

Default mode network abnormalities predict cutaneous allodynia in patients with episodic migraine without aura

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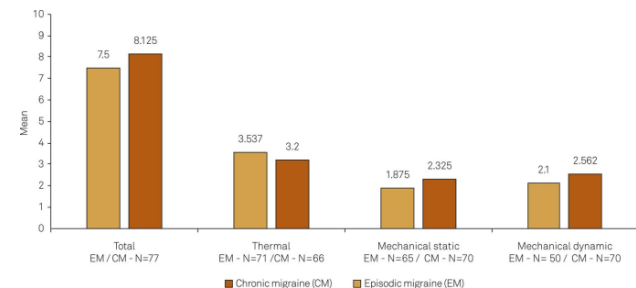
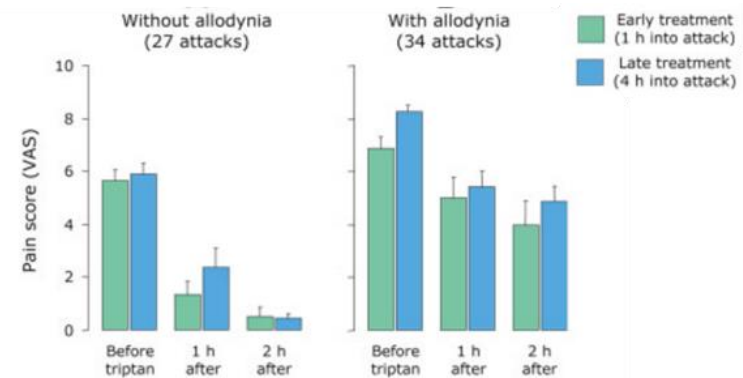
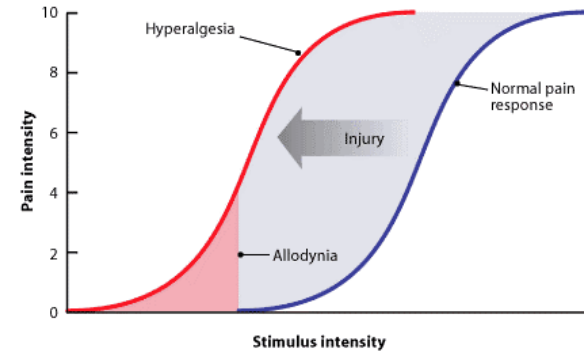


BACKGROUND

Cutaneous allodynia (CA) is the perception of skin discomfort induced by trivial stimuli

CA represents a negative predictor of response to symptomatic therapy with triptans during a migraine attacks

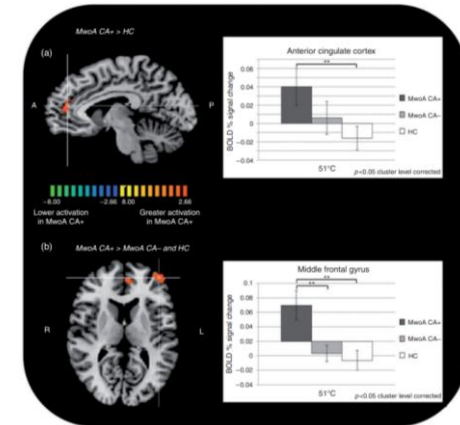
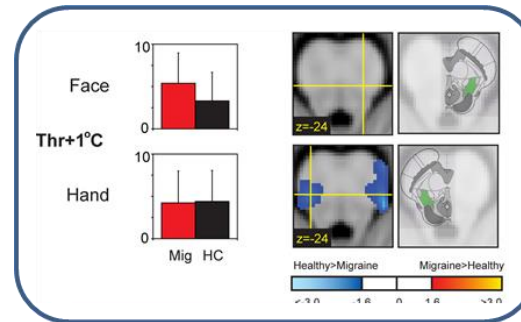
CA is a prognostic factor for migraine without aura (MwoA) chronification



