Sensory event related potentials slowing in migraine

Independent components GO/NOGO paradigm: a search for endophenotypes in migraine

TONY STEFFERT [a], ALEKSANDER VALJAMAE [b], JESSICA FERNANDEZ-MORALES [d], JURI KROPOTOV [e,f], PAUL F.M.J. VERSCHURE [b,c], AND PATRICIA POZO-ROSICH [d].

[a] Department of Psychology, Goldsmiths College, University of London, New Cross, London SE14 6NW, UK
[b] SPECS, Institute of Audiovisual Studies, Universitat Pompeu Fabra, Carrer de Roc Boronat, 138, 08018 Barcelona, Spain
[c] Catalan Institute of Advanced Studies (ICREA), Barcelona, Spain
[d] University Hospital Vall d'Hebron, Headache Unit, Department of Neurology, NA, Barcelona, 08035, Spain
[e] Institute of the Human Brain of Russian Academy of Sciences, 12 a ul. Academica Pavlova, St. Petersburg, 197376, Russia
[f] Institute of Psychology, Norwegian University of Science and Technology, Dragvoll, bld.12, 7491, Trondheim, Norway

Objectives: It is not clear to what extent migraine affects cognitive performance and its underlying neuronal substrate. Here we studied this question by combining a go-nogo task with quantitative electroencephalography (qEEG) and Independent component analysis (ICA) of event related potentials (ERP) thus establishing a quantitative endophenotype of migraine.

Background: Migraine is a widespread brain disorder that affects over 6 % of men and 15 % of women. The neuronal mechanism underlying migraine is still not well understood. However, a number of clinical signs, specialized tests and physiological studies have shown that the sympathetic nervous system (SNS) is dysfunctional. It can be hypothesized that this impairment can be reflected in patients cognitive performance. We address goal-directed behavior of patients in event-related potentials (ERP) study based on modified GO/NOGO paradigm (see Fig 1.). The new technique of decomposing ERP data into features with minimal mutual information and sLORETA imaging of the localised generators of these Independent components (ICs) has shown great promise in other areas such as ADHD [3]. THIS ALSO RAISES THE POSSIBILITY THAT IT ALSO AN BE USED TO DISAMBIGUATE THE SYMPTOMATHOLOGY OF MIGRAINE.

Methods: Twenty female patients with a mean age of 40 years old, diagnosed with chronic episodic migraine with or without aura [8] (10 with aura, 10 without aura) had EEG recorded from 19 electrodes of the International 10-20 system with a linked ears reference montage, sampling at 250 Hz rate giving a 0.3 – 70 Hz frequency range in the following conditions: **eyes closed** for 5 minutes, **eyes opened** for 5 minutes, and a modification version of a GO/NOGO task, **Visual Continuous Performance Task** (VCPT) (Fig 1) for 20 minutes.

EEG power (Fig 2) and EEG band power asymmetry (Not shown),as described in Bjork and Sand, 2008 [1], in all conditions and Independent component for event related potentials (ERP) (Fig 3) were compared with the corresponding age matched parameters from the Human Brain Institute (HBI) [16] normative database (Controls N.=172, females age 18 to 45 years old).

Results & Discussion: THE ANALYSIS OF THE ERROR RATES AND RT PERFORMANCE DID NOT SHOW SIGNIFICANT DIFFERENCES BETWEEN THE GROUPS: THE MEANS ARE 484 (SD=102), 480 (SD=76) AND AND 502 (SD=134) FOR MIGRAINEURS WITH AURA, WITHOUT AURA AND CONTROLS RESPECTIVELY. IN ADDITION, Independent component analysis of ERPs showed THAT:

1. Increase of P400 conflict monitoring component. (Fig 3, IC-4) This NOGO-related IC identified in the present study has a frontal distribution; it peaks at 400 ms, corresponding to the mean latency of response to GO cues. This component is generated in the anterior cingulate cortex. Taking in to account the involvement of the anterior cingulate cortex in a hypothetical conflict monitoring operation [13, 14, 15], we associate the P400 frontal-central IC selected in the present study with conflict monitoring. Indeed, in the two-stimulus paradigm used in the present study the subject develops a behavioral model: to press a button in response to two "animals" (A-A). When the second stimulus is a "plant" appearing after a prior "animal" (NOGO condition), this stimulus does not fit the behavioral model (a conflict) and this conflict seems to activate neurons in the anterior cingulate cortex that monitor this conflict situation.

