EMDR physopathological concepts
State-of-the-art

Marco Pagani

Senior Researcher Institute of Cognitive Sciences and Technologies, CNR
Rome, Italy
Chair of the Neuroimaging Committee of the European Association of Nuclear Medicine

WHAT DO WE DEAL WITH?

ANATOMY AND PHYSIOLOGY OF CENTRAL NERVOUS SYSTEM

METHODOLOGIES OF INVESTIGATION

PATHOPHYSIOLOGY OF PTSD

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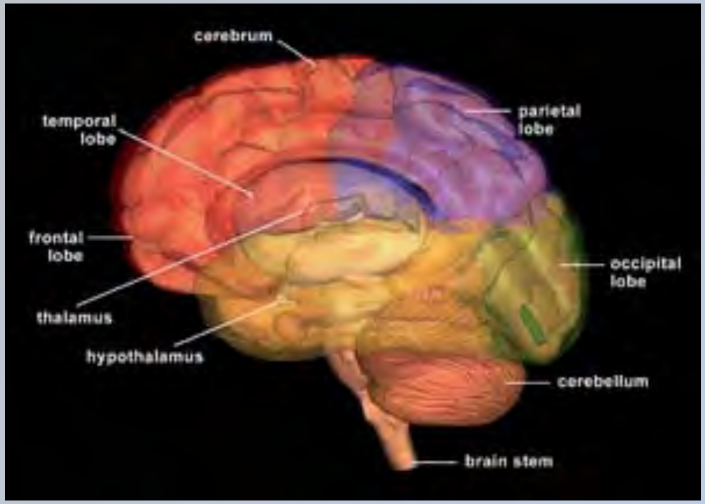
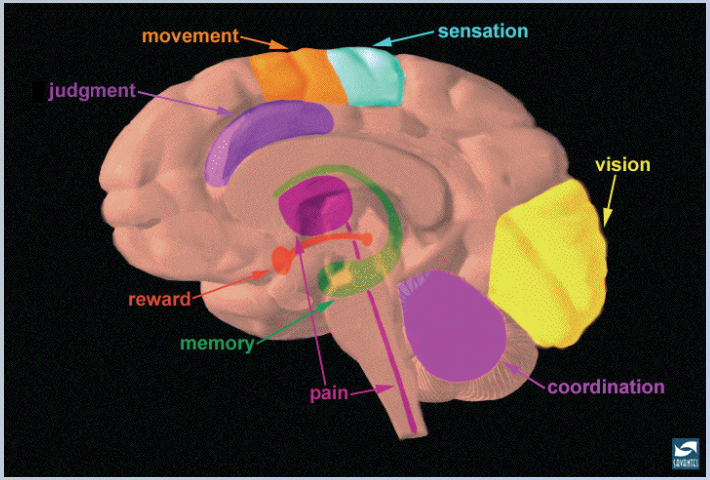
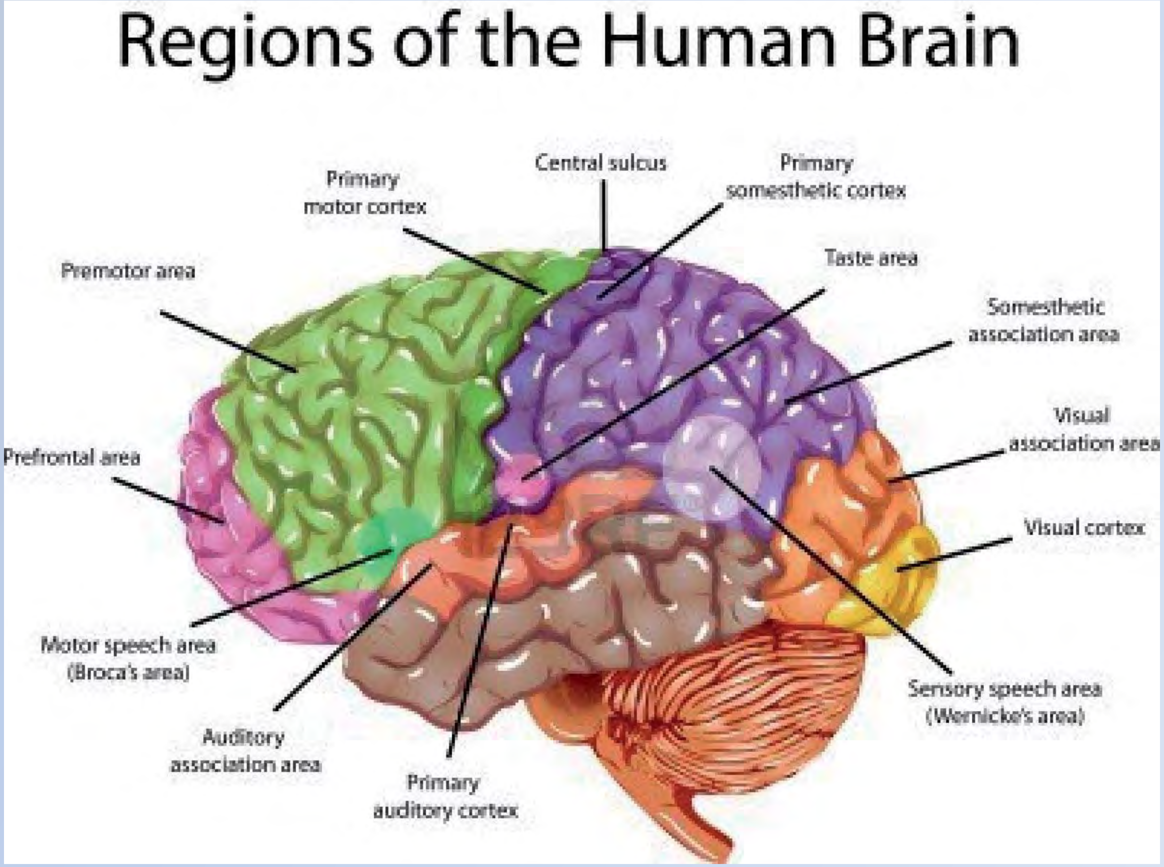
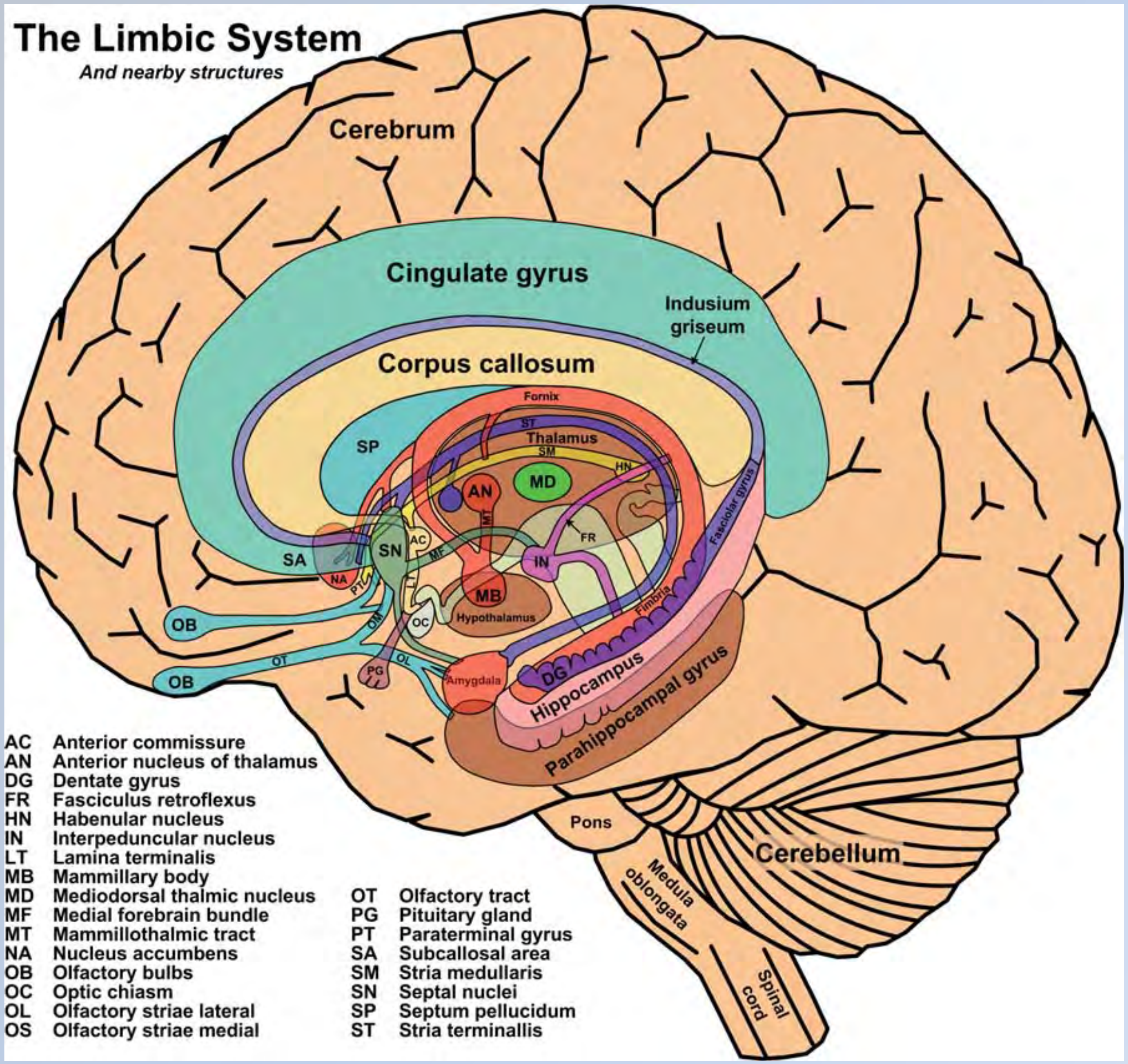
FUNCTIONAL BRAIN





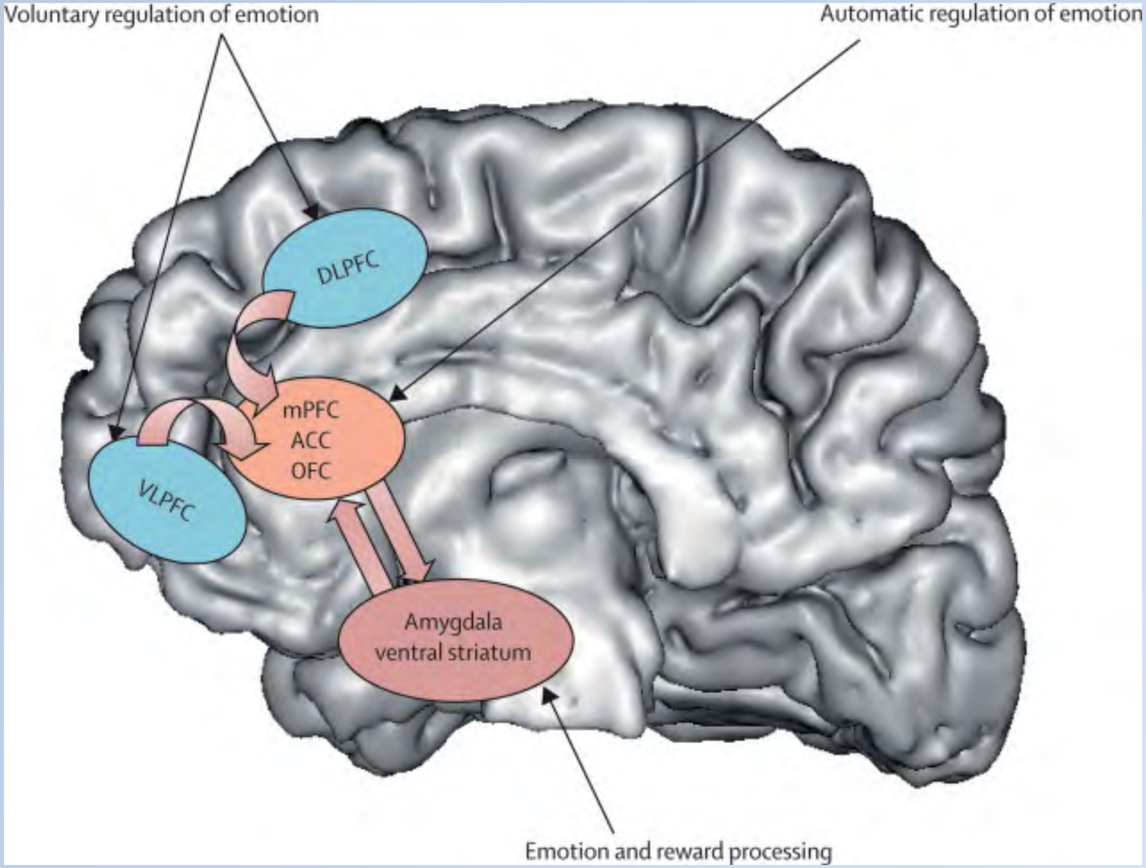


TARGET REGIONS



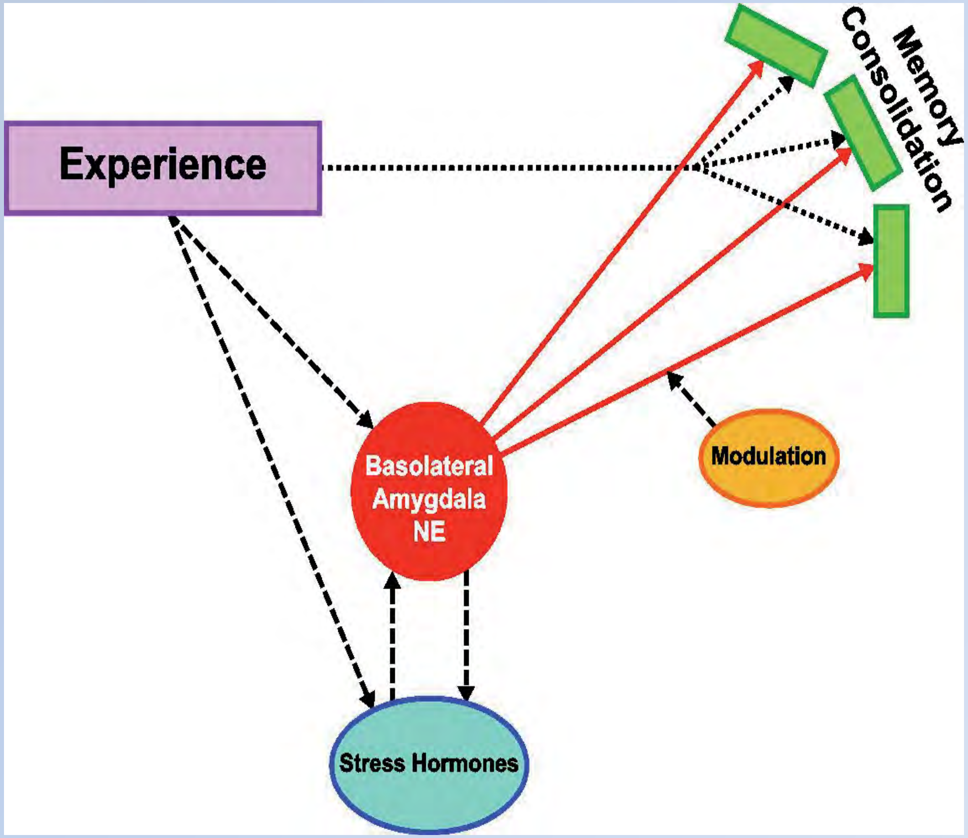
PREFRONTAL CORTEX

mPFC modulates emotional response inhibiting amygdala and estinguishing fear response



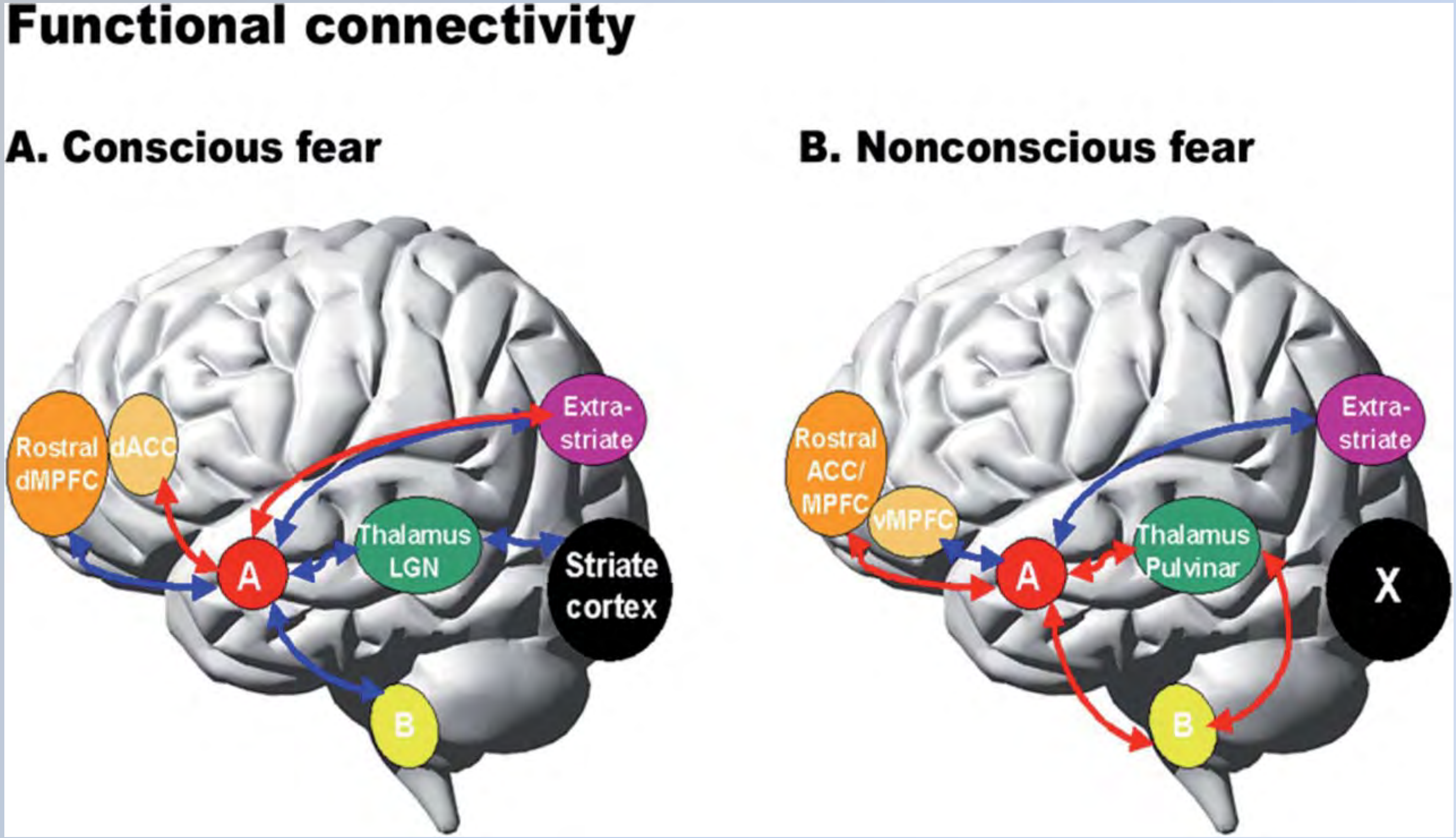
AMYGDALA

Amygdala has a central role in formation and preservation of emotional memories



Amygdala is also involved in memory modulation and consolidation

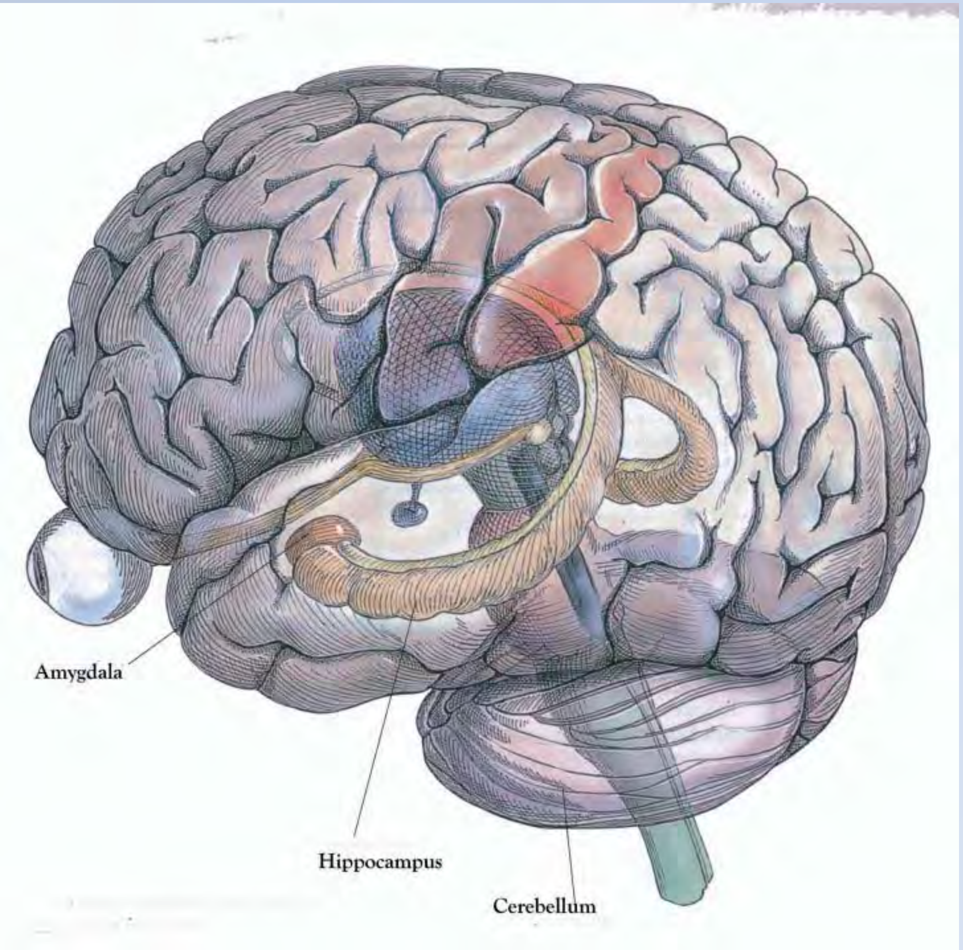
AMYGDALA



Inhibitory control from PFC on amygdala reduces the excessive firing of cortical and subcortical structures upon conscious fear