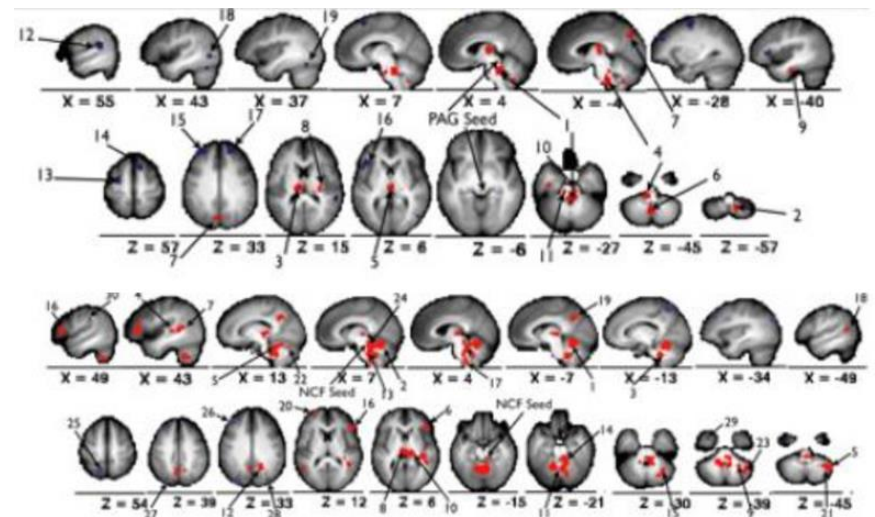
BACKGROUND-2

Advanced neuroimaging studies have showed in migraine patients:

- ✓ CA may be subtended by both a dysfunctional DPMS and abnormal internal representation of pain

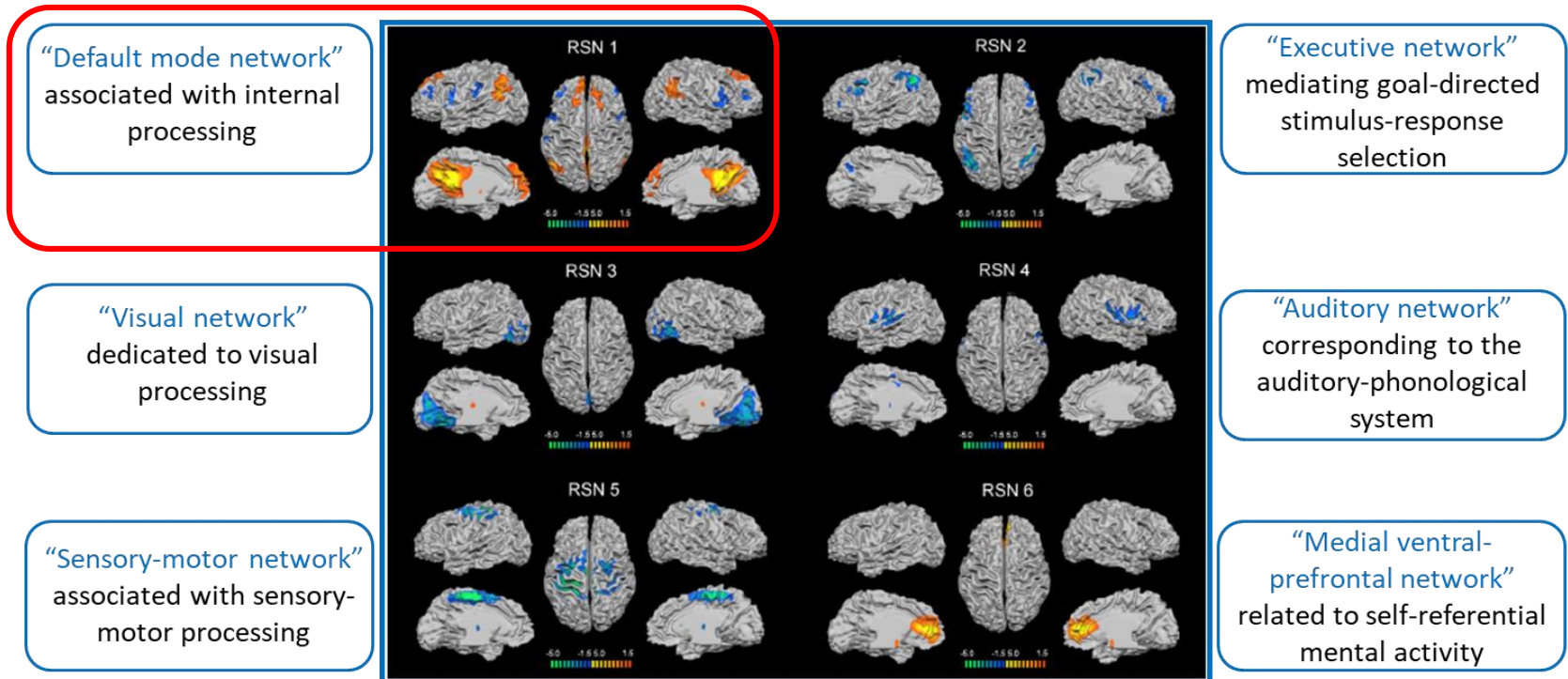


- ✓ CA is correlated to atypical RS-FC within the brainstem and between the brainstem and higher order cortical modulatory pain regions



