Electrocortical functional correlates of responsiveness to short-lasting preventive intervention with ketogenic diet (KD) in migraine: a multimodal evoked potentials study

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BACKGROUND

- Ketogenic diet (KD) is a dietetic regimen that mimics fasting in producing ketone bodies, which seems to have a potential role in treating migraine (Di Lorenzo et al., 2015).
- The molecular mechanisms underpinnings ketogenic diet effectiveness are only partially clear.
- However, from animal and human models emerges that KD might affects CNS at multiple levels: it is able to normalize cortical *dysexcitability*, probably via enhancement of *GABA* inhibition, and to reduce significantly *cortical spreading depression* velocity of propagation.

OBJECTIVE

- Here, with the aim of identifying cortical electrofunctional correlates (Coppola et al., 2013) of responsiveness to short-lasting preventive intervention with KD in migraine, we investigated EPs before and after KD.

DESIGN & METHODS

- Eighteen migraine patients (MO, ICHD-IIIbeta code 1.1) underwent the interictal recordings of median nerve somatosensory (SSEPs) (right stimulation, 500 sweeps, 4.4 repetition rate, 1.2 motor threshold) and visual (VEPs) (right eye stimulation, 600 sweeps, 3.1/s repetition rate, 15 min of arc check) evoked potentials, before and during ketogenesis, as confirmed by urinary sticks. We measured VEP N1-P1 and SSEP N20-P25 amplitudes respectively in 6 and in 2 sequential blocks of 100 sweeps and habituation as the slope of the linear regression between block 1 to 6 for VEPs or between 1 to 2 for SSEPs. We further subgrouped patients in those who received a very low calories KD – had a baseline BMI of 25 or more – and in those who received a normocaloric KD – had a baseline BMI of less than 25.

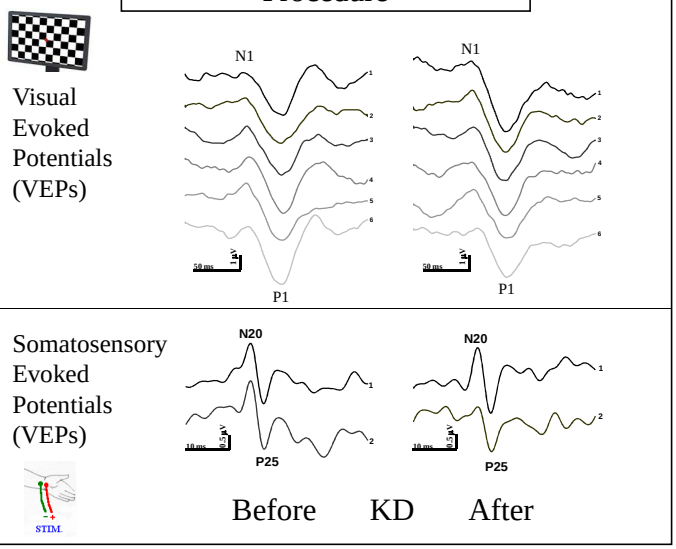
RESULTS

- After a period of 3 weeks of KD, a significant reduction of migraine frequency (from a mean of 4.44 to 1.33 attacks/month, $p<0.001$) and duration (from 50.72 to 15.8 hours/month, $p<0.001$) was observed.
- KD induced a significant normalization of the interictally reduced VEP and SSEP habituation (respectively $p=0.032$ and $p=0.004$).
- The subgroup analysis showed that the type of diet performed (very low calories KD or normocaloric KD) did not influence final results.

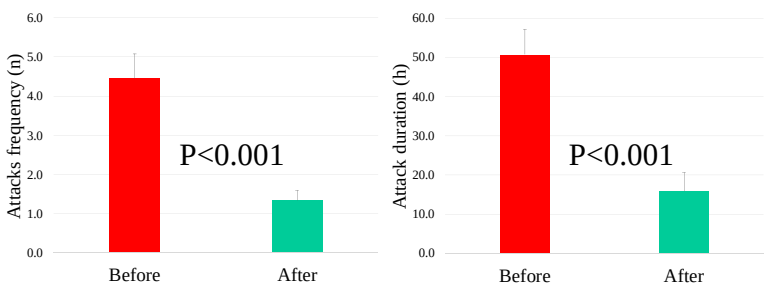
DISCUSSION

- These findings suggest that ketogenic diet may exert its prophylactic effect in migraine through the influence on the processing of information at the cortical level, independently from weight loss.

Procedure

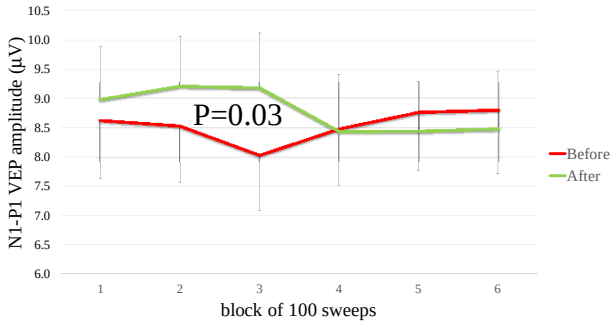


Headache features



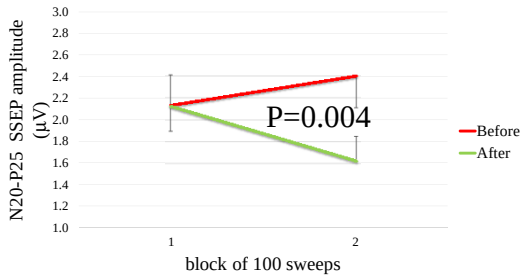
Significant clinical improvement after 3 weeks KD

Visual evoked potentials (VEPs)



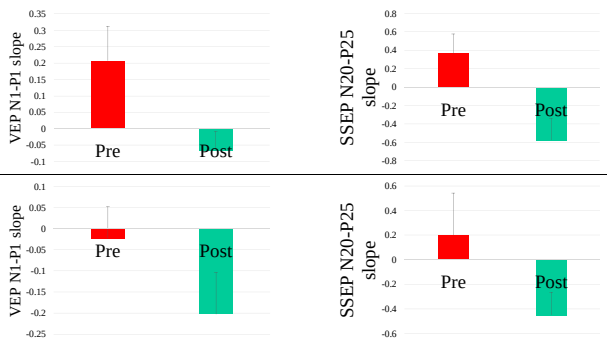
The baseline interictal deficient N1-P1 VEP amplitude habituation (in red) normalized after KD (in green).

Somatosensory evoked potentials (SSEPs)



The baseline interictal deficient N20-P25 SSEP amplitude habituation (in red) normalized after KD (in green).

Subgroup analysis



The subgroup analysis revealed that the type of diet performed (very low calories KD or normocaloric KD) did not influence final results of EPs normalization of the interictal habituation deficit.

REFERENCES

- Di Lorenzo C, Coppola G, Sirianni G, Di Lorenzo G, Bracaglia M, Di Lenola D, Siracusano A, Rossi P, Pierelli F. Migraine improvement during short lasting ketogenesis: a proof-of-concept study. Eur J Neurol. 2015 Jan;22(1):170-7.
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