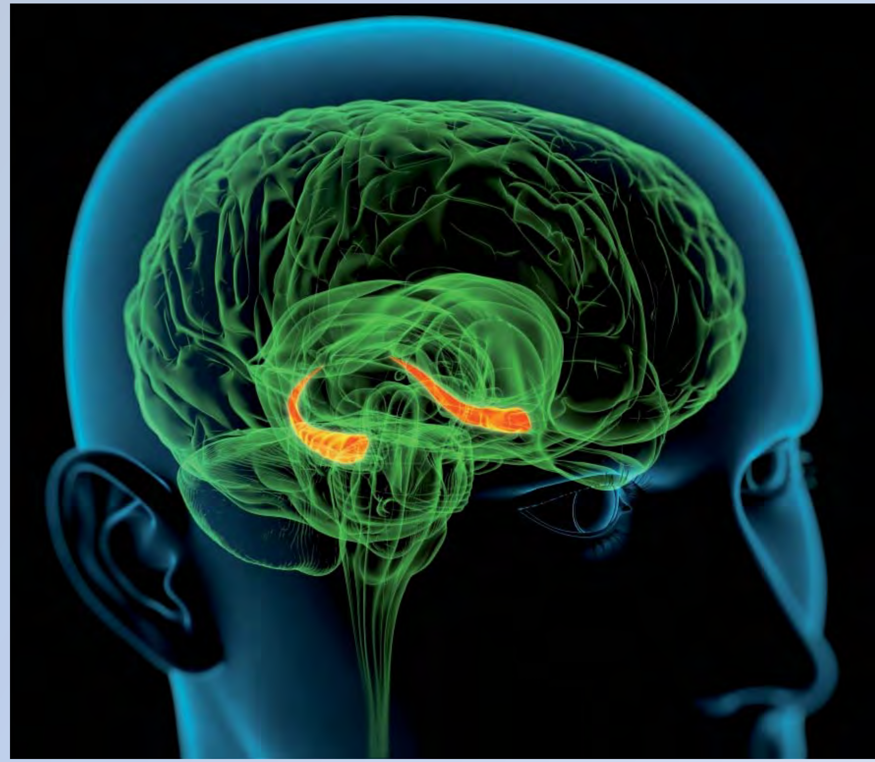
HIPPOCAMPUS

Hippocampus processes episodic and autobiographical memory and is essential in identifying "safe places"

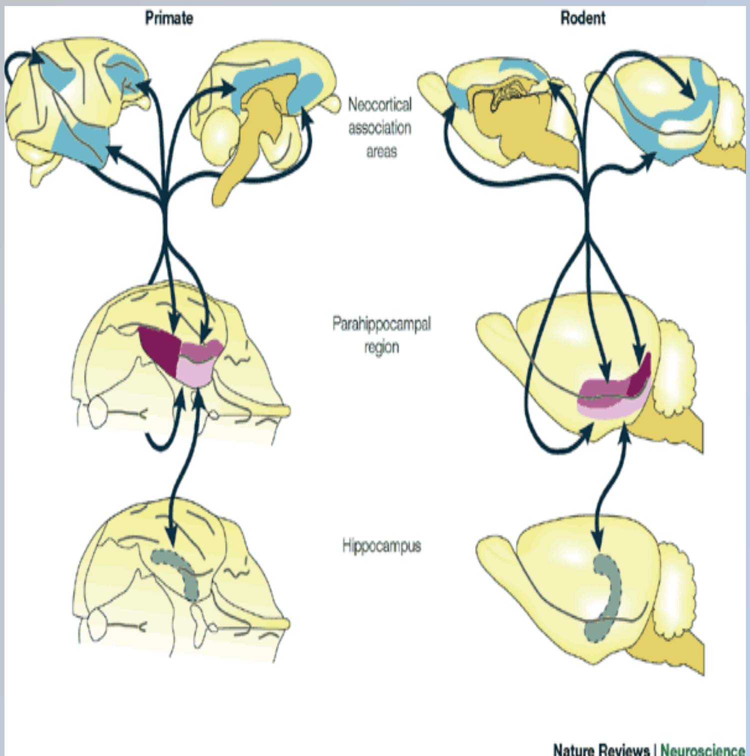


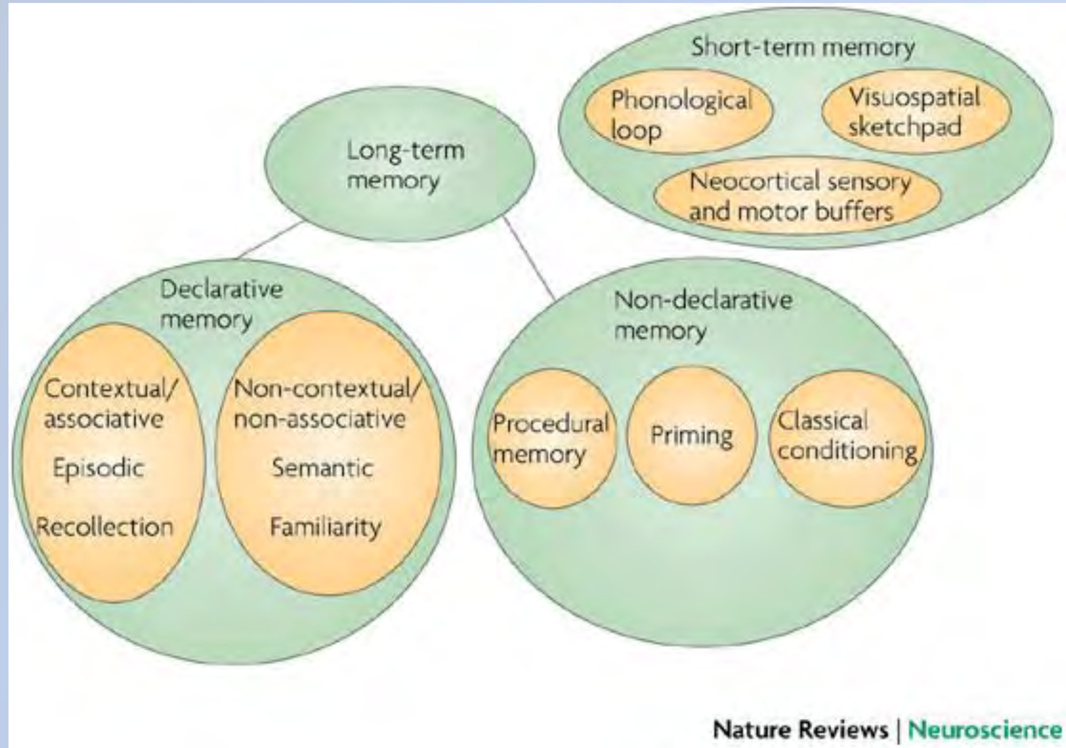
HIPPOCAMPUS

Hippocampus is extremely sensitive to stress and might decrease in volume and neuronal density following chronic cortisol secretion



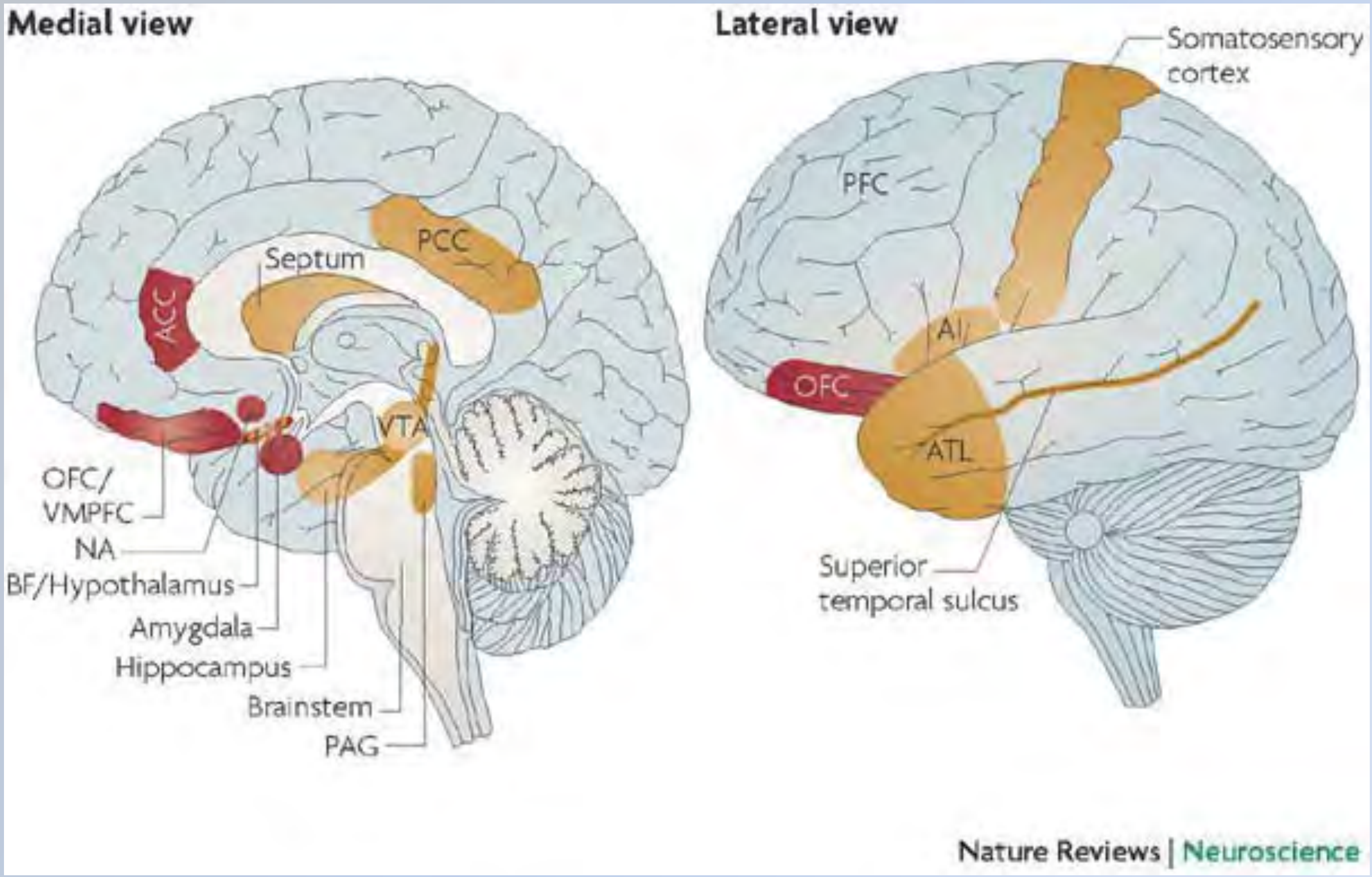
HIPPOCAMPUS





It has a central role in consolidation from short to long term memory, in declarative memory and spatial orientation

ANTERIOR AND POSTERIOR CINGULATE CORTEX



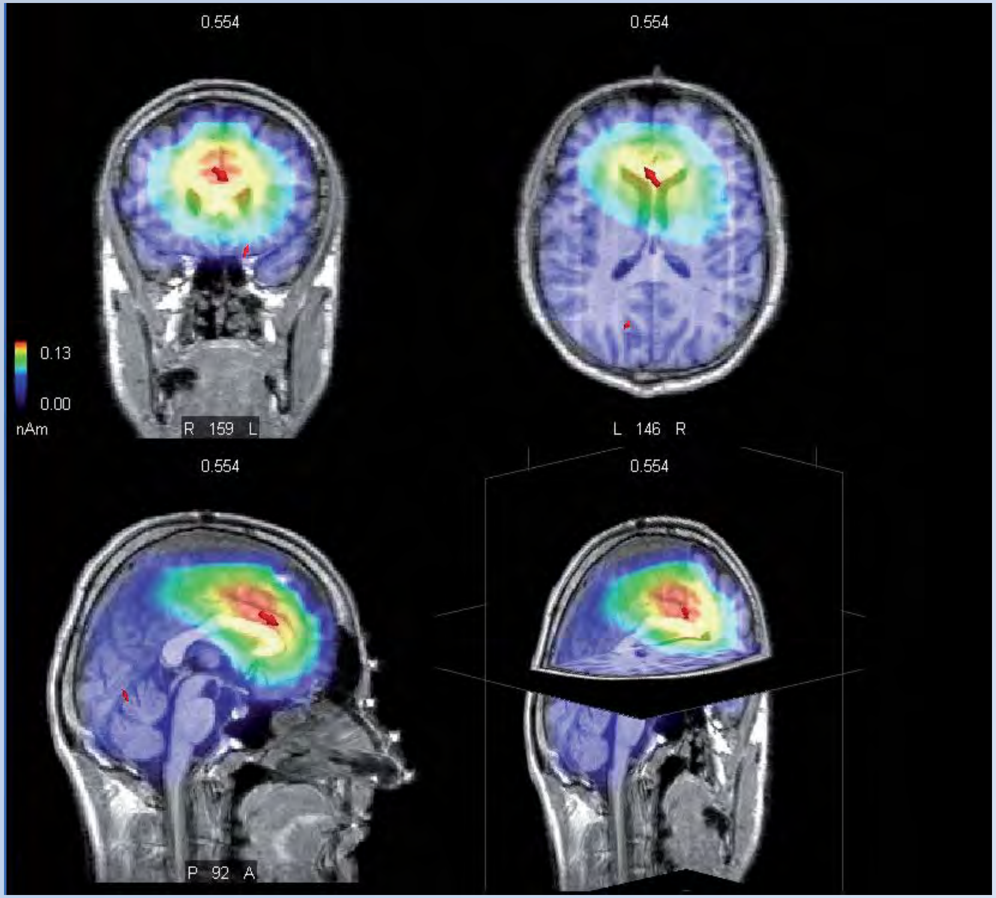
ANTERIOR CINGULATE CORTEX

With amygdala and insula modulates mood and anxiety

The tight connections with hippocampus contribute to memory formation

Connettivity with frontal cortex is related to self-esteem and self-evaluation

Anterior cingulate cohordinates hunger and sleep



POSTERIOR CINGULATE CORTEX

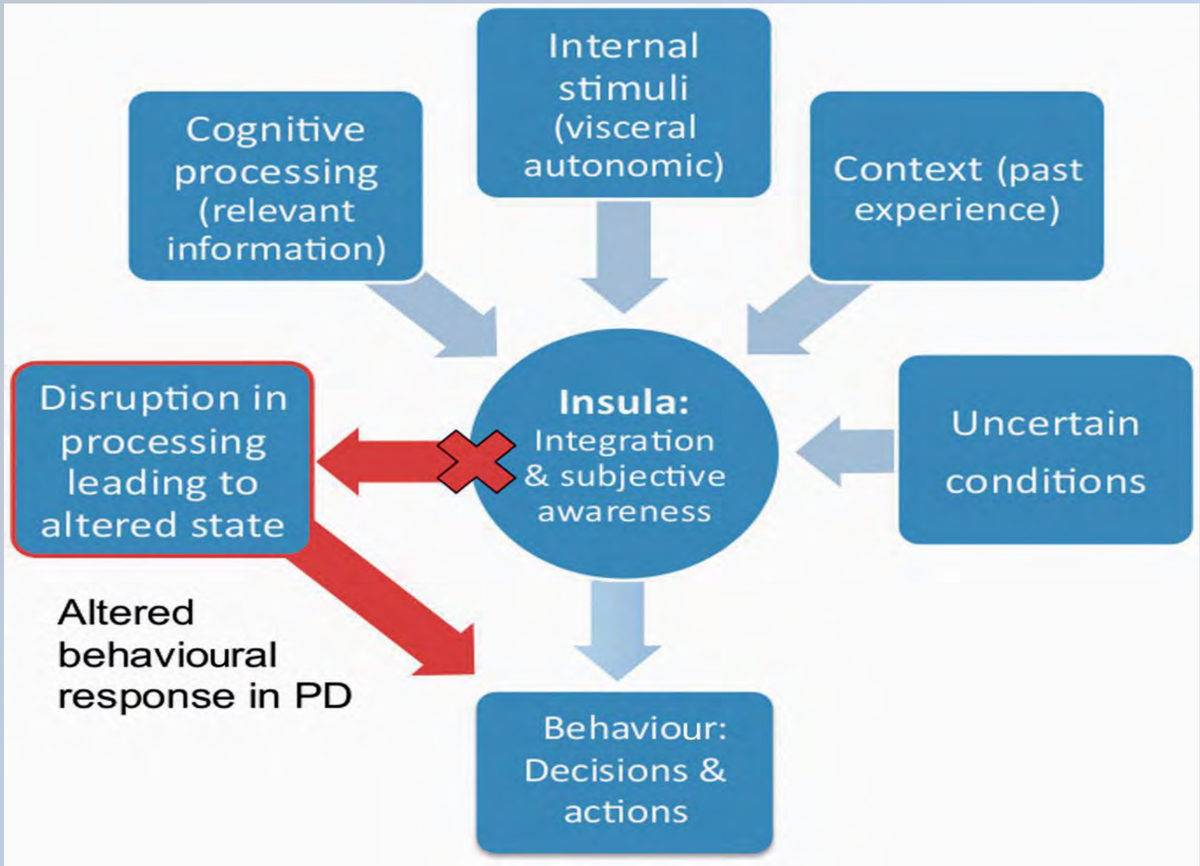
Posterior cingulate processes the “self” and conscious experiences of emotions and feelings

With precuneus it is involved in coping with physical threats and processing stressing material

INSULA

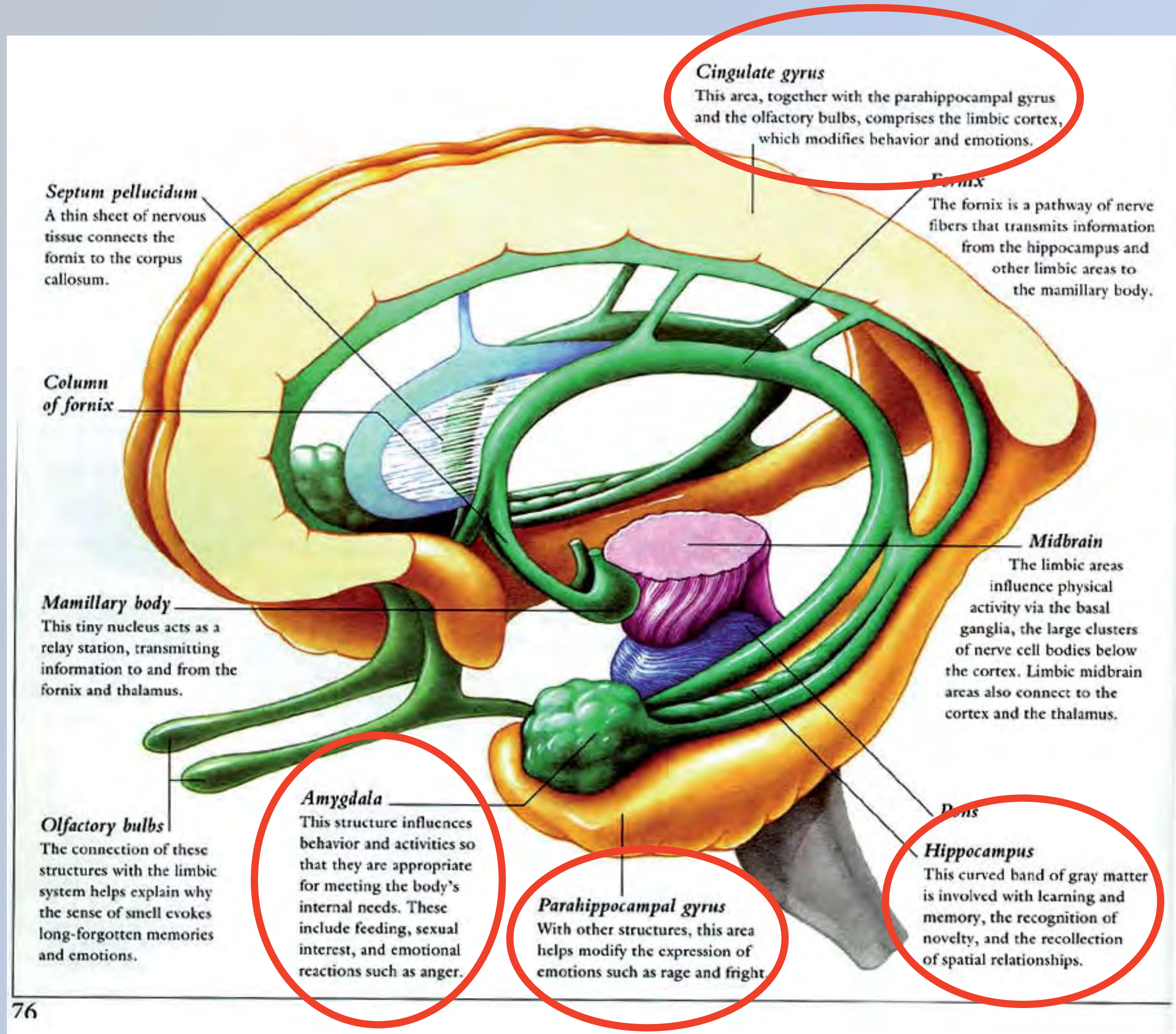
Insular activity has been correlated to anxiety, processing negative emotions and to the reliving of symptom severity