RESTING STATE NETWORKS

Although a plethora of studies have been conducted to investigate pattern of intrinsic brain FC in migraine, no studies have been conducted to investigate the prognostic role of specific pattern of intrinsic brain FC in the development of CA in migraine patients



AIMS

To investigate whether a specific pattern of Resting-state (RS) default mode network (DMN) intrinsic functional connectivity (FC), during interictal period, may predict the development of CA in patients with MwoA CA-

HYPOTHESIS

Migraine patients who will develop CA would show an altered resting-state brain FC during interictal period and even before the occurrence of this complication.

STUDY PROTOCOL

T_0 50 drug naive patients with MwoA with CA- 3 drop-out



3 tesla RS-fMRI brain scan



After 3 years

T_1 37 patients completed the ASC-12 10 drop-out



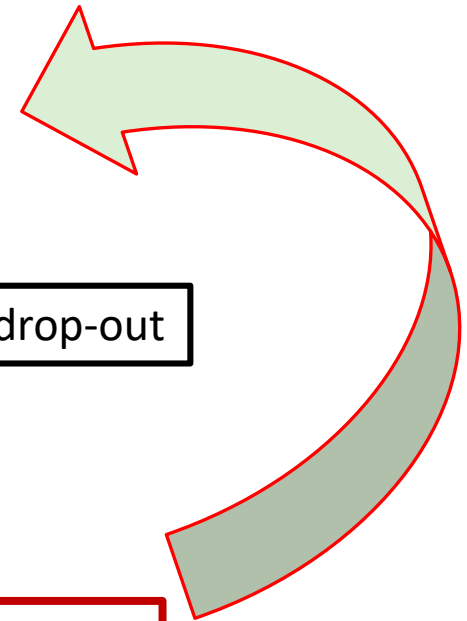
19 HC

VS

20 patients have developed CA (Mwoa dCA)

VS

17 patients have not developed CA (MwoA ndCA)



POPULATION

	Group	Mean \pm SD	p value
Gender	MwoA CA+	3M; 17F	0.08 ^a
	MwoA CA -	7M; 10F	0.23 ^b
	HC	6M; 13F	0.56 ^c
Age (years)	MwoA CA+	31.3 \pm 8.81	0.84 ^a
	MwoA CA -	30.7 \pm 8.86	0.06 ^b
	HC	28.84 \pm 6.3	0.18 ^c
Disease duration (years)	MwoA CA+	13.80 \pm 7.90	0.62
	MwoA CA -	12.35 \pm 9.80	
Frequency (days/month)	MwoA CA+	5.11 \pm 5.0	0.47
	MwoA CA -	4.0 \pm 2.98	
ASC-12 T0	MwoA	0	
ASC-12 T1	MwoA CA+	7.75 \pm 4.05	3.04 x 10 ⁻⁸
	MwoA CA -	0	
MIDAS	MwoA CA+	15.9 \pm 10.55	0.30
	MwoA CA -	12.17 \pm 11.06	
HIT-6	MwoA CA+	59.7 \pm 7.46	0.06
	MwoA CA -	54.41 \pm 9.18	
HAM-D	MwoA CA+	5,11 \pm 0,82	Parameter
	MwoA CA -	4,79 \pm 0,76	
HAM-A	MwoA CA+	5,71 \pm 0,96	0.28
	MwoA CA -	5,34 \pm 0,89	
VAS of attack intensity	MwoA CA+	8.36 \pm 1.14	0.11
	MwoA CA -	7.69 \pm 1.39	

