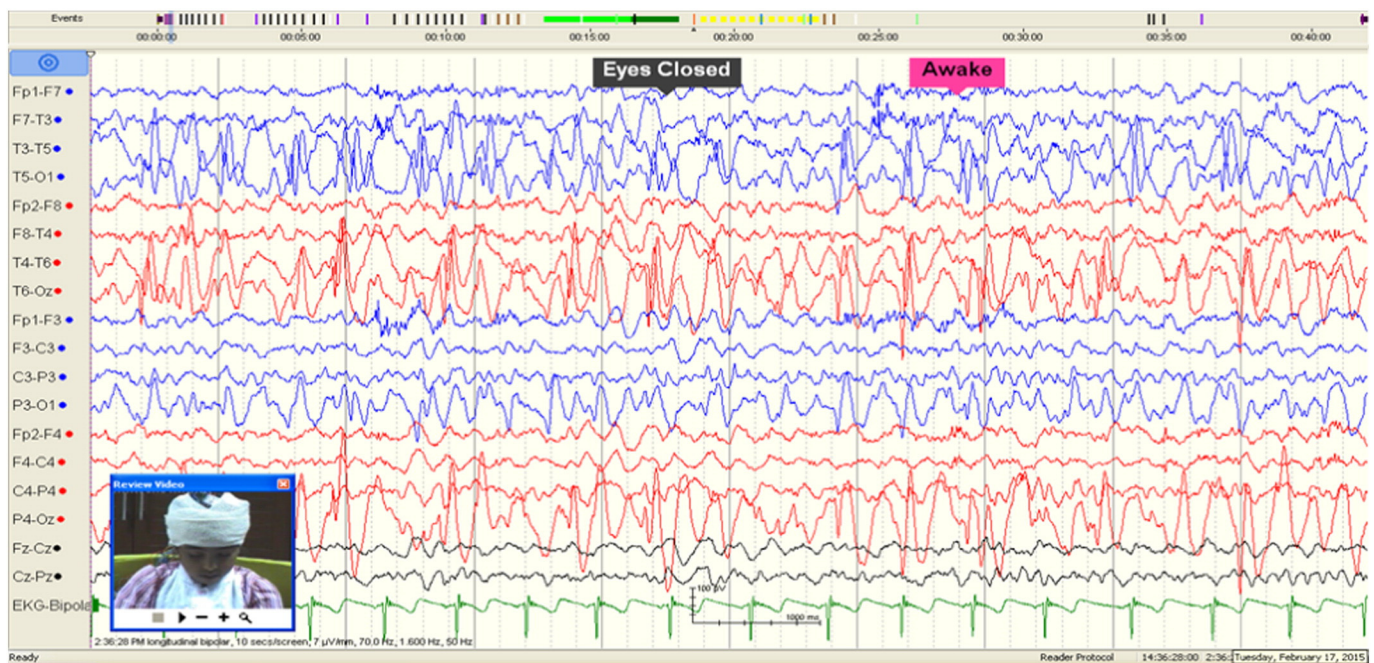


Fig. 3. Fixation-off sensitivity. EEG recording with lights on. High-voltage bilateral occipital epileptiform discharges reappeared when the child closed her eyes and persisted as long as her eyes were closed. Low-cut filter, 1.6 Hz; high-cut filter, 70 Hz.