INSULA



Insular hyperactivation is linked to the representation of psychological traumas at somatosensory level

LIMBIC SYSTEM - FUNCTIONAL ROLE



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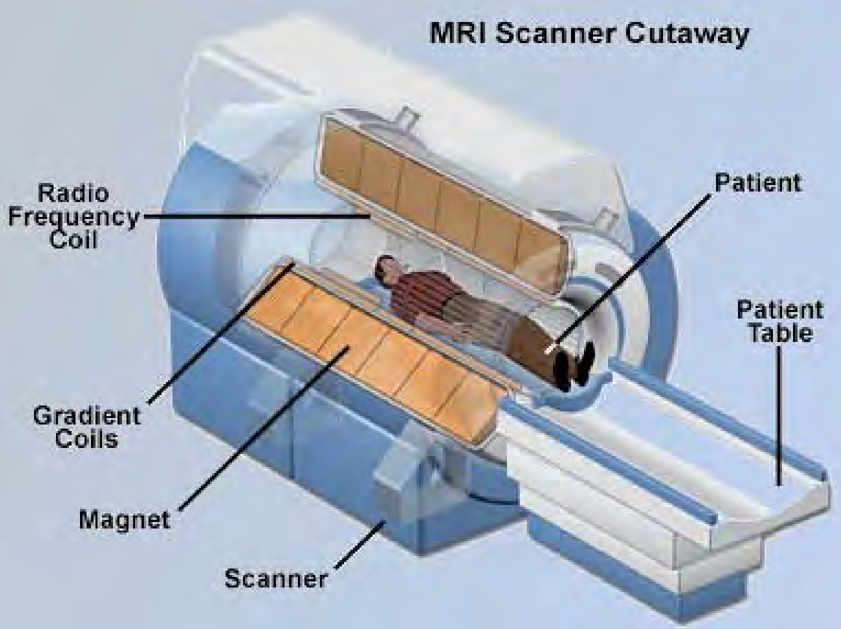
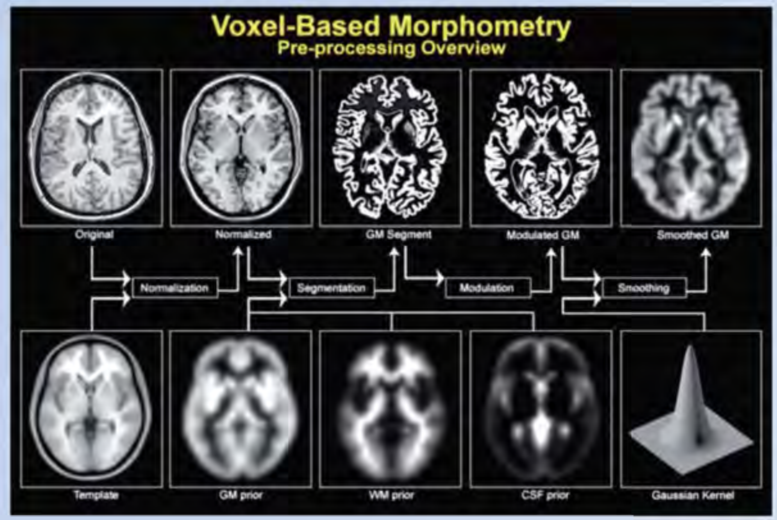
MAGNETIC RESONANCE

Magnetic resonance exploits magnetic fields to produce anatomical images

It is widespread and relatively cheap

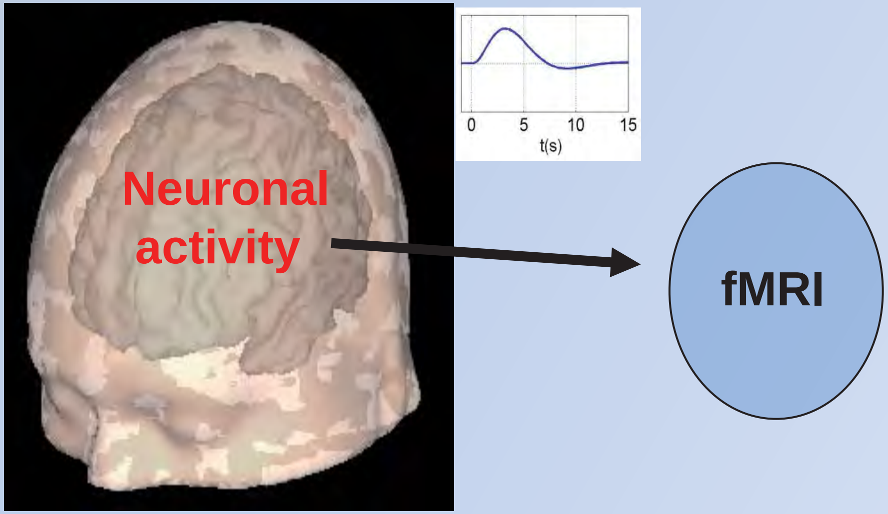




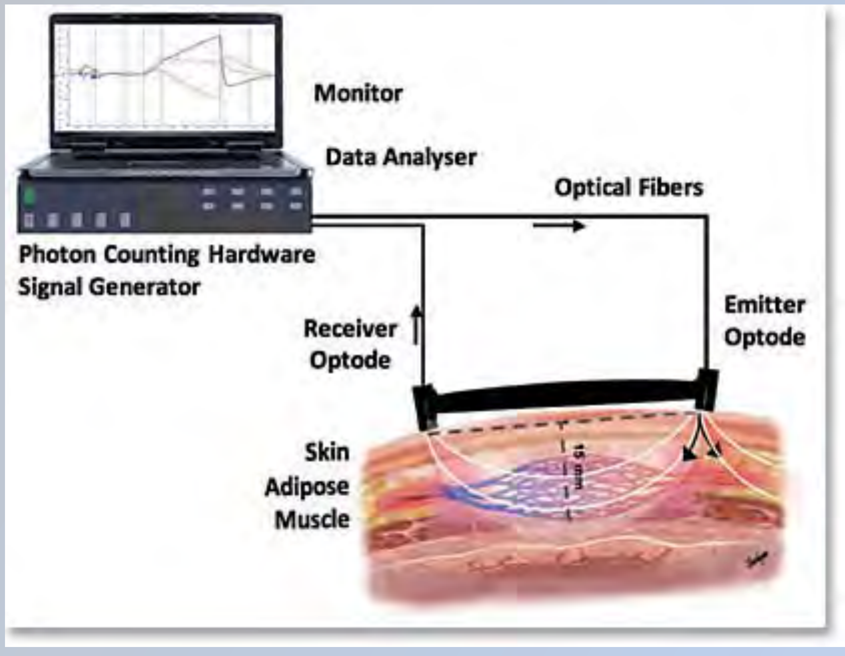
FUNCTIONAL MAGNETIC RESONANCE IMAGING

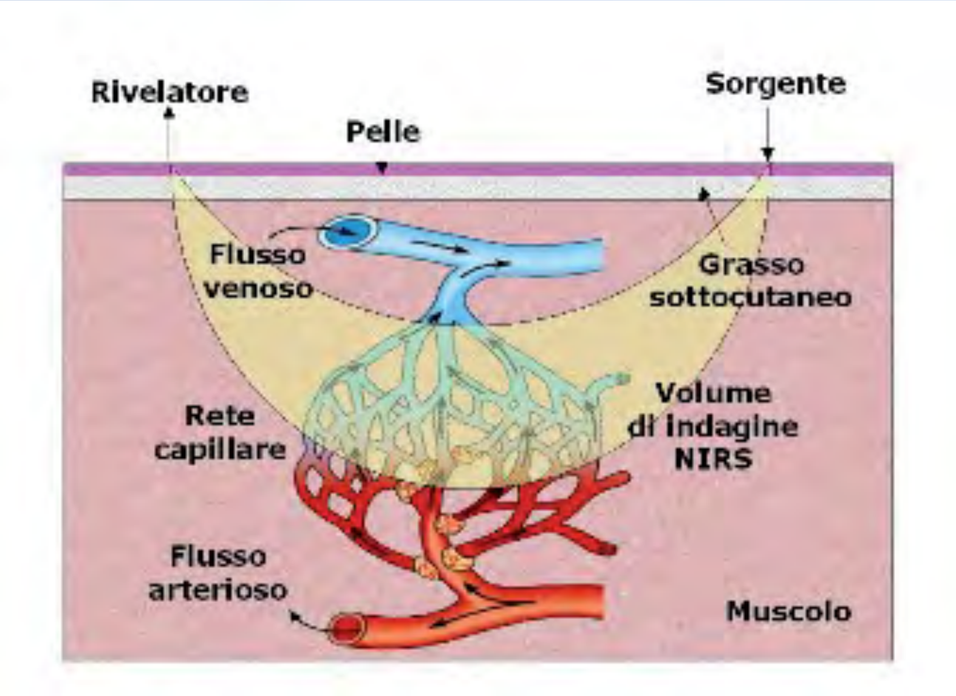
fMRI allows dynamic measurements of cerebral activity by quantifying oxygen consumption

Deoxygenated hemoglobin is found in neuronally active regions, highlighted by fMRI imaging



NIRS





Near Infra-Red Spectroscopy reveals tissue oxygenation within few centimeters from the probe

NIRS

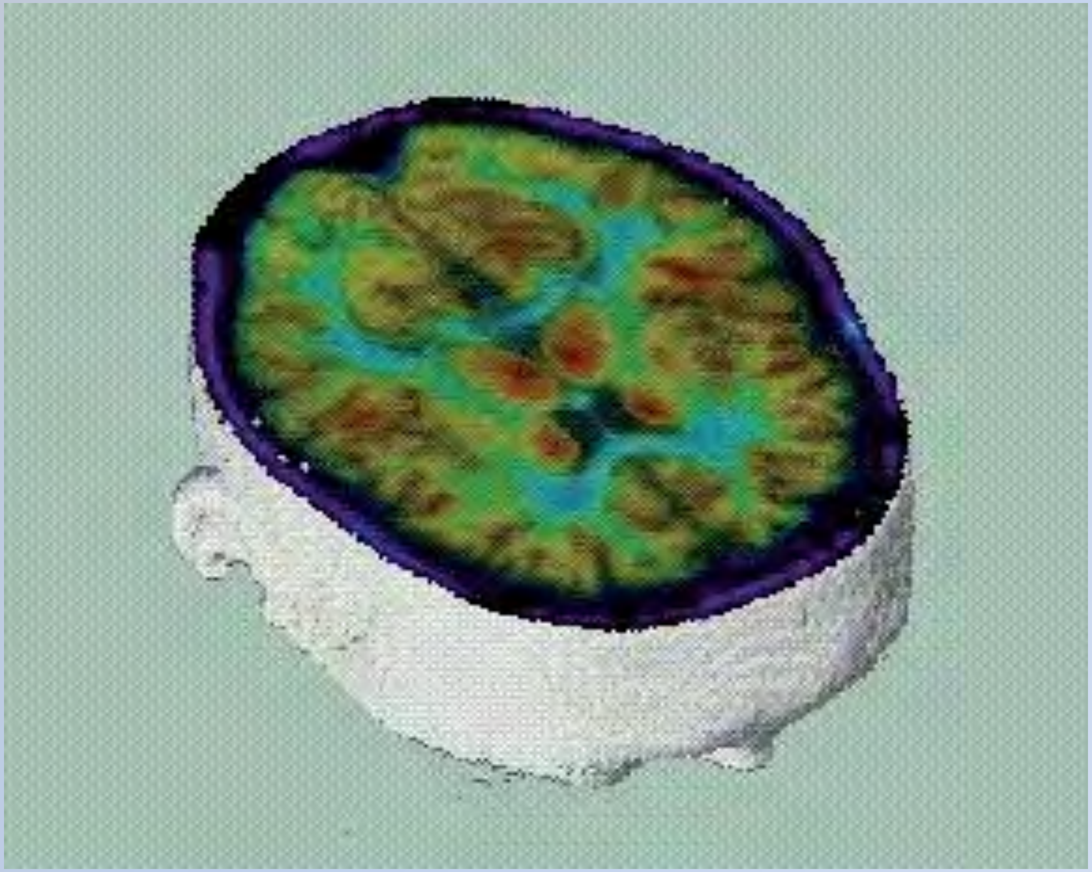
CURRENT: YES

EXPERIMENTAL: MAY BE

FUTURE!

SPECT and PET

Injected radioisotopes distribute in the brain proportionally to the function to be investigated (blood flow, metabolism or receptor density)



SPECT and PET

SPECT

- More diffuse
- Lower costs
- Versatile in somministration

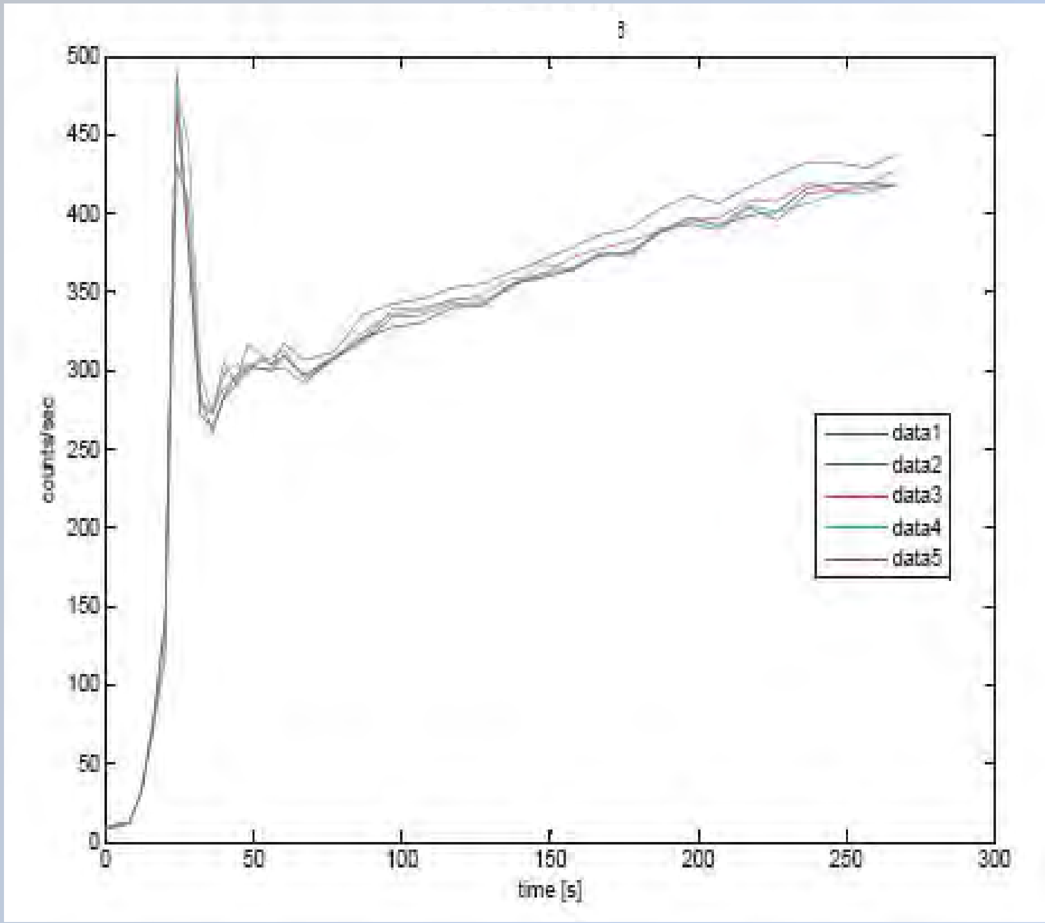
PET

- Better tracers choice
- Higher sensitivity
- Better spatial resolution

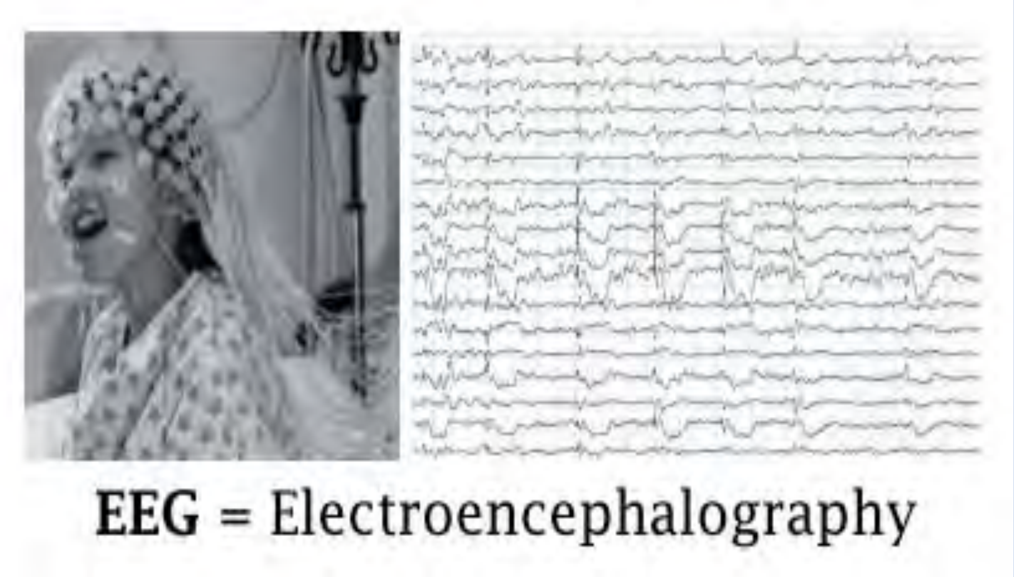
ADVANTAGE OF SPECT IN NEUROPSYCHOLOGY

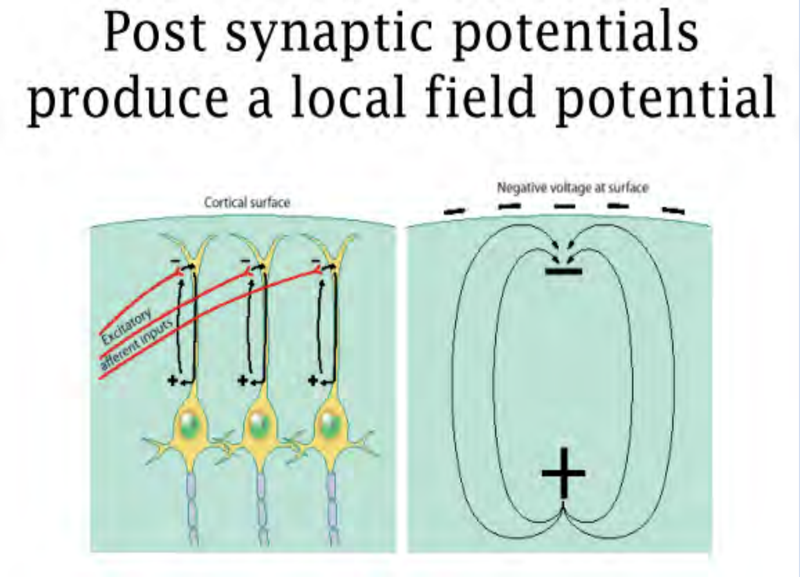
Tracer administration during brain stimulus or experimental condition

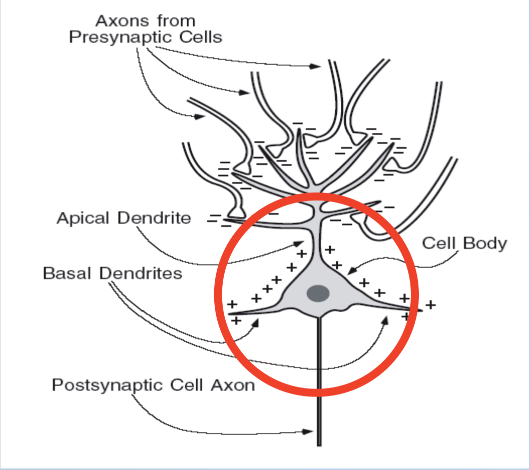
Brain scanning within 6 hours from injection

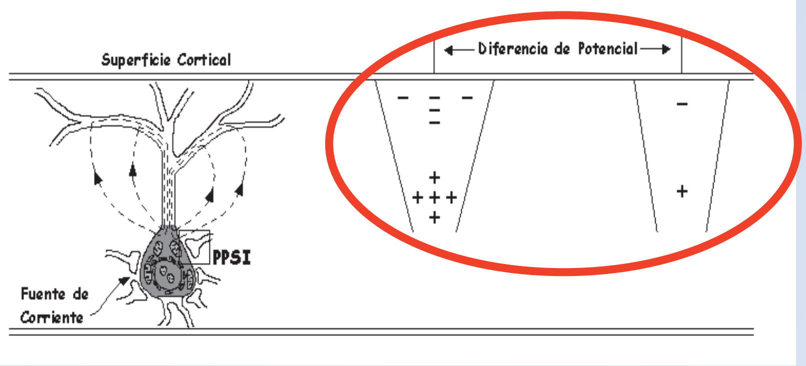


EEG


EEG = Electroencephalography


Post synaptic potentials produce a local field potential
Cortical surface
Negative voltage at surface
Excitatory afferent inputs

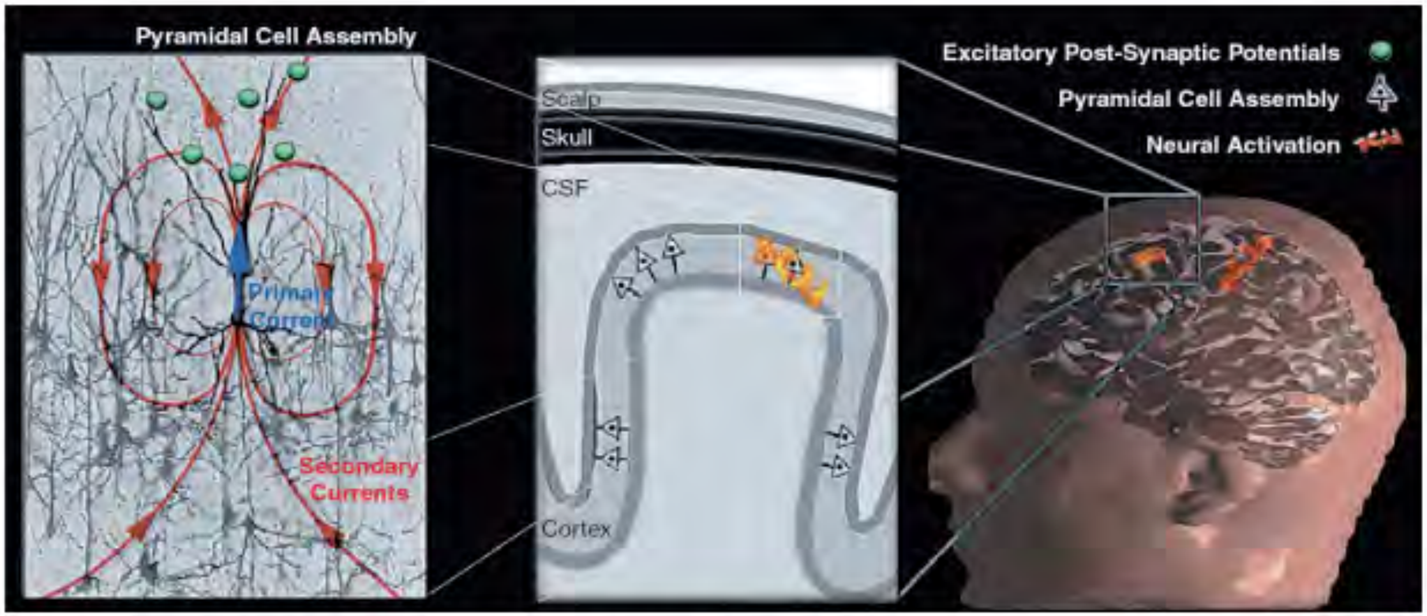

Axons from Presynaptic Cells
Apical Dendrite
Basal Dendrites
Cell Body
Postsynaptic Cell Axon


Superficie Cortical
Diferencia de Potencial
PPSI
Fuente de Corriente

NEUROIMMAGING IN EEG

- EEG enables higher temporal resolution, on the order of milliseconds, rather than seconds.
- Hardware costs are significantly lower for EEG sensors versus an fMRI (or MEG) machine.
- **EEG sensors can be deployed into a wider variety of environments than can a bulky, immobile fMRI machine (or MEG system).**
- **EEG is relatively tolerant of subject movement versus an fMRI (and MEG) (where the subject must remain completely still).**
- EEG can detect covert processing (i.e., processing that does not require a response).
- EEG is silent, which allows for better study of the responses to auditory stimuli.
- EEG does not aggravate claustrophobia (MEG yes).