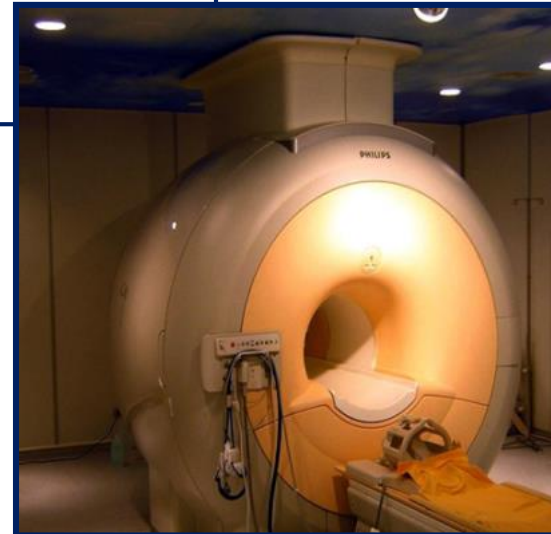
^a MwoA CA+ vs MwoA CA-

^b MwoA CA+ vs HC

^c MwoA CA- vs HC

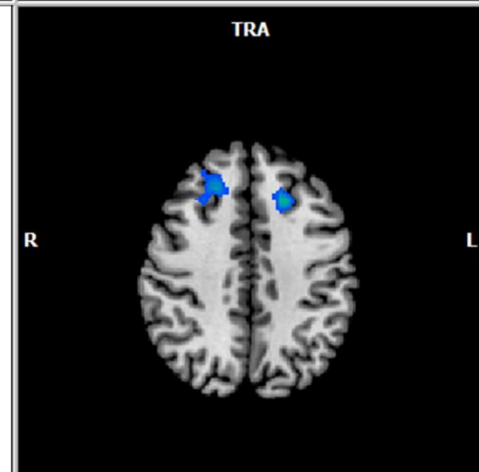
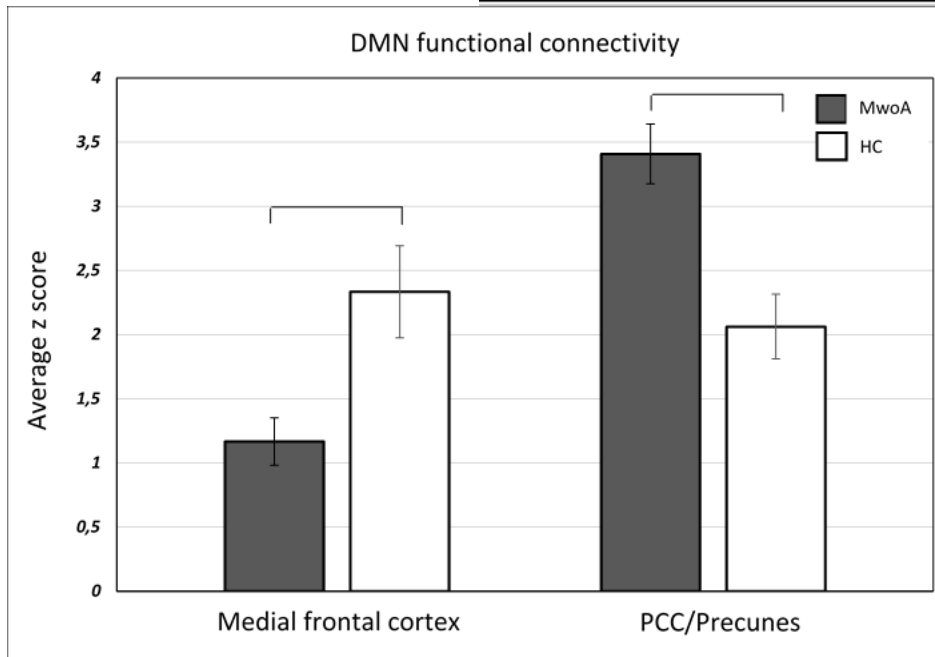
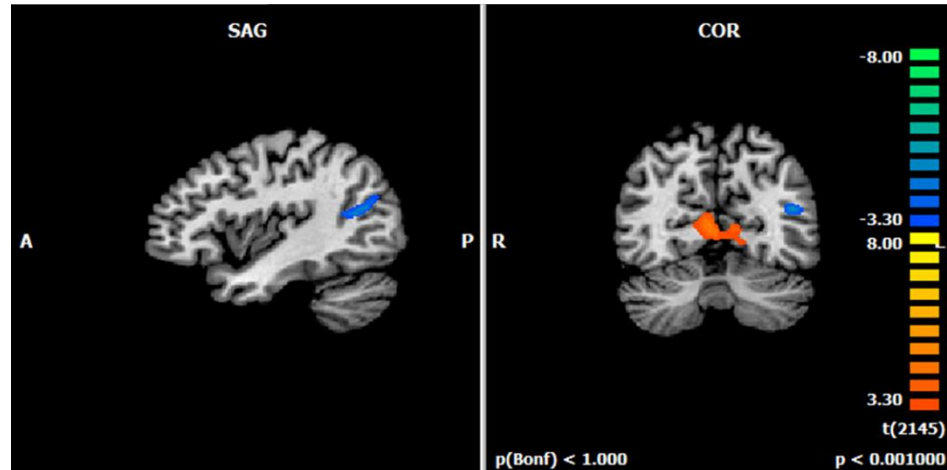
METHODS