2. Decrease of P300 motor suppression component. (Fig 3, IC-3) This component has a central distribution with a peak latency of 340 ms, which is 60 ms shorter than the mean latency of THE response, and is completely absent in response to GO cues. According to sLORETA [6] imaging this component is generated over the premotor cortex (Brodmann area 6). This component appears to correspond to subdurally recorded potentials found over pre-supplementary motor cortex in GO/NOGO tasks in epileptic patients in response to NOGO cues [10]. The involvement of this part of the cortex in motor inhibition was demonstrated previously by the fact that direct stimulation of the pre-supplementary motor cortex can inhibit ongoing, habitual motor actions [11]. A recent meta-analysis of fMRI studies in GO/NOGO tasks demonstrates that Brodmann area 8 is one of the most commonly activated areas of the cortex [12] thus supporting the involvement of this area in response selection and response inhibition. Thus we associate the centrally distributed P340 NOGO related IC separated in the present study with inhibition of a prepared motor action in response to NOGO cues.

Conclusions: Two main conclusions can be drown from ICA analysis of ERPs. First, it appears, that the anterior cingulate cortex in migraine patients is hyper-active in comparison to CONTROLS. Second, It appears that the premotor area in the migraine patients is hypoactivated. More patients data have to collected to further support these results and test whether ERPs analysis can be used for migraine diagnostics.

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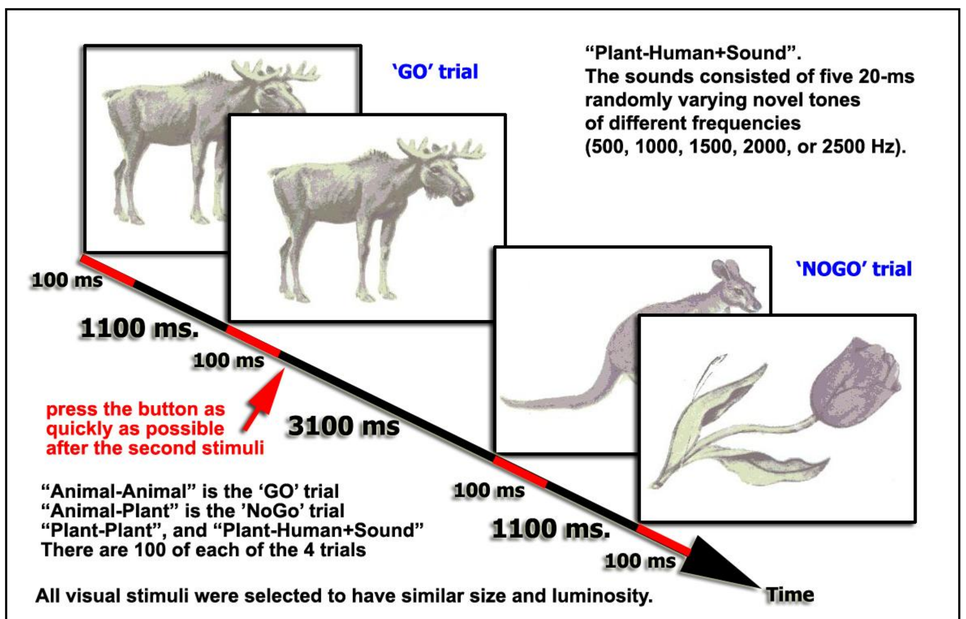

Figure 1. Visual Continuous Performance Task (VCPT). The VCPT is a 'Go-NoGo' task. There are three types of visual stimuli, presented in four different pairs of 100 trials each: The "Animal-Animal" is the 'GO' trial where the subject must press a button as quickly as possible after the second Animal stimulUS. The "Animal-Plant" is the 'NoGo' trial were they must refrain from responding, "Plant-Plant" is a discontinuous trial, and "Plant-Human" presented COMBINED with an artificial sound of five pure tones of 500, 1000, 1500, 2000 or 2500 Hz of 20 ms duration is a Novel trial. The trials are presented in random order with equal probability. The duration of stimuli is 100 ms. Inter-stimulus interval WITHin a pair is 1100 ms. Interval between trials is 3100 ms. The task lasts 20 minutes. [3] [4]