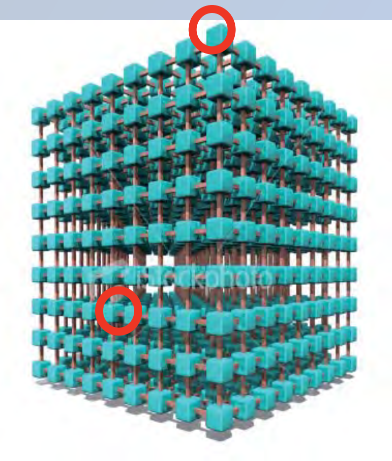
NEUROIMMAGING IN EEG



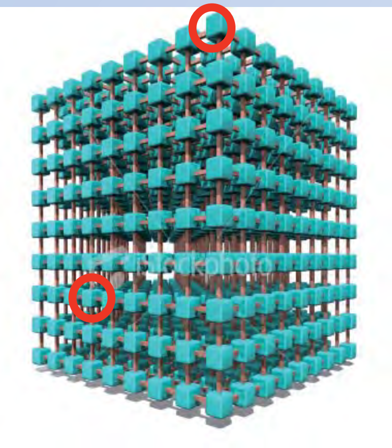
- The electrical current flowing in adjacent brain tissue produced by the firing of a single neuron is very small.
- When a large population of neurons are active together, they produce electrical currents (current flow) large enough to be detected by electrodes placed on the scalp.
- Electroencephalography is the recording of electric currents (potentials) generated in the brain, by means of electrodes applied to the scalp.
- Signals, recorded from the scalp, are small: 1 - 100 microvolts.

STATISTICAL ANALYSES

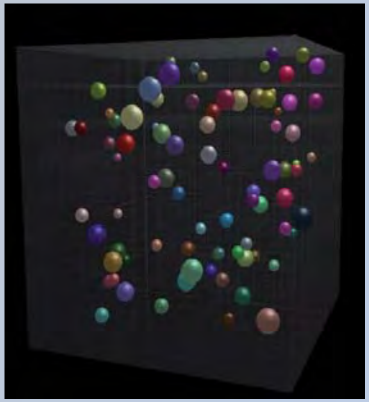
UNIVARIATE

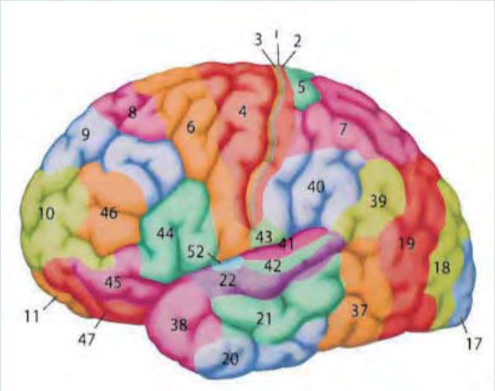


t-statistics

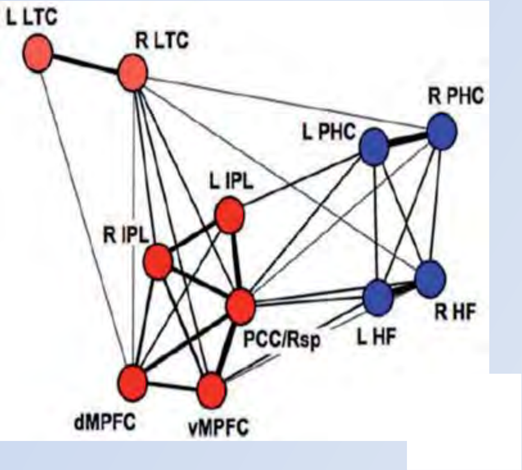


MULTIVARIATE



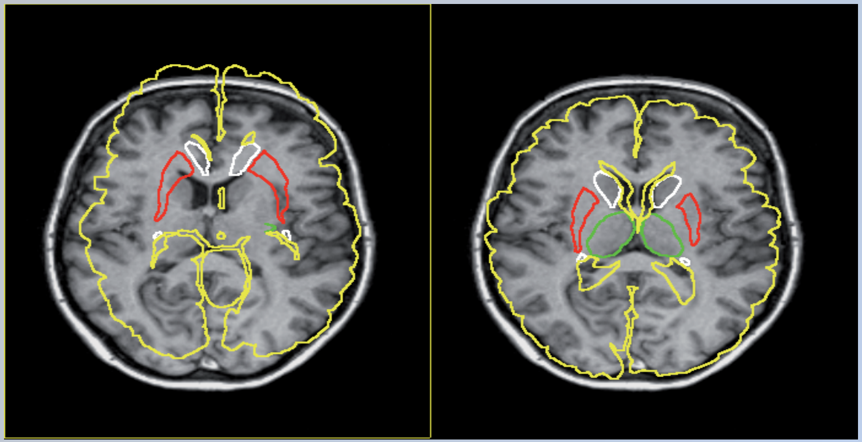


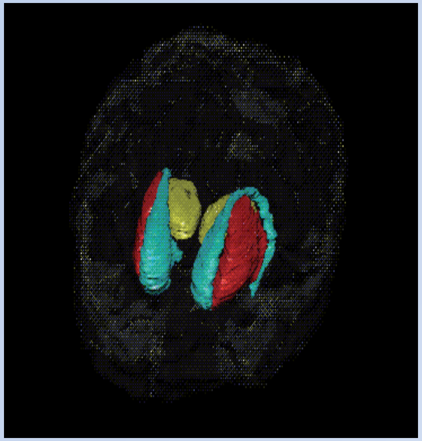
PCA/ICA



2D E 3D IMAGING

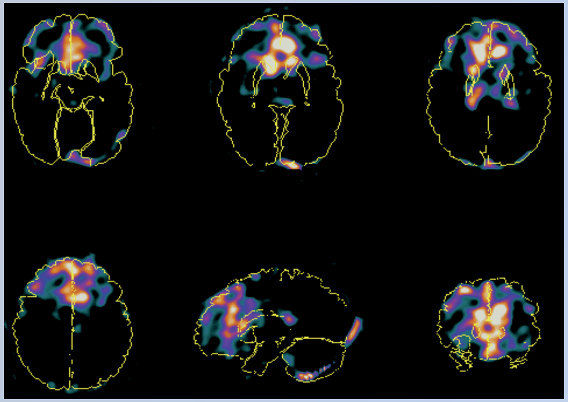
3D FITTING TO PRE-DEFINED MODELS



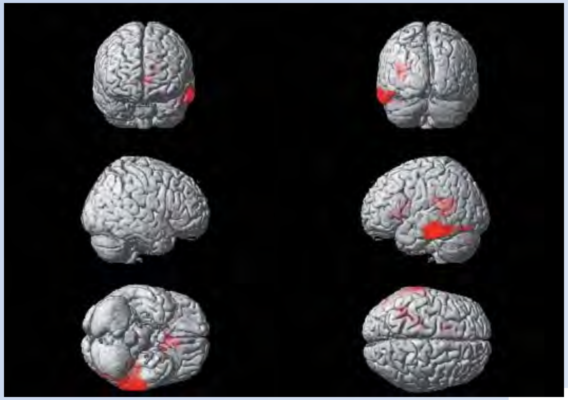


2D IMAGING

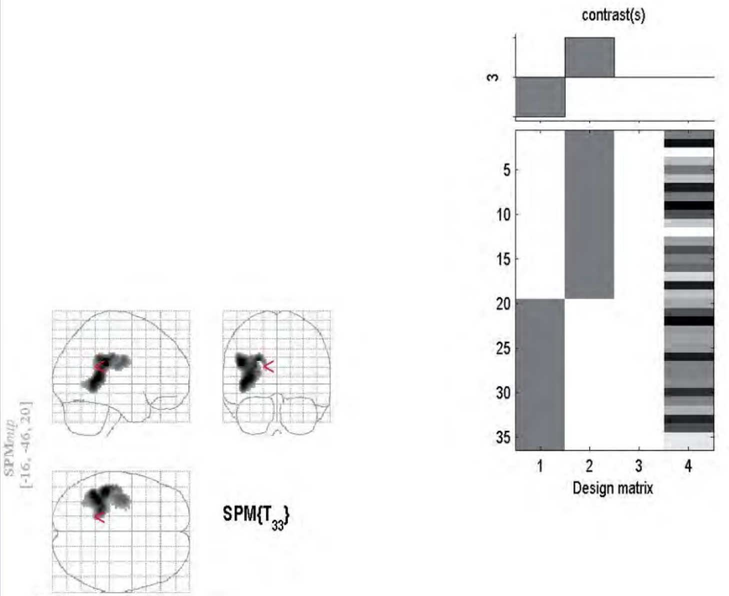
3D IMAGING



GROUP DIFFERENCES



VOXEL-BASED METHOD

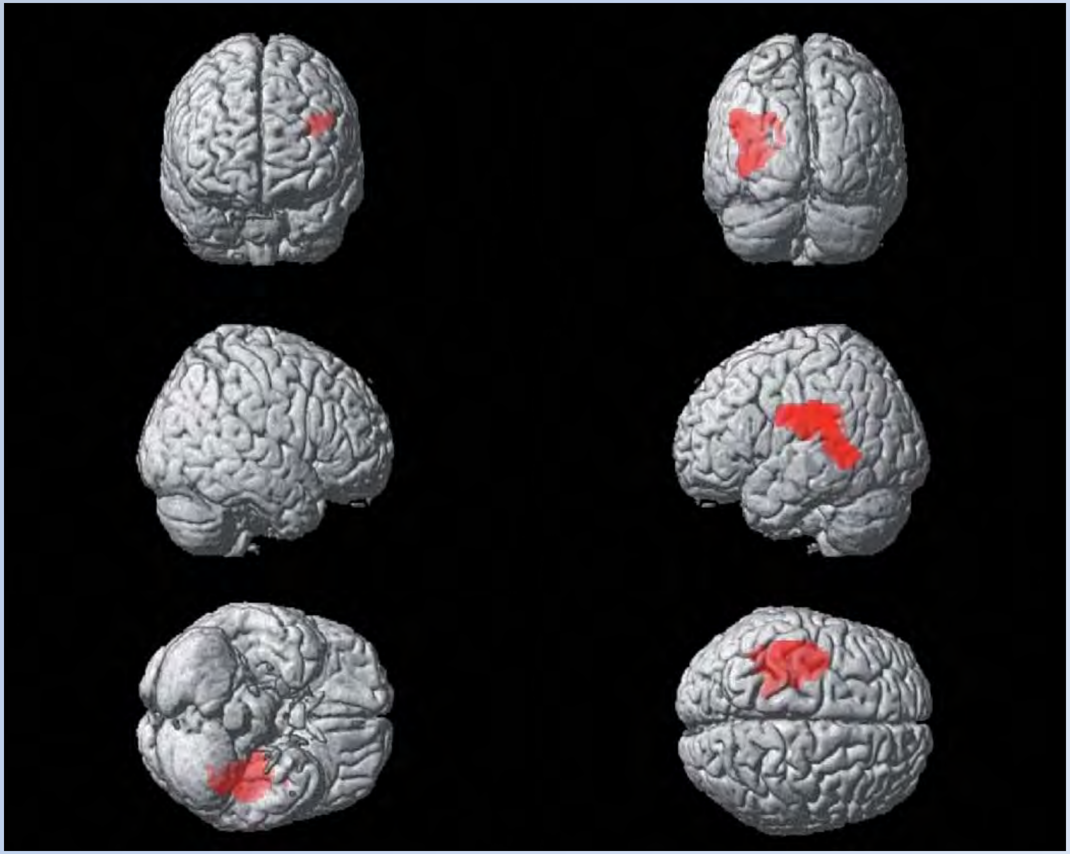


SPMresults: \PTSD_non PTSD SPM.mat
Height threshold T = 2.44
Extent threshold k = 1000 voxels

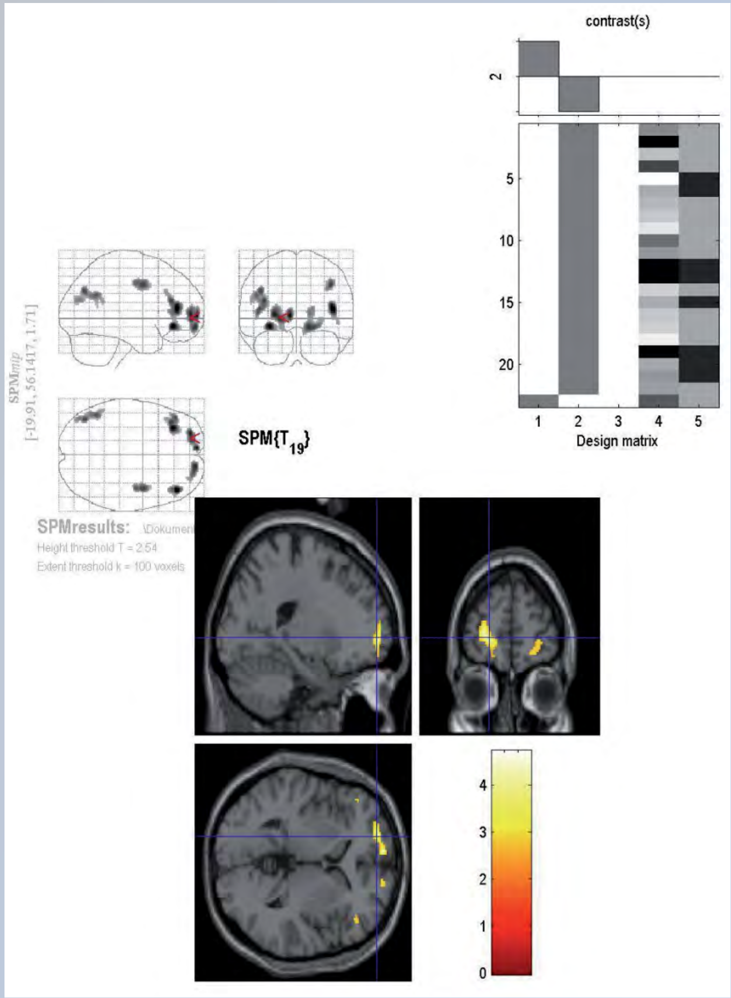
Statistics: ***p-values adjusted for search volume***

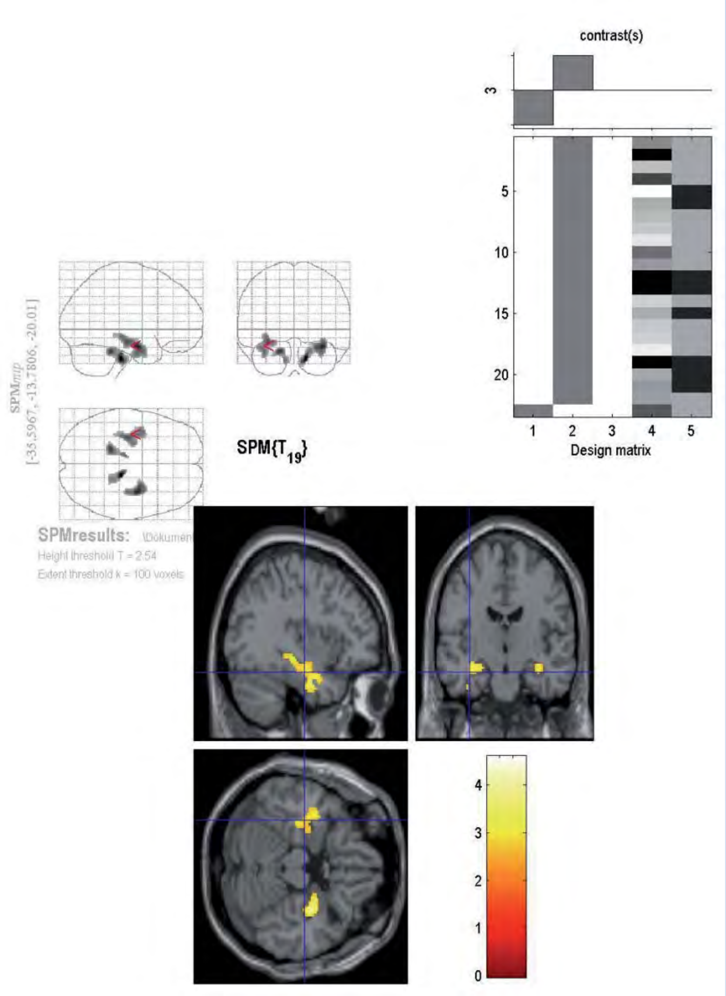
cluster-level			voxel-level					x,y,z {mm}
$p_{corrected}$	k_E	$p_{uncorrected}$	$p_{FWE-corr}$	$p_{FDR-corr}$	T	$(Z_\equiv)$	$p_{uncorrected}$	
0.050	**2036**	**0.004**	**0.852**	**0.568**	**3.66**	**3.33**	**0.000**	**-44 -32 24**
			0.870	0.568	3.63	3.30	0.000	-36 -44 6
			0.875	0.568	3.62	3.30	0.000	-42 -48 0
			0.907	0.568	3.55	3.24	0.001	-32 -42 10
			0.961	0.568	3.39	3.12	0.001	-24 -40 28
			0.962	0.568	3.39	3.11	0.001	-30 -38 18
			0.971	0.568	3.34	3.08	0.001	-26 -38 20
			0.985	0.568	3.25	3.01	0.001	-26 -36 28
			0.988	0.568	3.22	2.98	0.001	-50 -26 30
			0.996	0.568	3.09	2.87	0.002	-36 -12 24
			0.998	0.568	3.03	2.82	0.002	-36 -18 22
			0.998	0.568	3.02	2.82	0.002	-36 -8 26
			0.999	0.568	2.99	2.80	0.003	-32 -10 30
			0.999	0.568	2.98	2.79	0.003	-18 -44 26
			0.999	0.568	2.97	2.78	0.003	-48 -18 30
			1.000	0.568	2.85	2.68	0.004	-30 -14 26
			1.000	0.568	2.81	2.64	0.004	-46 -18 26
			1.000	0.568	2.72	2.57	0.005	-16 -46 20
			1.000	0.568	2.64	2.49	0.006	-32 -60 -2
			1.000	0.568	2.50	2.38	0.009	-26 -4 28

table shows 32 local maxima more than 4.0mm apart



VOXEL-BASED METHOD IN CLINICAL SETTING





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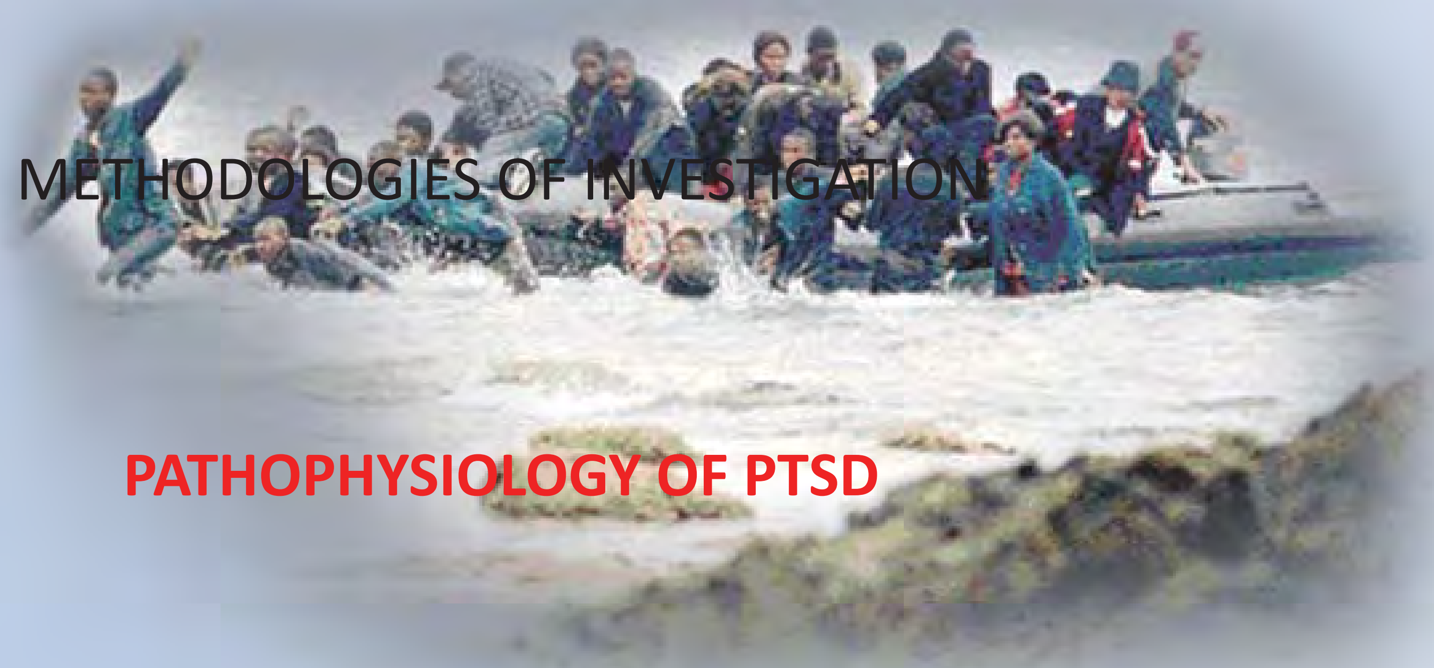