- ❖ Magnete 3 Tesla GE (General Electric, Minneapolis, MN, USA)
- ❖ Connettività funzionale (*Software Brain Voyager*)
 - Random effects analysis (**$p < 0.001$ cluster level corrected**)
- ❖ Analisi di correlazione post-hoc



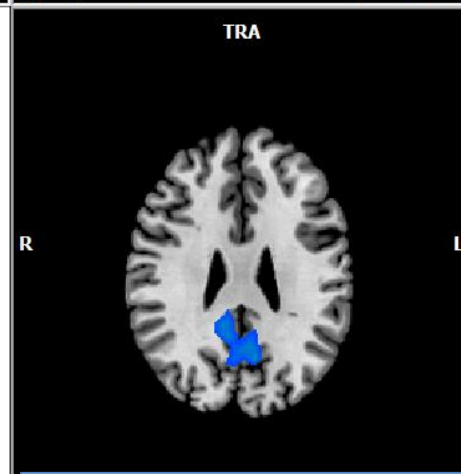
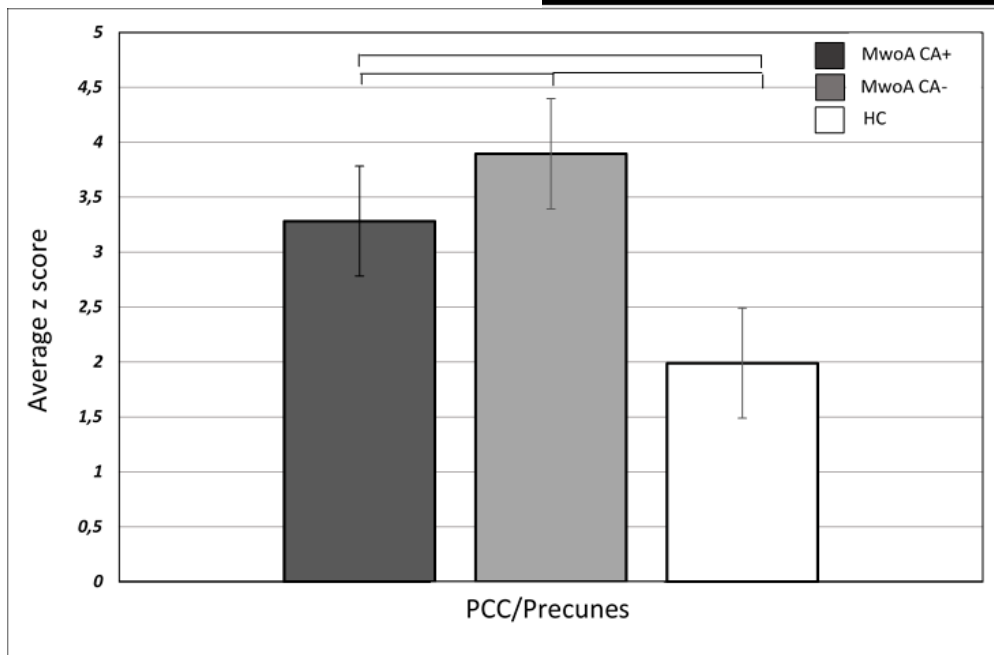
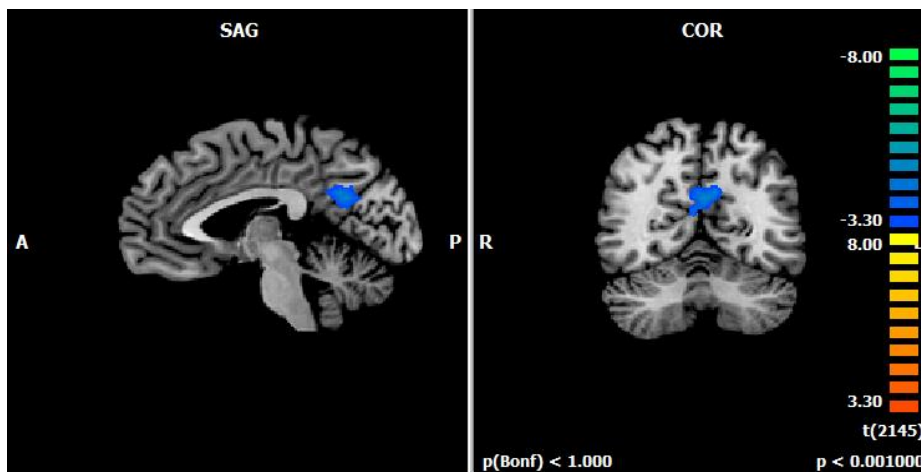
RESULTS-1