3. Discussion

Fixation-off sensitivity refers to forms of epilepsy or EEG discharges characterized by continuous focal or generalized spikes, spike-wave, or sharp-wave focal discharges, usually in occipital regions, that consistently occur within 1–3 s of eye closure, persist throughout the eye-closed state (i.e., when central vision and fixation are eliminated), and disappear immediately with eye opening [1] (Fig. 3). The diagnosis of FOS is confirmed only by demonstrating that the same abnormalities also occur by blocking central vision and fixation using semitransparent goggles (which, by reducing incoming light, obscure any visual input), Frenzel lenses (which produce refractive errors), translucent spherical lenses (which distort light refraction), or Ganzfeld stimulation (using a homogeneous visual field that gives the subjective visual experience of the surface fading away) in uncooperative patients [1]. The etiology, pathophysiology, and structural correlate underlying FOS remain unclear. Hassan et al. described a patient with persistent left-sided FOS following perinatal insult in which brain magnetic resonance imaging revealed gliosis and ulegyria over the left posterior occipital cortex corresponding to the topographic representation of the macula [9]. They suggested that the extensive denervation of the area representing the macula along with the presence of hyperexcitable ulegyric cortex is responsible for the phenomenon of FOS [9]. Fixation-off sensitivity should be differentiated from pure forms of scotosensitivity, in which EEG discharges or epileptic seizures are elicited by darkness [1], and from eye-closure sensitivity, in which the epileptiform discharges are triggered by eye closure, occur within 1 to 3 s after the positive deflection of the eye closure artifact, are self-limited and of brief duration, typically relate to photosensitivity, and are suppressed by complete darkness [2]. We document for the first time, to the best of our knowledge, two opposite phenomena in a female child with PS. The first was the reverse of FOS, a condition called iFOS, where occipital discharges were activated during eye opening and fixation and were suppressed by the elimination of central vision and fixation; in addition, during the same EEG recordings, FOS was unequivocally documented. Similar reports of iFOS have been described in two patients. Kumada et al. described an adolescent with Lafora disease whose myoclonus was suppressed by passive eye closure

[7]. Neurophysiologic studies disclosed that fixation was the most important enhancer of his myoclonus [7]. Another case of iFOS was described in a 6-year-old boy with ABPE [8]. Immediate inhibition of epileptiform activity was evident upon closure of the eyes and upon inhibition of fixation by the use of Frenzel lenses [8]. The explanation of these different mechanisms is difficult, but it seems that iFOS may be a variant phenomenon of FOS [8]. In Lafora disease, the presence of giant somatosensory-evoked potentials, indicating hyperexcitability of the sensorimotor cortex, is well known [10]. This hyperexcitability of the sensorimotor cortex in response to afferent stimuli indicates a severe impairment of inhibitory mechanisms in Lafora disease [7]. The authors stated that they did not know whether the iFOS represented an exaggeration of photosensitivity because of the impaired inhibitory mechanism or was based on another mechanism [7]. This patient was diagnosed with PS, a benign, age-related focal seizure disorder occurring in early and mid-childhood [11]. It is characterized by seizures, often prolonged, with predominantly autonomic symptoms, manifested mainly by emesis and by an EEG that shows shifting or multiple foci or both, often with occipital predominance [11]. Because of frequent EEG occipital spikes seen in patients with PS, it has been erroneously considered as occipital epilepsy [12]. In the present patient, the EEGs showed mainly occipital discharges. Ohtsu et al. indicated that the EEG foci in most patients with PS easily shift location, multiply, and propagate diffusely with age rather than persistently localizing in the occipital region and that the occipital EEG focus is seen most frequently between 2 and 5 years [13], as is the case with the present patient. The present patient has 1 sibling with a history of febrile seizures in addition to 3 more distant relatives diagnosed with epilepsy (Fig. 1). In PS, there is a high prevalence of febrile seizures of about 17% [12]. Although it is difficult to identify the classification of seizure types in these distant relatives, it is known that siblings and relatives of those with PS may, in rare instances, have the same type of seizures or Rolandic and idiopathic childhood occipital epilepsy [12]. Interestingly, FOS has EEG features that are the opposite of those observed during photosensitivity. Despite the conflicting corresponding mechanisms underlying these two phenomena [1], both FOS and photosensitivity can occur in the same patient, and one phenomenon may evolve into the