POST-TRAUMATIC STRESS DISORDER

In DSM-5 PTSD is defined by the coexistence of 4 clusters of symptoms

- re-experiencing (intrusive thoughts, flashbacks, nightmares)
- avoidance (memory impairment, feelings of detachment, efforts to avoid thoughts, places or people associated with the trauma, social withdrawal)
- negative alterations (mood and cognition)
- hyperarousal (abnormal startle responses, hypervigilance, irritability, sleep disturbance, difficulty concentrating)

PTSD AND NEUROIMAGING

It has become increasingly clear that a number of specific brain structures play a key role in the generation of PTSD symptoms

These structures are involved in emotional, memory, linguistic, visuospatial and motor processing, all of which might be affected in the disorder

PTSD AND NEUROIMAGING

Original Articles

Neural Correlates of Exposure to Traumatic Pictures and Sound in Vietnam Combat Veterans with and without Posttraumatic Stress Disorder: A Positron Emission Tomography Study

J. Douglas Bremner, Lawrence H. Staib, Danny Kaloupek, Steven M. Southwick, Robert Soufer, and Dennis S. Charney

The first neuroimaging studies on PTSD were performed in the USA at military hospitals including mostly Vietnam war veterans

Table 3. Areas of Decreased Blood Flow with Combat-Related Slides and Sounds Relative to Neutral Slides and Sounds in PTSD Patients and Comparison Subjects

PTSD patients (n = 10)					Comparison subjects (n = 10)				
	Talairach coordinates					Talairach coordinates			
Z score	x	y	z	Brain region	Z score	x	y	z	Brain region
5.04	−50	−10	0	L. superior temporal pole (22)	5.80	−58	−32	20	L. superior temporal gyrus (41)
4.88	−10	−22	12	L. Thalamus	5.66	−52	−6	8	L. precentral (6)
4.42	−36	−32	12	L. superior temporal (41)	5.09	−50	0	24	
4.59	8	20	−12	R. Mesofrontal (25)	4.77	−46	−4	24	
4.36	−8	18	−12	L. Mesofrontal (25)	4.14	−40	−28	28	L. inferior pariental lobule (40)
4.23	−34	−86	16	L. visual area (19)	4.13	56	−6	8	R. superior tempral pole (22)
3.60	−22	−90	20		3.06	62	−34	8	
3.98	−8	52	0	L. anterior cingulate (32)	3.61	2	−12	32	Posterior cingulate (23)
3.87	50	−4	0	R. superior temporal gyrus (21)	3.53	12	−54	−4	R. cerebellum
3.66	−56	−32	−4	L. middle temporal gyrus (21)	3.09	18	−50	−12	
					3.05	8	−56	0	R. posterior parahippocampus (lingual) (19)

Z score > 3.00, p < .001.

PTSD AND NEUROIMAGING

Regional Cerebral Blood Flow During Script-Driven Imagery in Childhood Sexual Abuse-Related PTSD: A PET Investigation

Lisa M. Shin, Ph.D., Richard J. McNally, Ph.D., Stephen M. Kosslyn, Ph.D., William L. Thompson, B.A., Scott L. Rauch, M.D., Nathaniel M. Alpert, Ph.D., Linda J. Metzger, Ph.D., Natasha B. Lasko, Ph.D., Scott P. Orr, Ph.D., and Roger K. Pitman, M.D.

TABLE 5. Brain Regions of Sexually Abused Subjects With PTSD (N=8) and Without (N=8) That Showed Significantly Different Changes in Cerebral Blood Flow in Response to Audiotaped Scripts of Traumatic Events Relative to Neutral Events (Condition-by-Group Interaction)

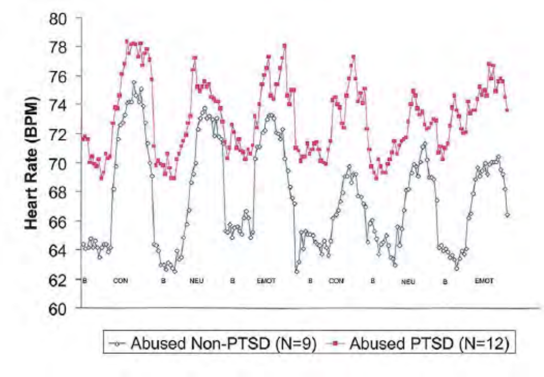
Region	z Score	Coordinate of Activation Focus (mm)[a]		
		x	y	z
Greater increases in PTSD group				
Orbitofrontal cortex	3.98	26	38	–16
	3.48	26	30	–20
	3.50	4	10	–20
Anterior temporal pole	3.31	–24	15	–28
Greater decreases in PTSD group				
Middle frontal gyrus				
46[b]	4.48	42	46	8
9/10[b]	3.69	–24	52	12
Superior frontal gyrus				
9[b]	4.43	14	50	28
10[b]	3.52	–20	48	24
Inferior frontal gyrus	3.96	48	16	8
Superior temporal gyrus	4.64	–40	–52	16
	4.03	48	–22	0
Middle temporal gyrus	4.64	62	–12	–8
Parahippocampal gyrus	3.70	–20	–20	–12
Inferior parietal lobule	3.69	60	–36	32
	3.67	26	–56	36
	3.52	–44	–46	32
Greater increases in comparison group				
Anterior cingulate gyrus	3.31	7	38	0
Posterior cingulate gyrus	3.55	4	–52	24

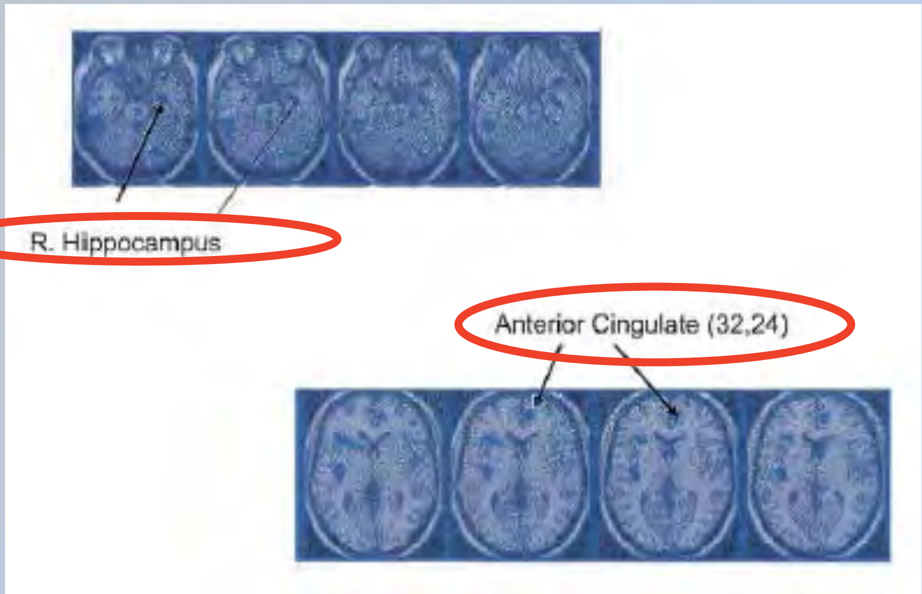
NEUROIMAGING IN ABUSE RELATED PTSD

Neural Correlates of the Classic Color and Emotional Stroop in Women with Abuse-Related Posttraumatic Stress Disorder

J. Douglas Bremner, Eric Vermetten, Meena Vythilingam, Nadeem Afzal, Christian Schmahl, Bernet Elzinga, and Dennis S. Charney

BIOL PSYCHIATRY 2004;55:612–620





Decreased Blood Flow

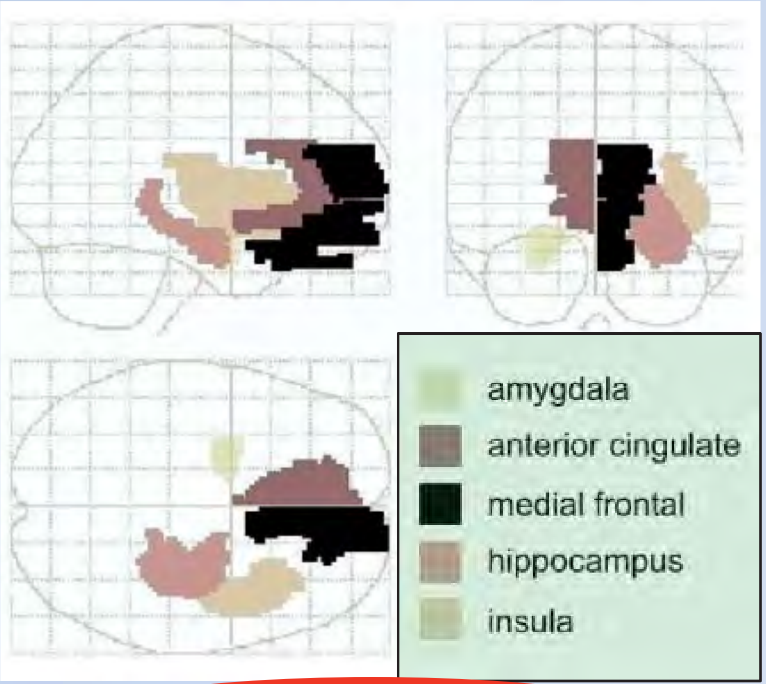
Z Score[a]	Talairach Coordinates x	y	z	Brain Region
4.27[b]	−46	22	24	L middle frontal gyrus (46)
3.67	−24	14	−2	L putamen
3.64	−42	24	4	L inferior frontal gyrus (45)
3.52[b]	−32	4	56	L middle frontal gyrus (6)
3.88[b]	−52	−40	−28	Cerebellum
3.86[b]	−38	−12	2	Insula
3.73[b]	26	−2	−28	Uncus
3.12	42	−16	−18	R hippocampal region
3.39[b]	4	−24	−22	Midbrain
3.23[b]	24	−74	−30	Cerebellum
2.62	22	−82	−46	
3.14[b]	10	48	20	R anterior frontal cortex (9)
3.07	6	30	32	R anterior cingulate (32)
3.04	16	54	10	R anterior frontal cortex (10)
3.78[b]	−64	−48	14	L superior temporal gyrus (22)

CONNECTIVITY IN CIVILIAN TRAUMAS

Neurophysiological Responses to Traumatic Reminders in the Acute Aftermath of Serious Motor Vehicle Collisions Using [^{15}O]-H_2O Positron Emission Tomography

Elizabeth A. Osuch, Mark W. Willis, Robyn Bluhm, CSTS Neuroimaging Study Group, Robert J. Ursano, and Wayne C. Drevets

BIOL PSYCHIATRY 2008;64:327–335



Functional connectivity

Amygdala has strong connections with anterior cingulate, insula and hippocampus

MALTREATMENT AND CONNECTIVITY

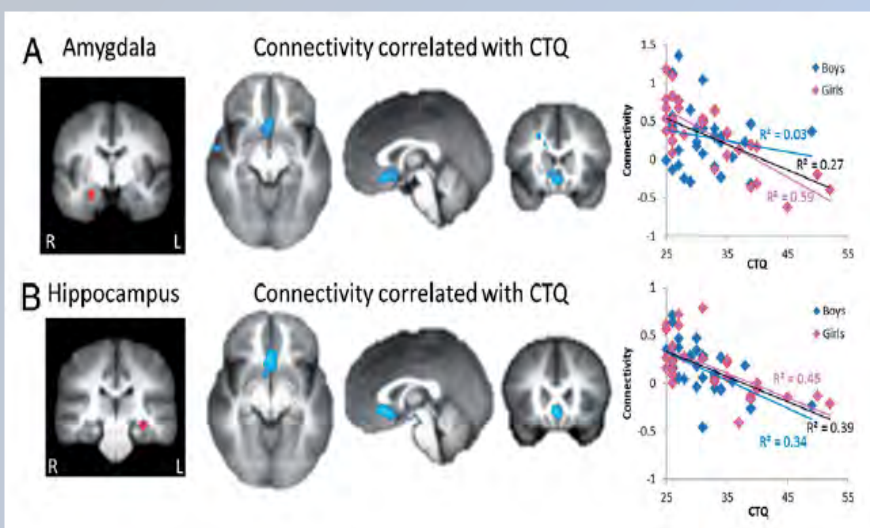
Childhood maltreatment is associated with altered fear circuitry and increased internalizing symptoms by late adolescence

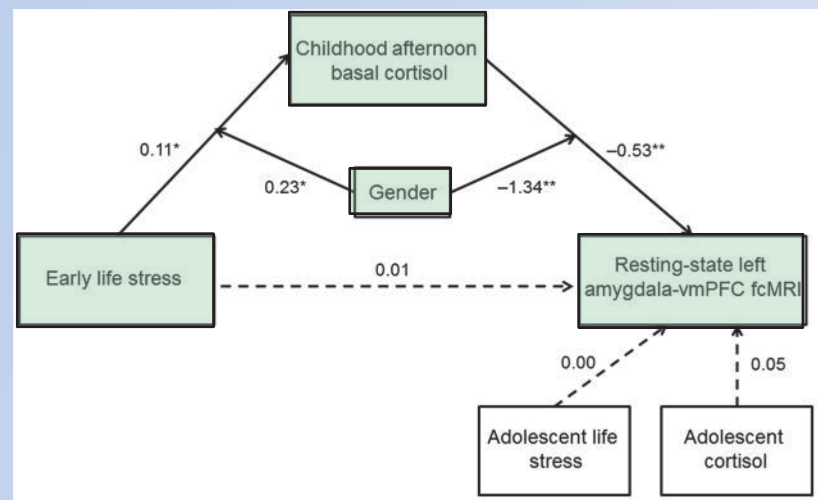
Ryan J. Herringa[a,1,2], Rasmus M. Birn[a,b,1], Paula L. Ruttle[a], Cory A. Burghy[c], Diane E. Stodola[c], Richard J. Davidson[a,c,d], and Marilyn J. Essex[a,2]

PNAS | November 19, 2013 | vol. 110 | no. 47 | 19119–19124

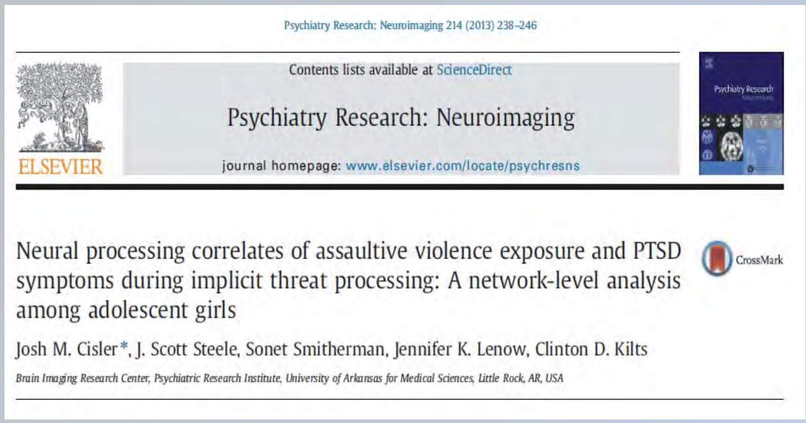
Maltreatment in childhood also at subthreshold level alters the capability of brain to regulate the fear response and leads to a symptoms internalization during teenage causing anxiety and depression

This suggests in case of childhood maltreatment to implement as soon as possible specific treatments preventing serious problems, especially in females





ASSAULTIVE VIOLENCE AND CONNECTIVITY



Psychiatry Research: Neuroimaging 214 (2013) 238–246

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

ELSEVIER

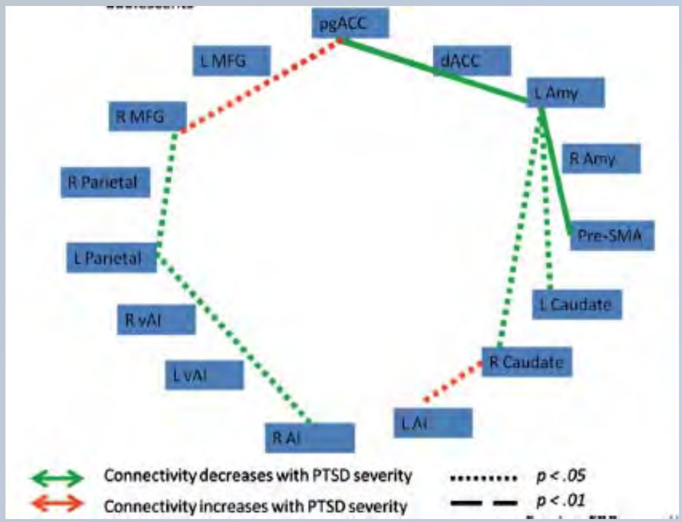
Neural processing correlates of assaultive violence exposure and PTSD symptoms during implicit threat processing: A network-level analysis among adolescent girls

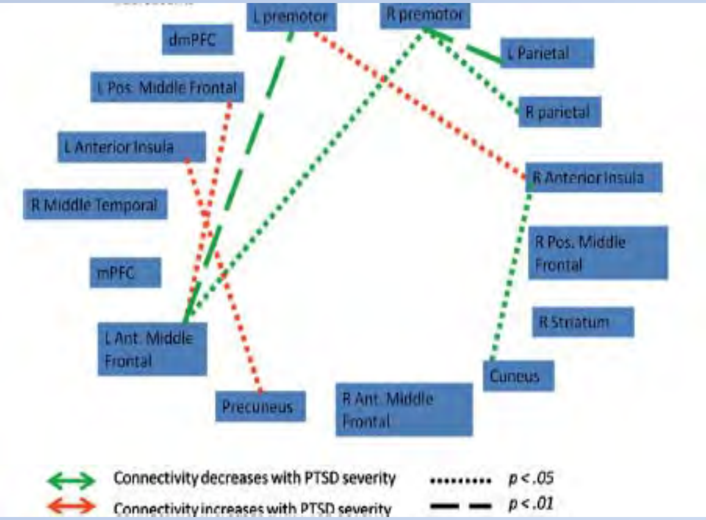
Josh M. Cisler*, J. Scott Steele, Sonet Smitherman, Jennifer K. Lenow, Clinton D. Kilts

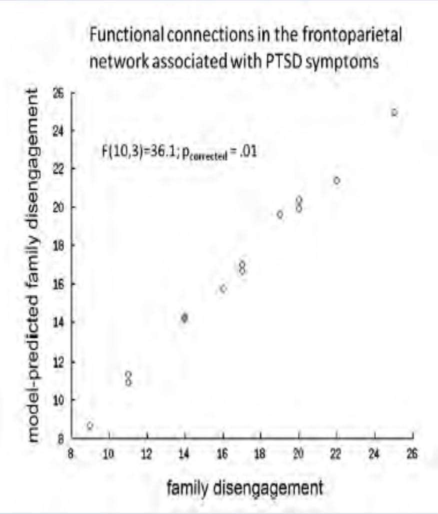
Brain Imaging Research Center, Psychiatric Research Institute, University of Arkansas for Medical Sciences, Little Rock, AR, USA

There is in adolescence a clear association between the violence suffered, PTSD and functional organization of brain cortex upon emotional process

Of utmost importance is the impact of care-giver derangement suggesting a worsening of neural connectivity in case of wanting family support