Patients with MwoA *vs* HC



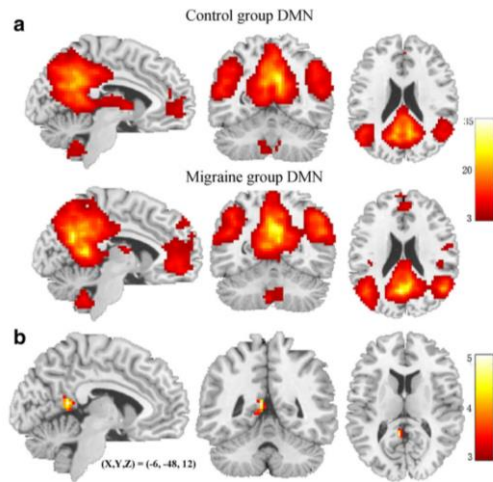
RESULTS-2

Patients with MwoA dCA vs MwoA ndCA vs HC



No correlation between RS-FC PCC and clinical parameters of disease severity

DISCUSSION-1



✓ Increased DMN–FC in patients with MwOA

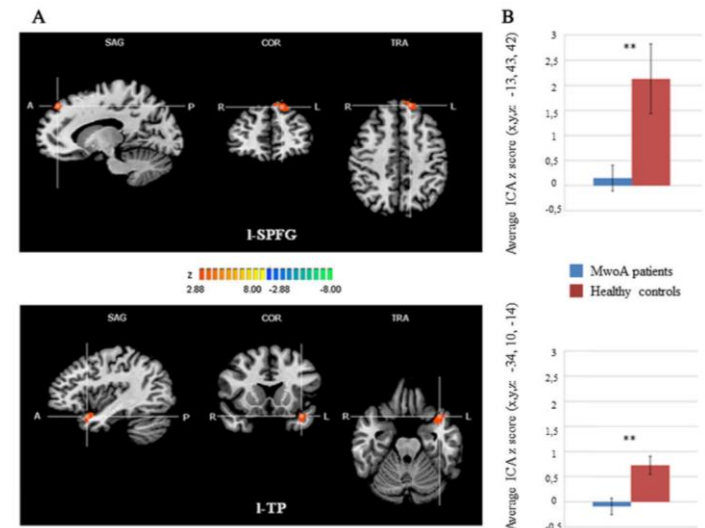


Precuneus and post. cingulate cortex (PCC)

✓ Decreased DMN-FC in patients with MwOA



Medial prefrontal (mPFC) and temporal cortex



DISCUSSION-2

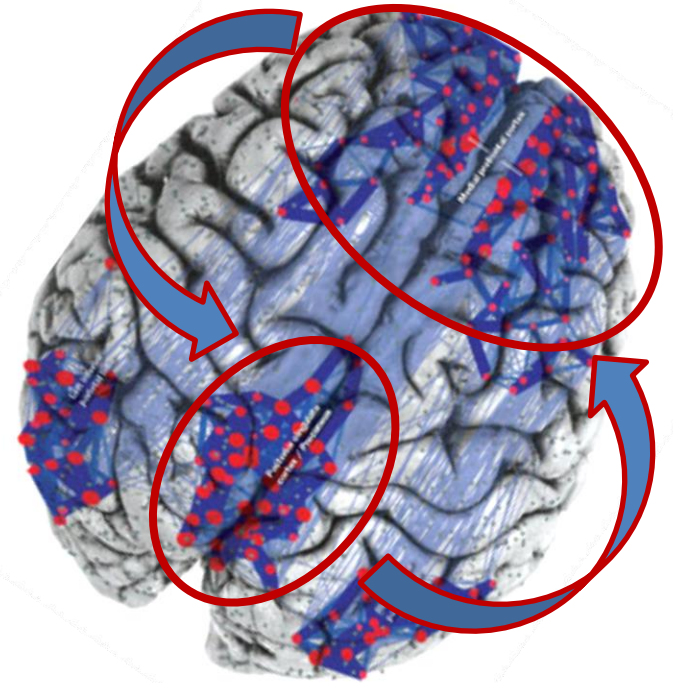
Functional differentiation within DMN comes from task-based studies