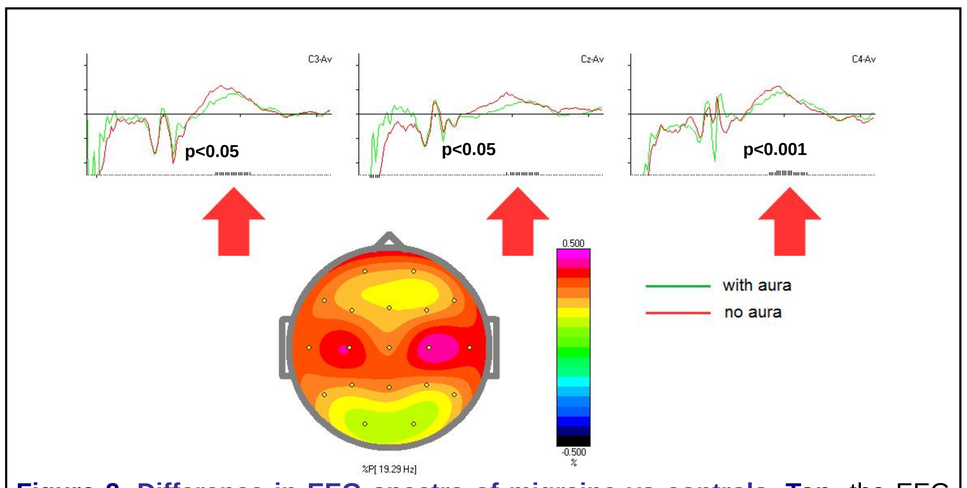

Figure 2. Difference in EEG spectra of migraine vs controls. Top: the EEG Spectral of each Migraine group is subtracted from the control group to generate a "difference wave". The small black bars indicated by the red arrows show a statistically significant increase p<0.05 or p<0.001 in the 'low Beta' frequency band (13-20 Hz) over the sensory motor strip (C3, Cz, C4).
Bottom: The head map of the power difference of the statisticalLY significanT frequencies BETWEEN MIGRAINE PATIENTS AND CONTROLS SHOWING A hyperactivation of this part of the cortex in migraine patients.

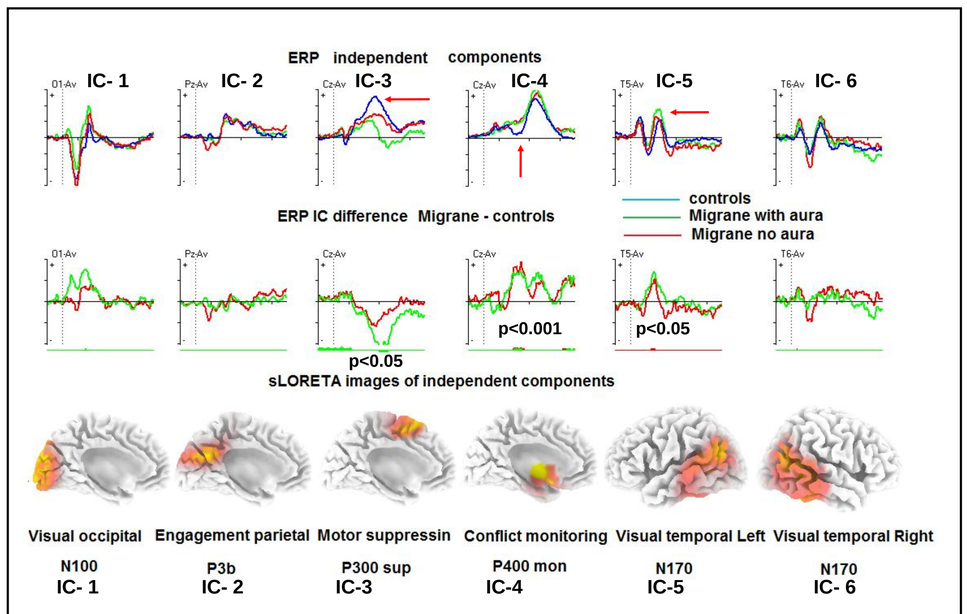

Fig 3: Independent Component Analysis of ERP's. The top row plots SHOW the ERPs. Controls (Blue), Migraine with Aura (Green) and Migraine withOUT Aura (Red). The vertical 'Y' axis to the dotted vertical line represents the 100 ms when the second stimulus of the "Animal-Plant" trial is displayed. It can be seeN in the 3rd "Motor Suppression" (IC-3) and 4th, "Conflict Monitoring" (IC-4) components THAT the blue "controls" line is significantly different from both Migraine groups.

The central row is the difference wave, where each of the Migraine groups has been subtracted from the control group. The small red and green bars beneath the 3rd, 4th, and 5th component, indicate a statistical significance difference of either p<0.05 for the smallest bars, p<0.01, for the medium bars or p<0.001 for the largest bar above the line is positive and below is negative. The bottom row shows 3-D sLORETA [6] images of the brain generators of the independent components of the ERP's. [6] [2]

✉aleksander.valjamae@upf.edu