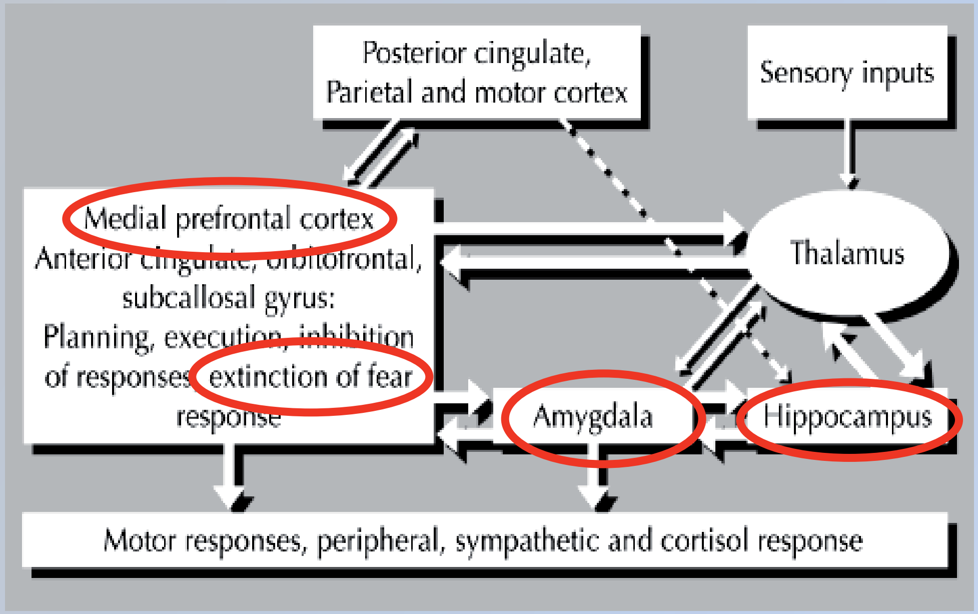


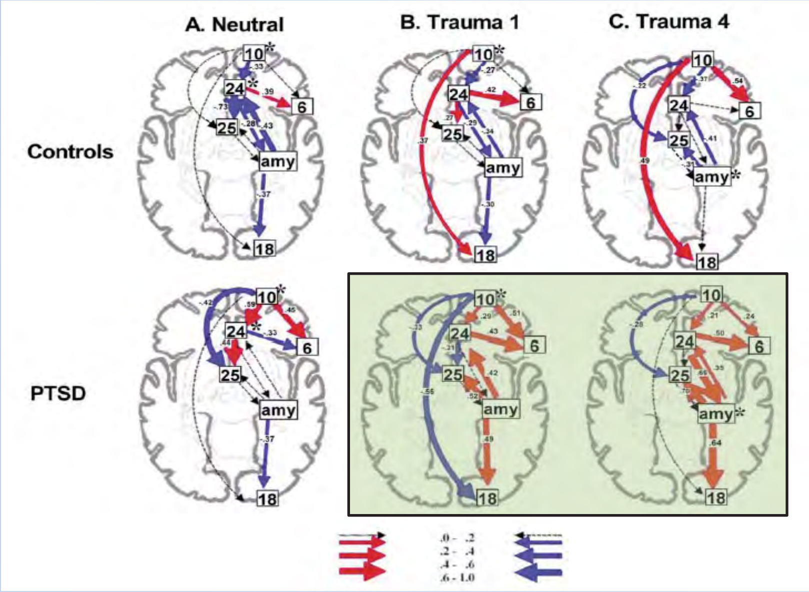


PTSD AND NEUROIMAGING

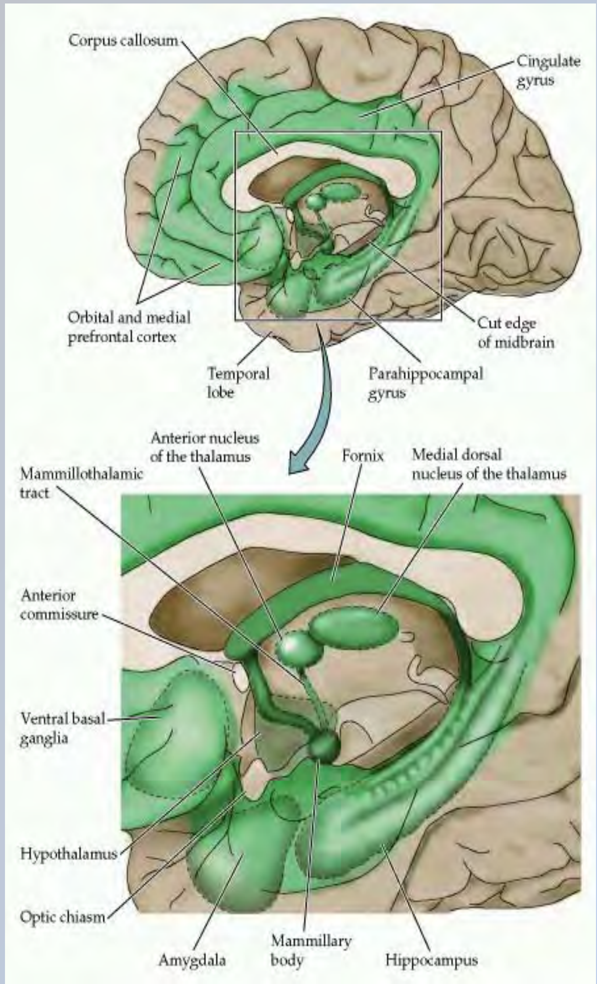
Bremner et al. Current Psychiatry Reports 2002, 4:254–263

Gilboa et al. Biol Psych 2004; 55:263–272





PTSD AND NEUROIMAGING



All neuroimaging studies converge in identifying as implicated in PTSD:

- prefrontal cortex (PFC)
- amygdala
- hippocampus
- insula
- Anterior and posterior cingulate cortex

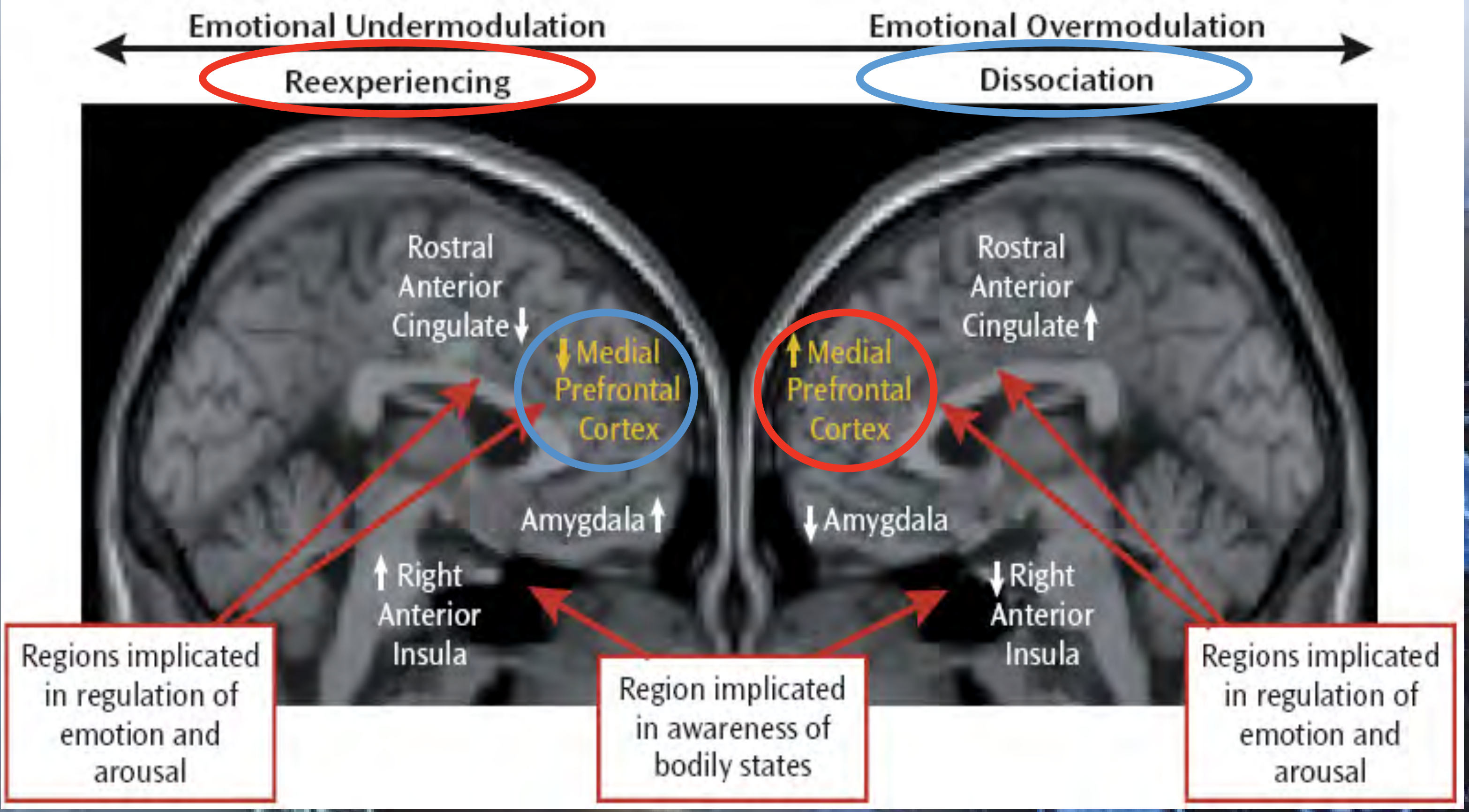
The impairment of PFC associated with a hyper-reactivity of the amygdala constitutes the core neural correlate of PTSD

Ruth A. Lanius, M.D., Ph.D.
Eric Vermetten, M.D., Ph.D.
Richard J. Loewenstein, M.D.
Bethany Brand, Ph.D.
Christian Schmahl, M.D.
J. Douglas Bremner, M.D.
David Spiegel, M.D.

Emotion Modulation in PTSD: Clinical and Neurobiological Evidence for a Dissociative Subtype

Am J Psychiatry 167:6, June 2010

Distacco da contenuti emozionali non sopportabili. Compromissione di memoria, identità, sensazioni corporee e percezione del sè e dell'ambiente circostante



PTSD AND DISSOCIATION

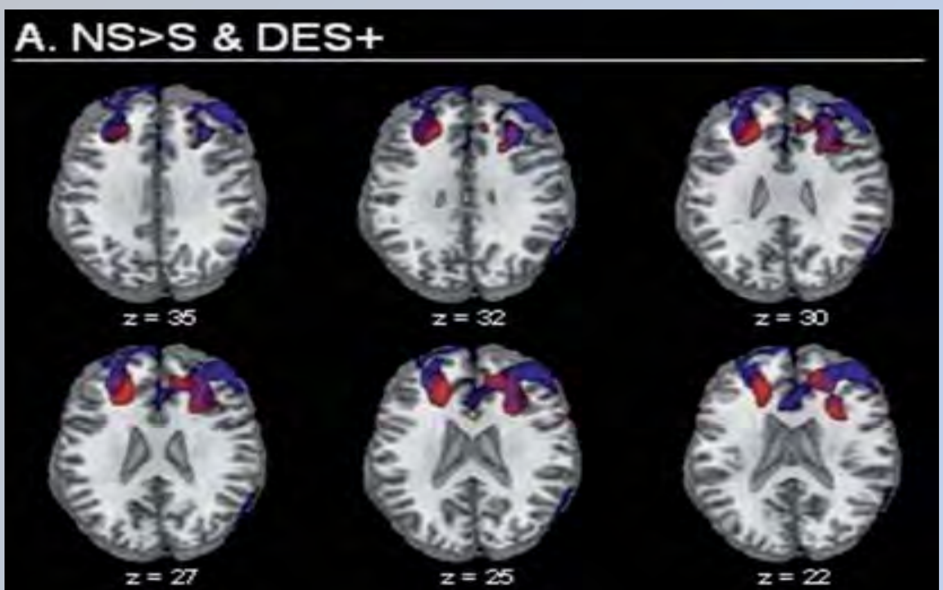
Acta Psychiatrica Scandinavica

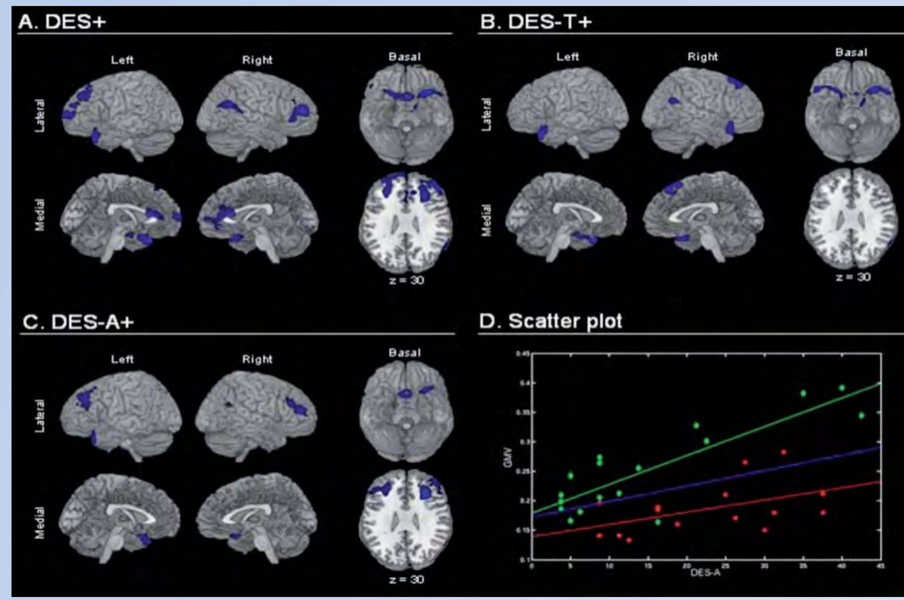
Acta Psychiatr Scand 2013: 128: 222–233
All rights reserved
DOI: 10.1111/acps.12026

ACTA PSYCHIATRICA SCANDINAVICA

Gray matter volume alterations related to trait dissociation in PTSD and traumatized controls

Nardo D, Högberg G, Lanius RA, Jacobsson H, Jonsson C, Hällström T, Pagani M. Gray matter volume alterations related to trait dissociation in PTSD and traumatized controls.





Regions in which grey matter density correlates inversely with PTSD symptoms (in red) and positively (in blue) with overall trait dissociation score

Regions in which pathological and non - pathological Dissociative Experience Scales correlate with grey matter density

WHAT CAN WE DO?

NEUROBIOLOGY OF PSYCHOTHERAPIES

NEUROBIOLOGY OF EMDR

WHAT CAN WE DO?

NEUROBIOLOGY OF PSYCHOTHERAPIES

NEUROBIOLOGY OF EMDR

NEUROIMAGING and PSYCHOTHERAPY

Neuroimaging techniques have been used in an attempt to shed light on the neurobiological correlates of various psychotherapies revealing their neurobiological effects

Despite positive clinical outcomes functional and neuroanatomical studies are still poorly randomized and insufficient to draw robust conclusions

NEUROIMAGING and PSYCHOTHERAPY
ETCR - SPECT

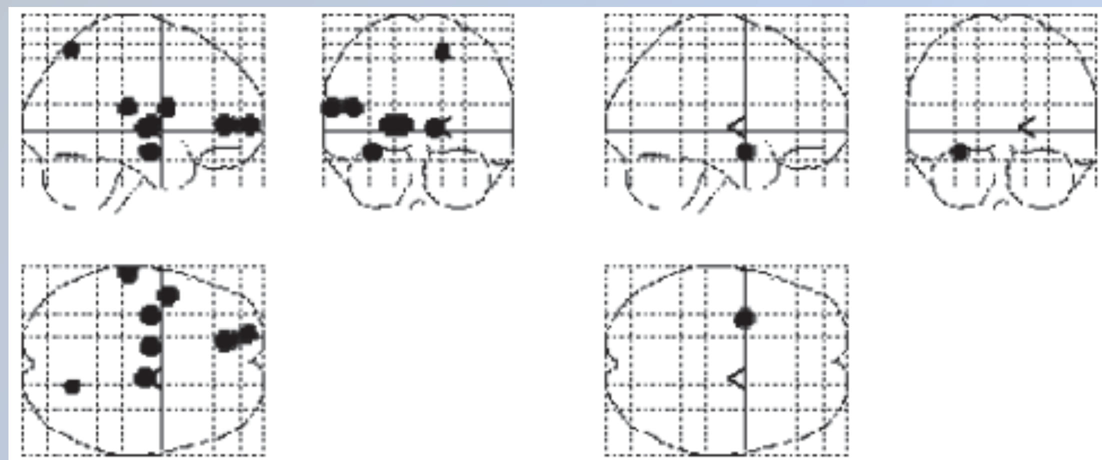


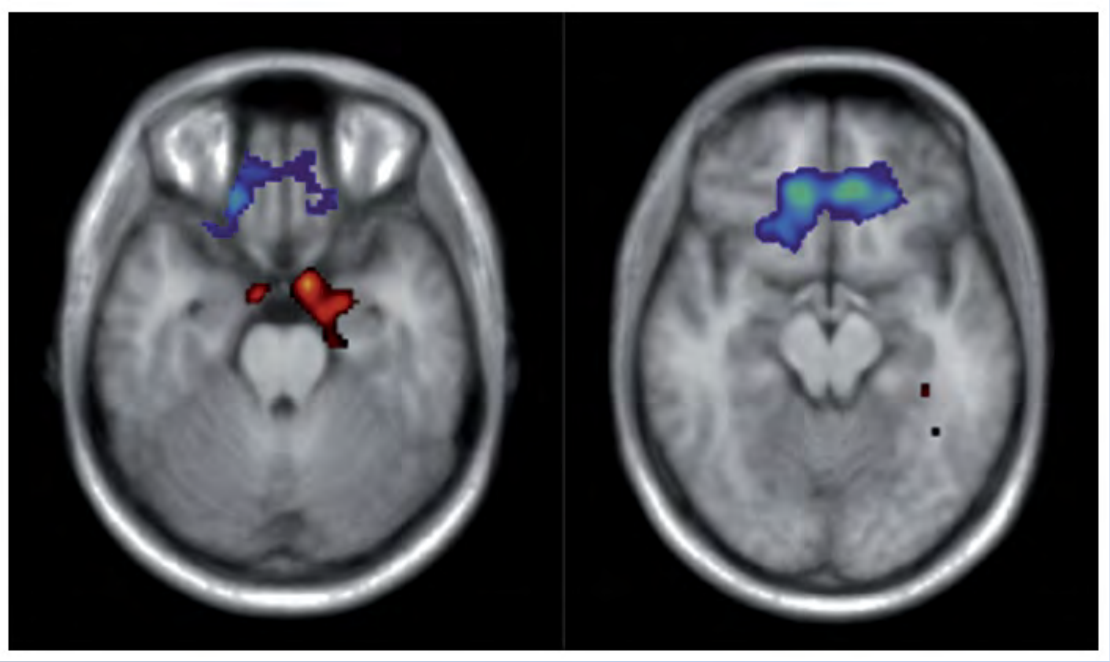
Table 2. *Results from SPM analysis*

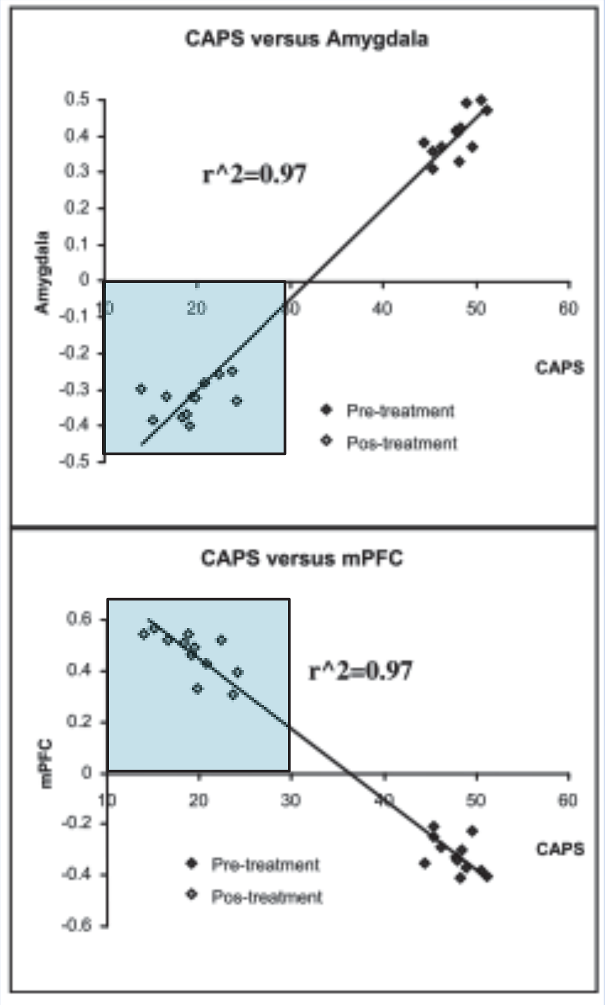
Region	Brodmann	Cluster	x	y	z	Z score
Increased activity after psychotherapy						
Left anterior cingulate	32	4	−13	+43	+4	3·58
Left Broca's area	44	12	−47	+5	+16	3·26
Left hippocampus		39	−32	−9	−15	3·71
Left parietal	40	18	−61	−23	+16	3·51
Left prefrontal cortex	10	42	−20	+62	+4	3·79
Left thalamus		25	−11	−7	+4	3·60
Right parietal	7	7	+18	−63	+56	3·46
Right thalamus		9	+12	−12	+2	3·34
Decreased activity after psychotherapy						
Left amygdala		26	−30	−1	−15	3·39

Location and peaks of significant clusters of activation and deactivation after psychotherapy were set to threshold $t = 3·34$ corresponding to $p < 0·001$.