✓ mPFC

- recall best action/emotional response to specific events
- leading role in decision making/coping

✓ PCC/precuneus

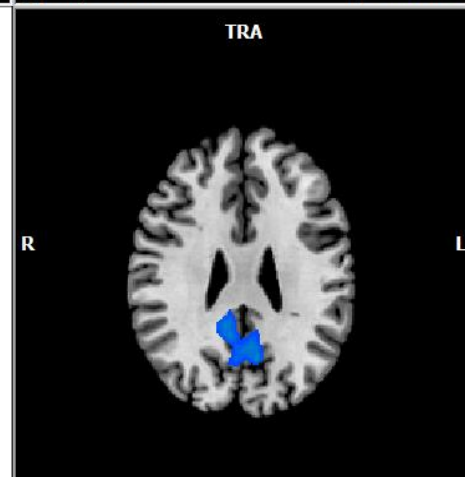
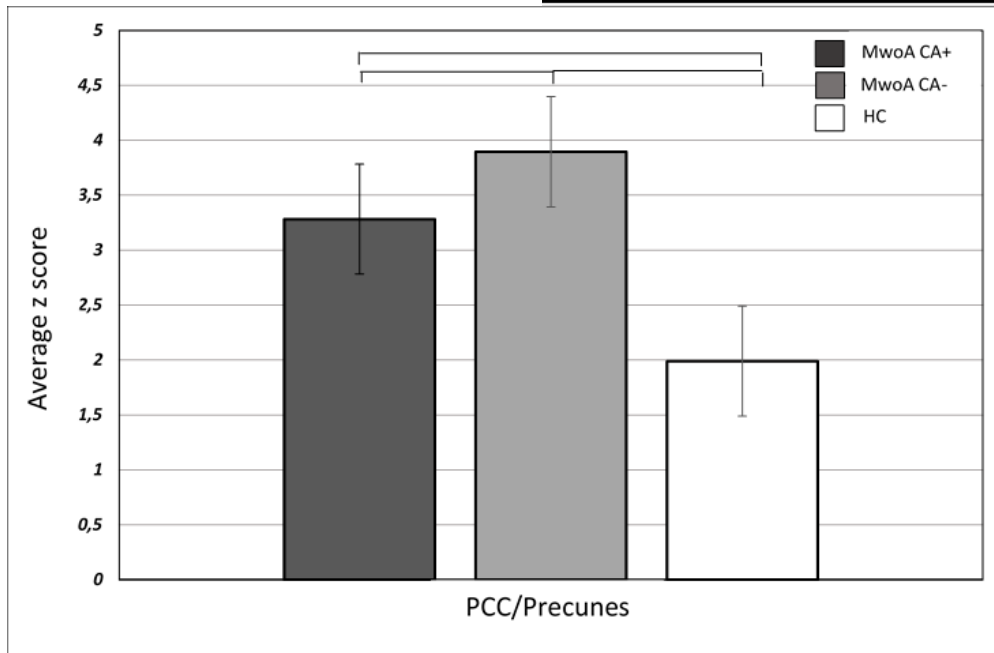
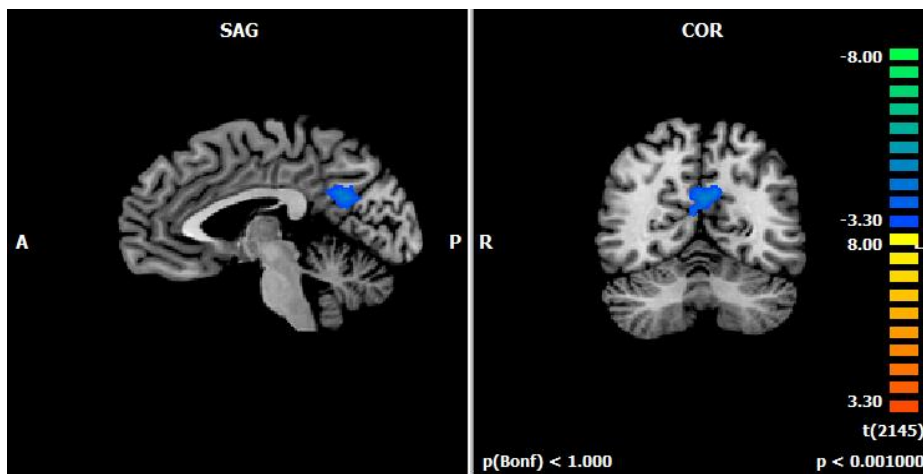
- state of arousal
- internally/externally focused attention
- pain sensitivity/perception
- multisensory integration