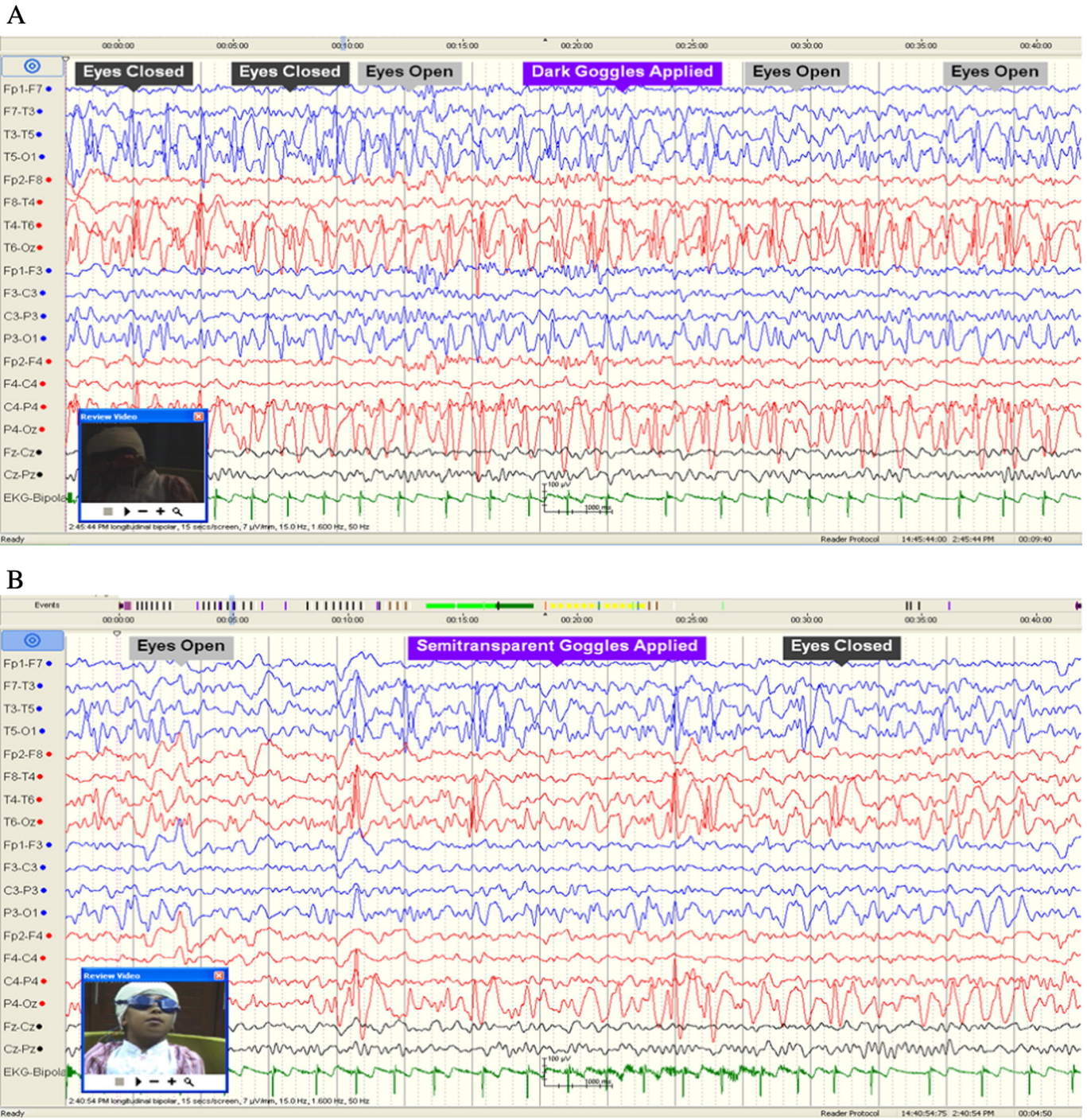


Fig. 4. EEG recording done with the patient (A) wearing dark goggles (complete darkness) and (B) wearing semitransparent goggles, both of which did not abolish the bilateral occipital epileptiform discharges, which confirms the diagnosis of fixation-off sensitivity. Low-cut filter, 1.6 Hz; high-cut filter, 50 Hz.

other [1,2]. In conclusion, FOS is a rare phenomenon, and its variant iFOS has been diagnosed previously in only 2 patients. We document, for the first time, the coexistence of the two conditions in a child with PS.

Abbreviations

- FOS fixation-off sensitivity
- iFOS inverted fixation-off sensitivity
- PS Panayiotopoulos syndrome
- ABPE atypical benign partial epilepsy
- EEG electroencephalography

Consent

Parental written informed consent was obtained for publication of this case report and any accompanying images.

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Disclosure

None of the authors has any conflict of interest to disclose.

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