Peres et al. 2007; Psychological Medicine 37:1481-1491

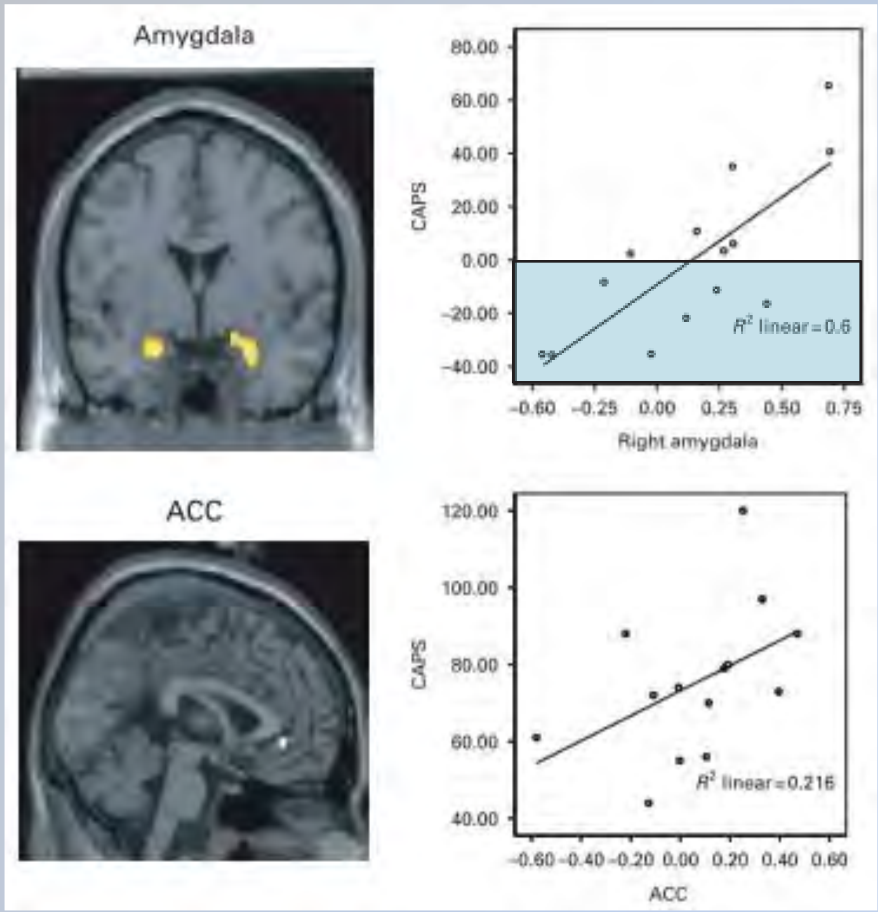
NEUROIMAGING and PSYCHOTHERAPY
ETCR - fMRI

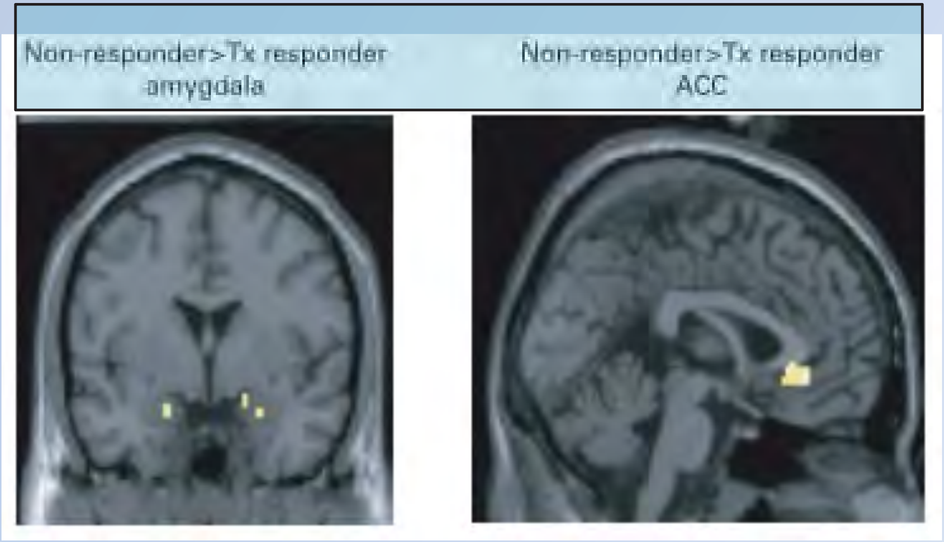




Peres et al. 2011 – J Psychiatry Research 45:727-734

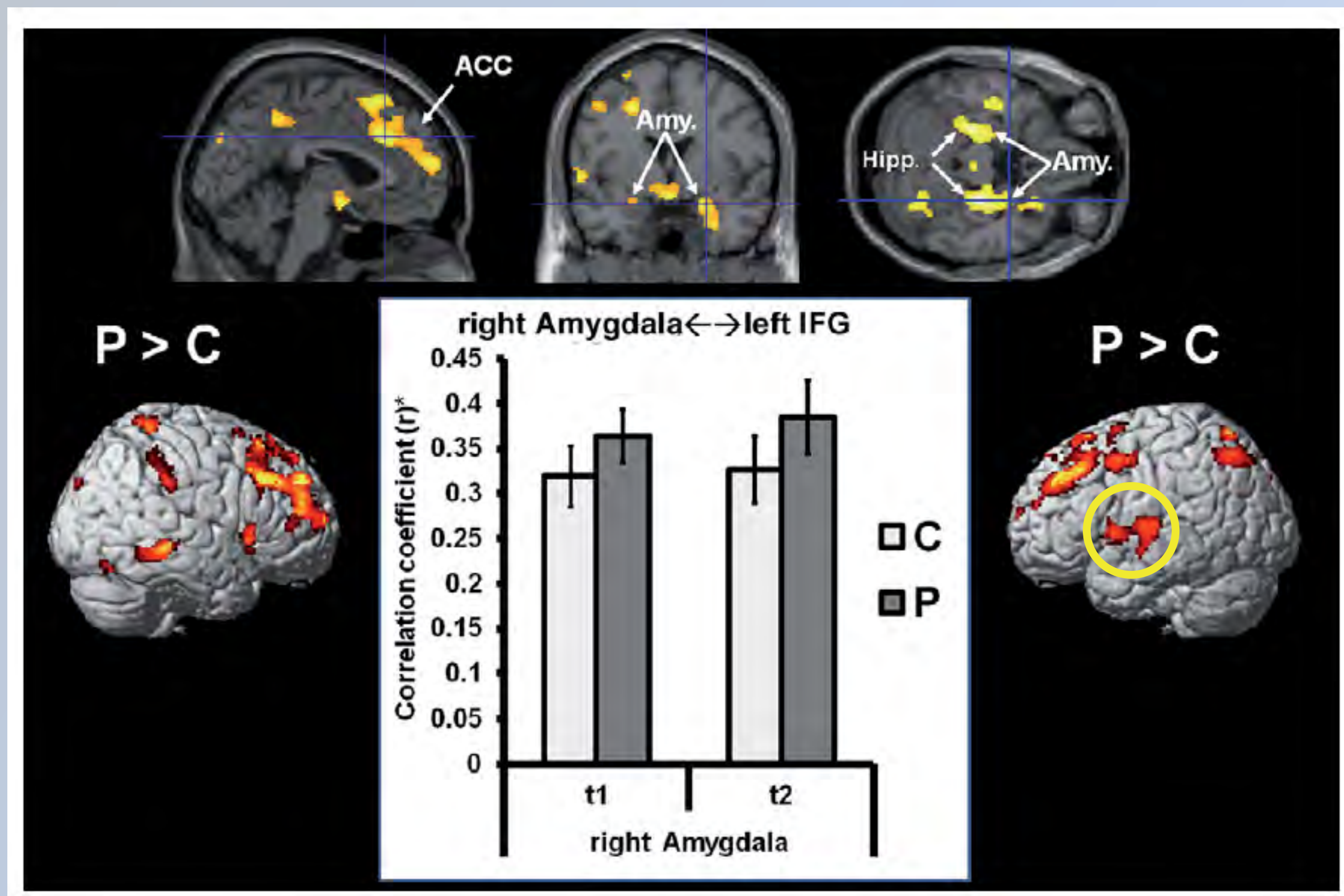
NEUROIMAGING and PSYCHOTHERAPY
CBT - fMRI





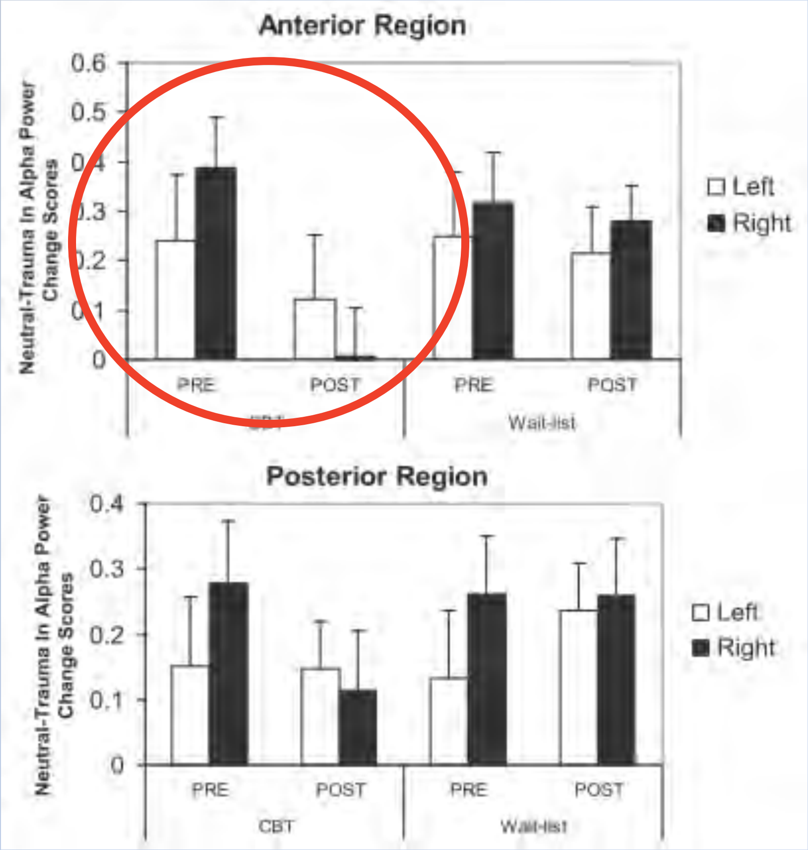
Bryant et al. 2008; Psychological Medicine 38:555-561

NEUROIMAGING and PSYCHOTHERAPY
CBT - fMRI



Kircher et al. 2013 – Biological Psychiatry 73:93-101

NEUROIMAGING and PSYCHOTHERAPY
CBT - EEG



Rabe et al. 2008 – Psychosomatic Medicine 70:13-19

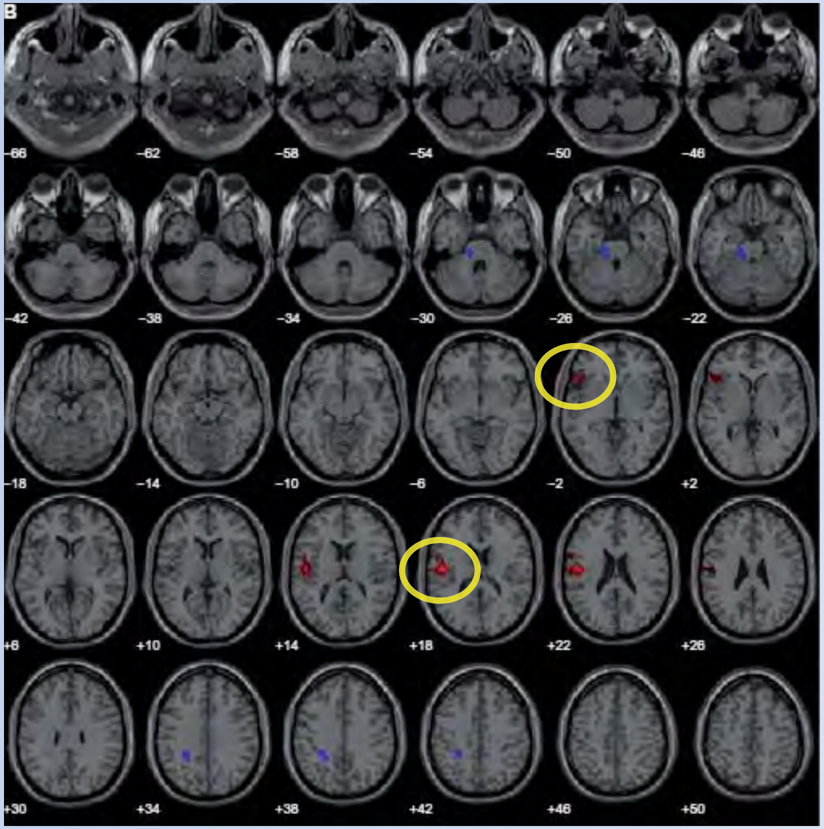
NEUROIMAGING and PSYCHOTHERAPY
CTT-BW - fMRI

Neuropsychiatric Disease and Treatment
Dovepress
ORIGINAL RESEARCH

Changes in cerebral blood flow after cognitive behavior therapy in patients with panic disorder: a SPECT study

Table 3 Changes in regional cerebral blood flow in subjects after cognitive behavior therapy (n=14)

Brain region	Brodmann area	x	y	z	Z score
Area of increase after CBT					
Left parietal lobe, postcentral gyrus	43	−64	−12	20	5.11
Left frontal lobe, precentral gyrus	4	−60	−6	24	4.05
Left frontal lobe, inferior frontal gyrus	9	−58	6	24	3.74
Left frontal lobe, inferior frontal gyrus	47	−50	24	−2	4.59
Area of decrease after CBT					
Left brain stem, pons		−16	−24	−26	3.97



NEUROIMAGING and PSYCHOTHERAPY
MINDFULNESS

Psychiatry Research: Neuroimaging 191 (2011) 36–43

Contents lists available at ScienceDirect

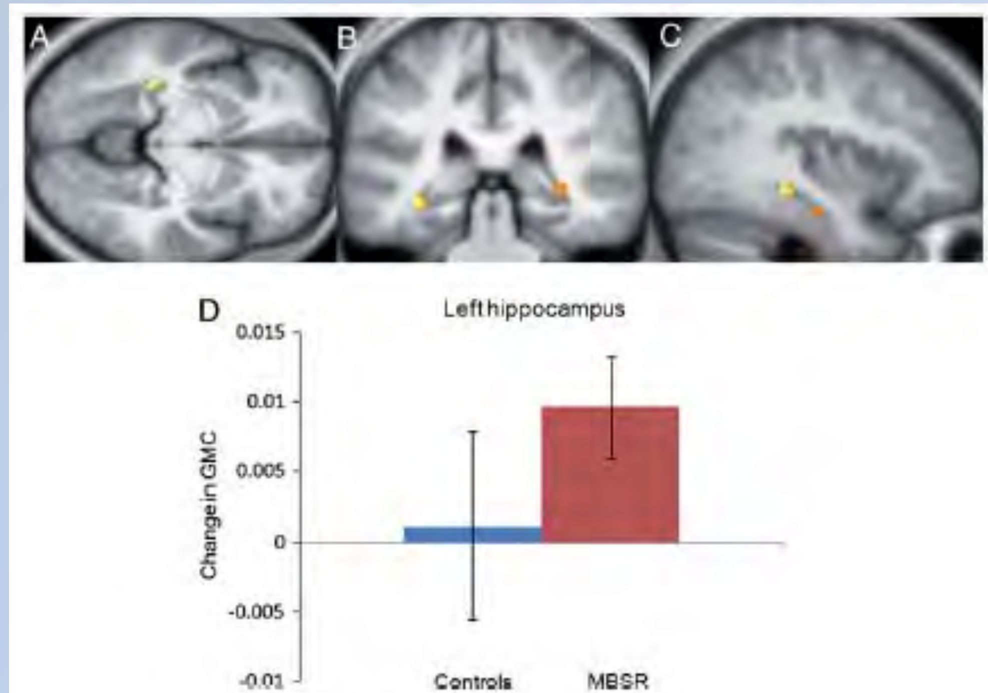
Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Mindfulness practice leads to increases in regional brain gray matter density

Britta K. Hölzel[a,b,*], James Carmody[c], Mark Vangel[a], Christina Congleton[a], Sita M. Yerramsetti[a], Tim Gard[a,b], Sara W. Lazar[a]

Study	Meditation tradition	*N* meditators/ controls	Morphological measures	Regions identified greater in meditators than controls
Lazar et al. (2005)	Insight	20/15	Cortical thickness	Right anterior insula and right middle and superior frontal sulci
Pagnoni and Cekic (2007)	Zen	13/13	Gray matter volume (VBM in SPM5)	Meditators showed no age-related decline in the left putamen as compared to controls
Hölzel et al. (2008)	Insight	20/20	Gray matter density (VBM in SPM2)	Left inferior temporal lobe, right insula, and right hippocampus
Vestergaard-Poulsen et al. (2009)	Tibetan Buddhist	10/10	Gray matter density and volume (VBM in SPM5)	Medulla oblongata, left superior and inferior frontal gyri, anterior lobe of the cerebellum and left fusiform gyrus
Luders et al. (2009)	Zazen, Vipassana, Samatha and others	22/22	Gray matter volume (VBM in SPM5)	Right orbito-frontal cortex, right thalamus, left inferior temporal lobe, right hippocampus
Grant et al. (2010)	Zen	19/20	Cortical thickness	Right dorsal anterior cingulate cortex, secondary somatosensory cortex



NEUROIMAGING and PSYCHOTHERAPY
PSYCHODYNAMIC PSYCHOTHERAPY

frontiers in HUMAN NEUROSCIENCE
ORIGINAL RESEARCH ARTICLE
published: 16 August 2013
doi: 10.3389/fnhum.2013.00410

Changes in brain activity of somatoform disorder patients during emotional empathy after multimodal psychodynamic psychotherapy

Moritz de Greck[1,2], Annette F. Bölter[3], Lisa Lehmann[4], Cornelia Ulrich[5], Eva Stockum[3], Björn Enzi[6], Thilo Hoffmann[7], Claus Tempelmann[8], Manfred Beutel[1], Jörg Frommer[3] and Georg Northoff[9]*

Psycodinamic psychotherapy aimed at improve comprehension of emotional conflicts

Parahippocampal girus is involved in emotional memory and its diminished activation might reflect the repression of emotional memories, that is the core expression of somatoform disorder

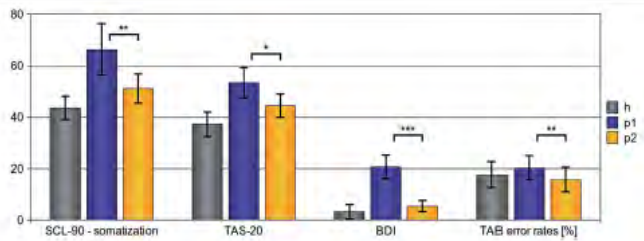
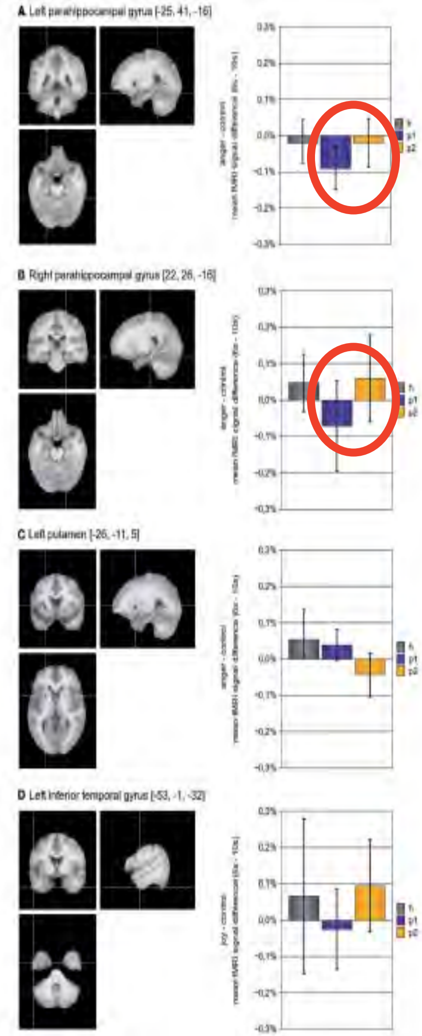


FIGURE 1 | Behavioral results—effects of psychotherapy. After psychotherapy we observed a significant reduction of somatization severity (SCL-90 - somatization scores), to enhanced emotional awareness (TAS-20 scores), and to a reduction of depressive symptoms (BDI scores). In addition, emotion recognition abilities improved after psychotherapy as shown by a significant reduction of error rates in the TAB. (Explanations: *h*, *p*1, and *p*2 refer to the scores of healthy subjects (h), pre-treatment somatoform patients (p1), and post-treatment somatoform patients (p2); error bars indicate the 95%-confidence-interval; *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, with regard to one-tailed *t*-tests.)