Increased PCC-FC could represent an effort of adaptive response to stressful events and repetitive migraine attacks

RESULTS-2

Patients with MwoA dCA vs MwoA ndCA vs HC

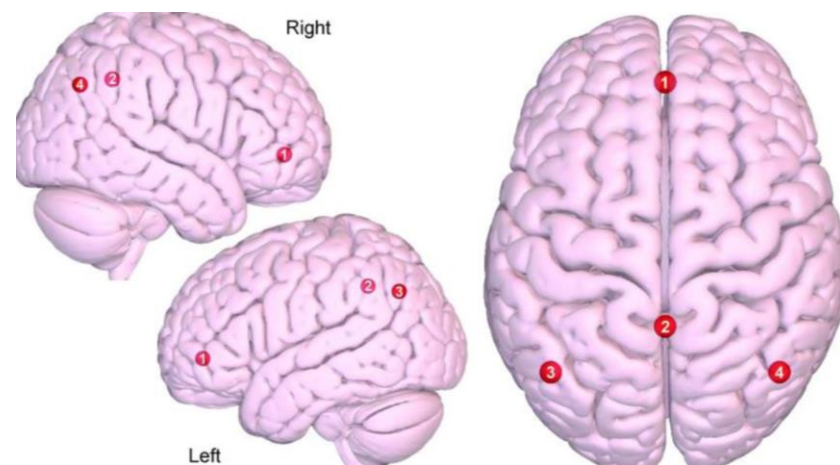
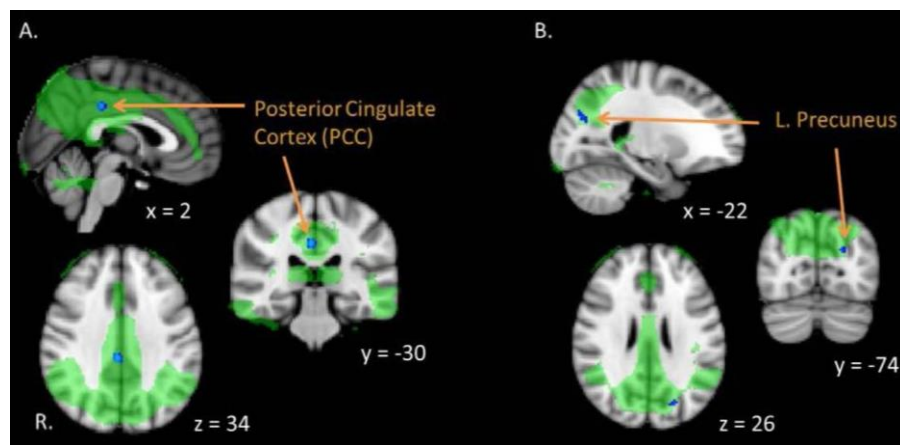


DISCUSSION-3

Reduced PCC-FC makes less effective this adaptive attempt, leading to abnormal

- internally/externally focused attention
- pain sensitivity/perception
- multisensory integration → from “touch” to pain → CA

Reduced PCC-FC in MwoA dCA is similar to DMN changes observed in several *chronic* pain condition as well as in CM



CONCLUSIONS

We believe that:

- ✓ Reduced PCC-FC observed in patients with MwoA dCA could represent a putative “phenotypic/prognostic biomarker” able to identify migraine subgroups in clinical and research scenario
- ✓ DMN-FC findings are not correlated with clinical parameters of disease severity, therefore abnormal PCC-FC may be “*per se*” and not related to years lived with migraine, migraine frequency, attacks severity, etc.

Aknowledgments

Dept. Neurology

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- A. Russo
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