NEUROIMAGING and PSYCHOTHERAPY

OPEN ACCESS Freely available online PLOS one

Changes in Prefrontal-Limbic Function in Major Depression after 15 Months of Long-Term Psychotherapy

Anna Buchheim[1*], Roberto Viviani[1,2], Henrik Kessler[3,4,5], Horst Kächele[4,6], Manfred Cierpka[7], Gerhard Roth[8], Carol George[9], Otto F. Kernberg[10], Georg Bruns[11], Svenja Taubner[12,6,3]

we investigated recurrently depressed (*DSM-IV*) unmedicated outpatients ($N = 16$) and control participants matched for sex, age, and education ($N = 17$) before and after 15 months of psychodynamic psychotherapy. Participants were scanned at two time points, during which presentations of attachment-related scenes with neutral descriptions alternated with descriptions containing personal core sentences previously extracted from an attachment interview. Outcome measure was the

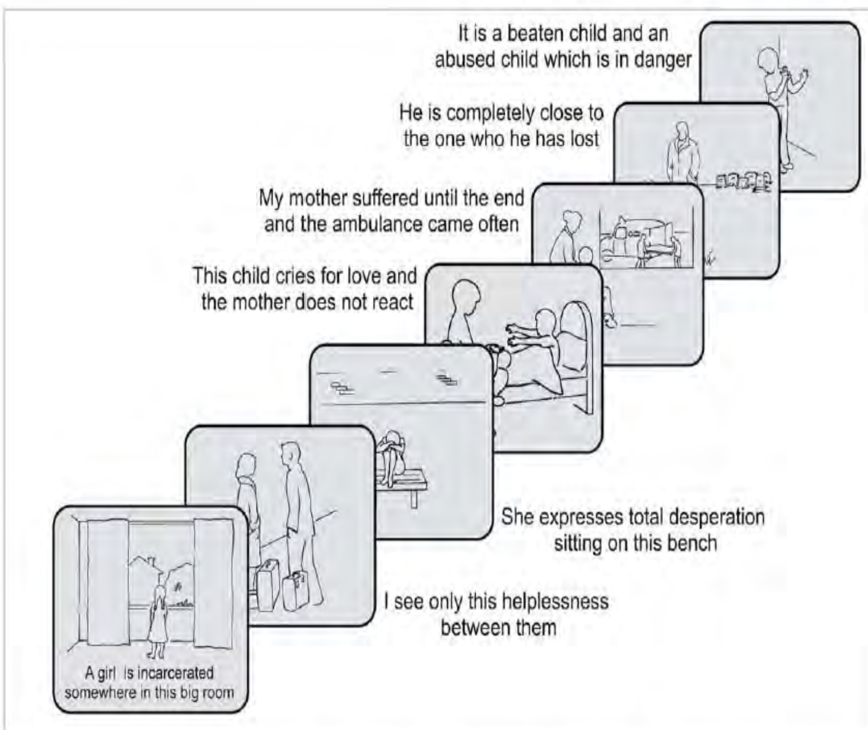
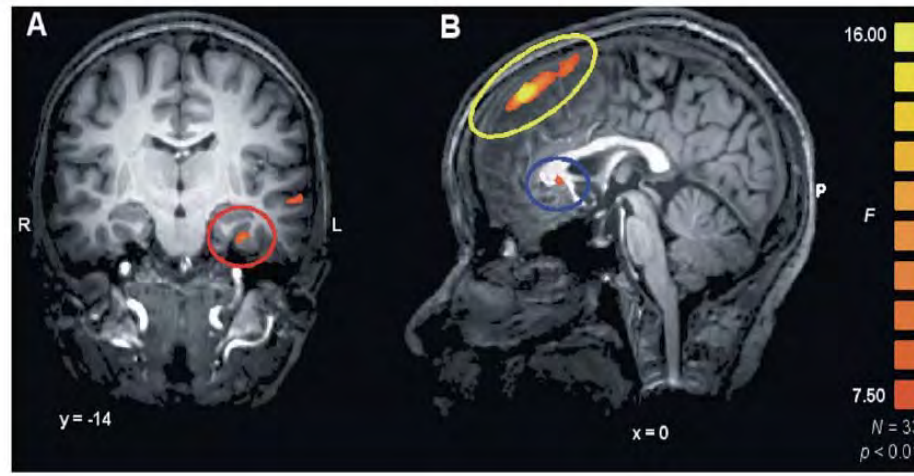
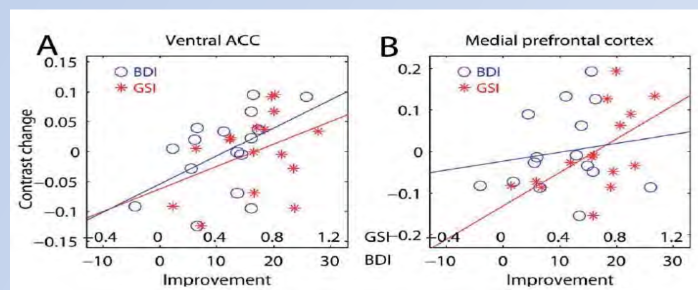


Figure 1. Stimuli. Prototypical presentation with personally relevant sentences from the AAP Picture System.





NEUROIMAGING and PSYCHOTHERAPY

Functional and anatomical studies support the evidence of neurobiological models explaining the changes which take place following PTSD-related psychotherapies

These findings call for continued commitment to unravelling the pathophysiological mechanisms underlying these effective treatments of PTSD

WHAT CAN WE DO?

NEUROBIOLOGY OF PSYCHOTHERAPIES

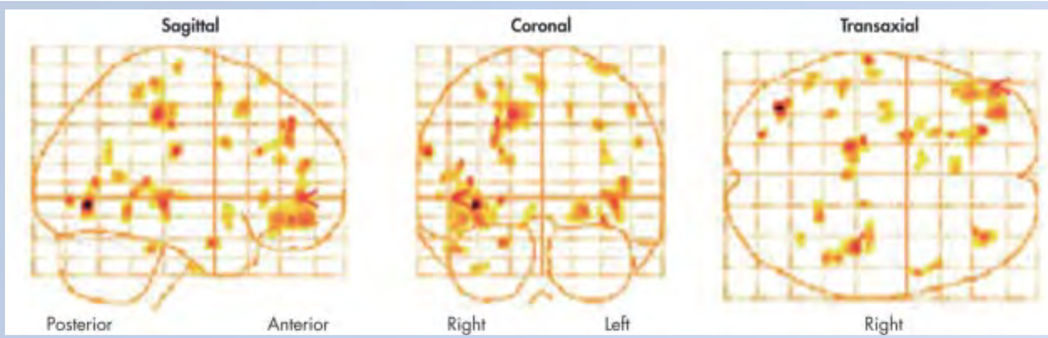
NEUROBIOLOGY OF EMDR

EMDR AND SPECT

TABLE 1. Summary of SPM Results: Voxel-Level Gray Matter Activations and Deactivations from Pre- to Post-EMDR (N = 6)

Brain Region	Talairach Coordinates (x, y, z)	Valence	*t*-value
Occipital lobe			
Right lingual gyrus (BA 18)	18, −80, −12	Deactivation	13.84*
Left cuneus/precuneus	0, −74, 30	Deactivation	6.68*
Sub-lobar thalamus			
Right pulvinar	22, −28, 10	Deactivation	13.14*
Frontal lobe			
Right precentral gyrus (BA 4)	52, −12, 42	Deactivation	10.23*
Left middle frontal gyrus (BA 11)	−44, 36, −12	Activation	6.81*
Left inferior frontal gyrus (BA 44)	−48, 48, 0	Activation	7.92*
Left superior frontal gyrus (BA 8)	−24, 42, 42	Activation	9.55*
Left medial ventral frontal gyrus (BA 9)	−18, 36, 20	Activation	5.77**
Parietal lobe			
Left postcentral gyrus (BA 40)	−52, −28, 50	Deactivation	7.68*

*Significant at p = <0.001, uncorrected for multiple comparisons
** Significant at p = <0.005, uncorrected for multiple comparisons
SPM = statistical parametric mapping
BA = Brodmann's area



Lansing et al. 2005; J Neuropsychiatry and Clinic Neuroscience; 17:526-532

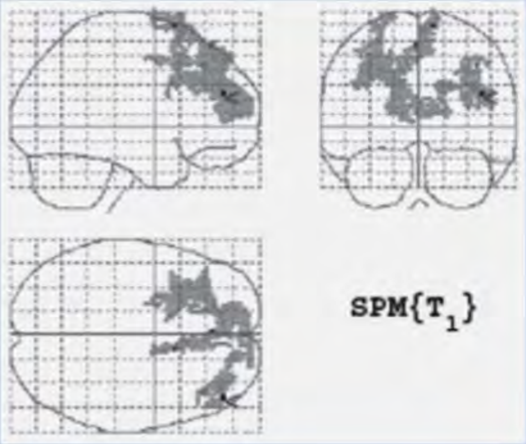
EMDR AND SPECT

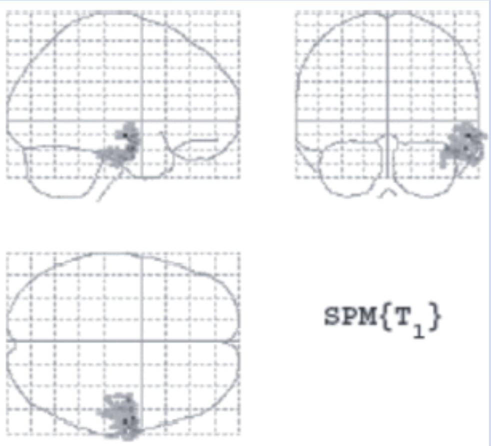
TABLE 1. Significantly Activated Regions in the Cerebral Perfusion after EMDR

Coordinate	Z Value	Region	Brodmann Area
44, 48, 24	4.46	Right middle frontal gyrus	46
40, 34, 44	4.06	Right middle frontal gyrus	8
40, 44, 30	3.69	Right superior frontal gyrus	9
10, 14, 72	4.30	Right superior frontal gyrus	6
–8, 48, 58	3.95	Left superior frontal gyrus	8
8, 66, 14	3.44	Right superior frontal gyrus	10
–6, 64, 14	3.39	Left medial frontal gyrus	10

TABLE 2. Significantly Deactivated Regions in the Cerebral Perfusion After EMDR

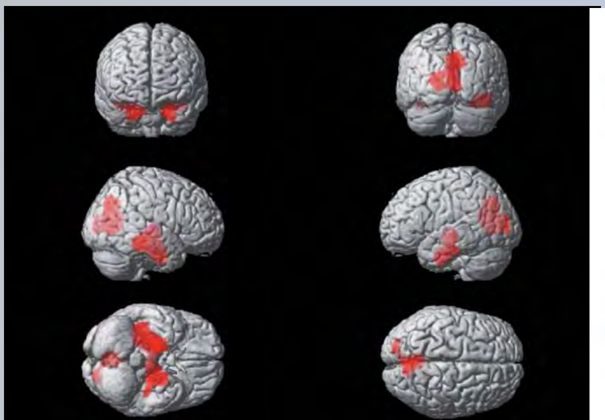
Coordinate	Z Value	Region	Brodmann Area
60, 12, –10	3.81	Right middle temporal gyrus	21
58, 6, 20	3.73	Right middle temporal gyrus	21
44, 10, –20	3.69	Right subgyral	20

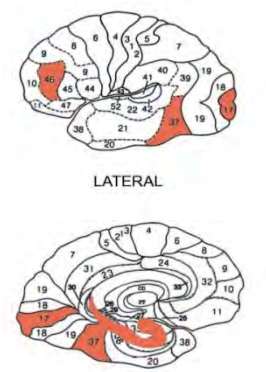




Oh & Choi 2007; J EMDR Practice and Research; 1:24-30

EMDR AND SPECT





Effects of EMDR psychotherapy on ^{99m}Tc-HMPAO distribution in occupation-related post-traumatic stress disorder

Marco Pagani[a,b], Göran Högberg[c], Dario Salmaso[b], Davide Nardo[d], Örjan Sundin[e], Cathrine Jonsson[a], Joaquim Soares[f], Anna Åberg-Wistedt[g], Hans Jacobsson[a], Stig A. Larsson[a] and Tore Hällström[c]

Nuclear Medicine Communications 2007, 28:757–765

Table 1 Means and SD for significant volumes of interest in the comparison of responders versus non-responders to eye movement desensitization and reprocessing

Brain area	Responders (n=11)		Non responders (n=4)		F(1,13)	P-value
	Mean	SD	Mean	SD		
BA17	46.4	1.9	49.2	1.9	6.414	0.025
BA37	41.6	1.5	44.0	1.8	6.397	0.025
BA46	43.0	0.6	41.9	1.2	6.220	0.027
Hippocampus	41.8	1.4	44.3	1.1	10.078	0.007

BA, Brodmann's area.

EMDR AND MRI

Journal of Psychiatric Research 44 (2010) 477–485

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Journal of Psychiatric Research

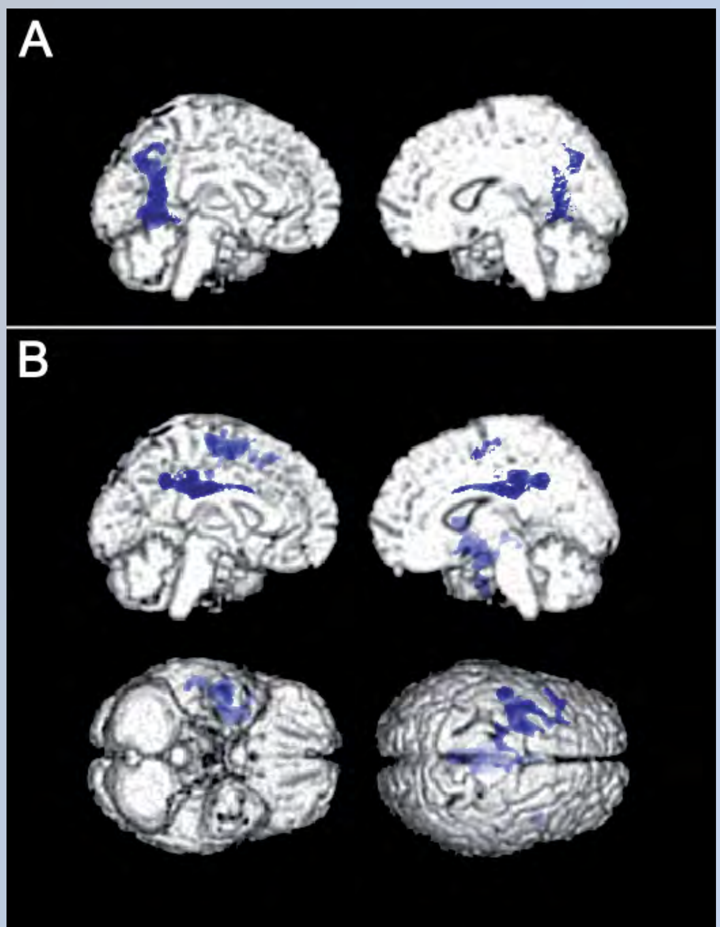
journal homepage: www.elsevier.com/locate/jpsychires

Gray matter density in limbic and paralimbic cortices is associated with trauma load and EMDR outcome in PTSD patients

Davide Nardo [a,*], Göran Högberg [b], Jeffrey Chee Leong Looi [c], Stig Larsson [d], Tore Hällström [b], Marco Pagani [d,e]

PTSD
NS>S

EMDR
R>NR



cluster p(cor)	cluster K	voxel Z	voxel p(unc)≤	TAL x	TAL y	TAL z	Region
0.054	9132	3.59	0.001	-10	-60	3	L Lingual Gyrus BA18
		3.18	0.001	-23	-57	-2	L Parahippocampal Gyrus BA19
		3.05	0.001	-17	-55	32	L Posterior Cingulate BA31
		3.00	0.001	-3	-61	33	L Precuneus BA7
		2.99	0.001	7	-50	2	R Posterior Cingulate BA29

cluster p(cor)	cluster K	voxel Z	voxel p(unc)≤	TAL x	TAL y	TAL z	Region
0.036	7048	4.54	0.001	1	-27	36	R Posterior Cingulate BA 31
		3.78	0.001	-3	-27	33	L Posterior Cingulate BA 23
		3.40	0.001	-2	-32	31	L Posterior Cingulate BA 31
0.029	7300	4.03	0.001	-35	9	58	L Middle Frontal Gyrus BA 6
		3.18	0.001	-46	-10	57	L Precentral Gyrus BA 4
		3.00	0.001	-3	0	50	L Medial Frontal Gyrus BA 6
0.025	7471	3.16	0.001	41	12	7	R Insula BA 13
		3.09	0.001	31	-5	-11	R Parahippocampal Gyrus/Amygdala

WHY EMDR?

EMDR AND BET

Brief eclectic psychotherapy *v.* eye movement desensitisation and reprocessing therapy in the treatment of post-traumatic stress disorder: randomised controlled trial

Mirjam J. Nijdam, Berthold P. R. Gersons, Johannes B. Reitsma, Ad de Jongh and Miranda Olff

BJPsych The British Journal of Psychiatry
1–8. doi: 10.1192/bjp.bp.111.099234

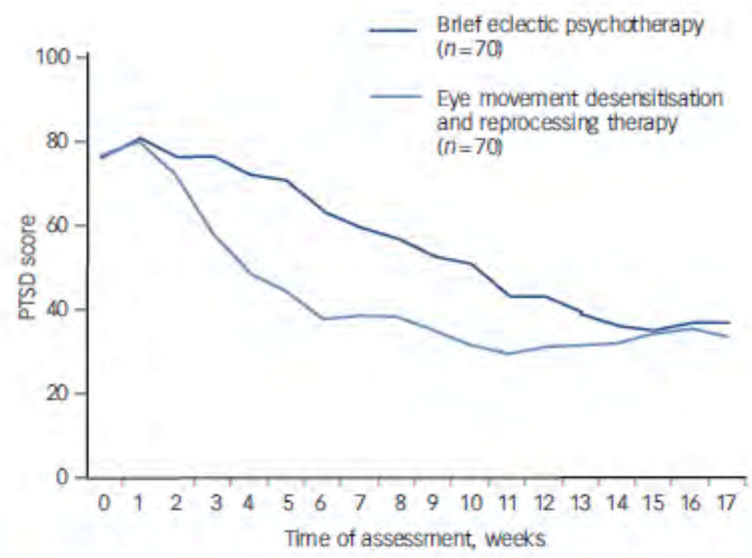


Fig. 2 Changes in post-traumatic stress disorder (PTSD) scores on the Impact of Event Scale – Revised for intent-to-treat analysis.

Mean values at assessment points from a repeated measures model adjusted for baseline value of PTSD score.

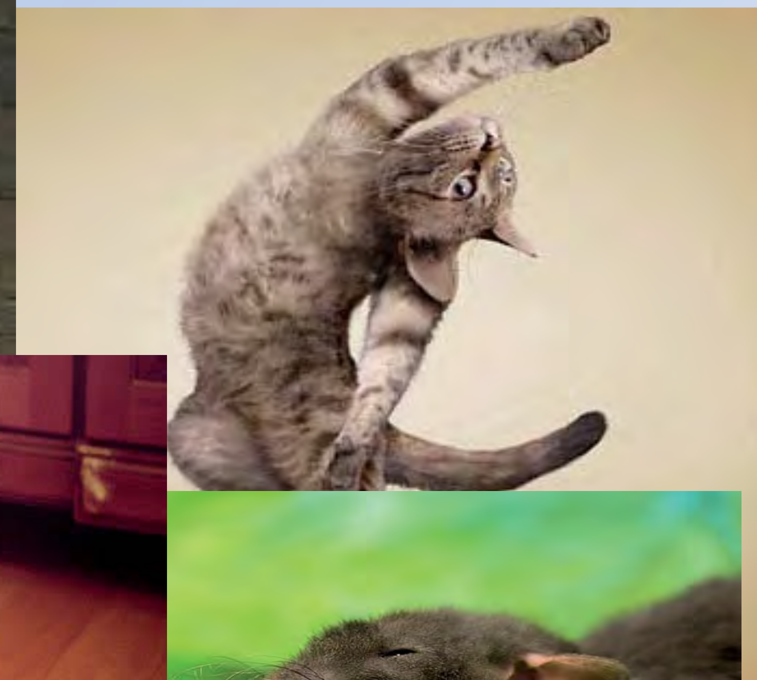
Both treatment are effective but EMDR results in a faster disappearance of symptoms

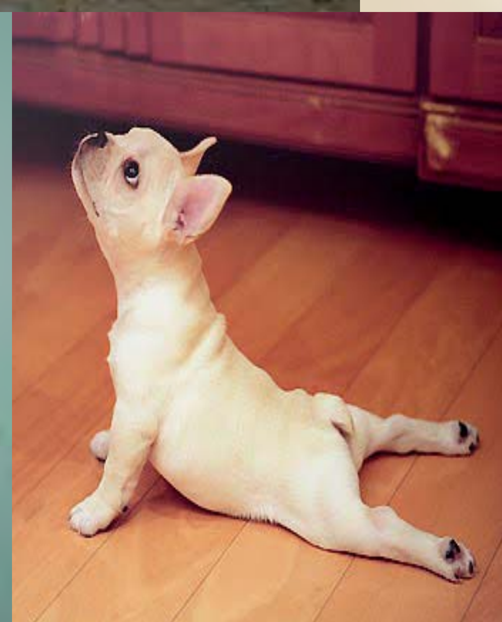
NEUROIMAGING AND PSYCHOTHERAPY

- Studies have probed into psychotherapies' mechanism of action providing evidence of an association between functional changes and treatment efficacy
- However, none of them investigated real-time firing neurons in response to the stimuli induced by psychotherapies since activations/deactivations were only recorded before and after treatment
- This has restricted the reported information to static conditions not describing in details the dynamics of regional activation during psychotherapy

A BIT TIRED?

5 MINUTES OF REST AND STRETCHING!





EMDR AND EEG

OPEN ACCESS Freely available online

PLOS | ONE

Neurobiological Correlates of EMDR Monitoring – An EEG Study

Marco Pagani[1]*, Giorgio Di Lorenzo[2], Anna Rita Verardo[3], Giampaolo Nicolais[4], Leonardo Monaco[2], Giada Lauretti[3], Rita Russo[3], Cinzia Niolu[2], Massimo Ammaniti[5], Isabel Fernandez[3], Alberto Siracusano[2]

1 Institute of Cognitive Sciences and Technologies, Consiglio Nazionale delle Ricerche (CNR), Rome, Italy, 2 Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy, 3 EMDR Italy Association, Bovisio Masciago (MI), Italy, 4 Department of Developmental and Social Psychology, "Sapienza University of Rome", Rome, Italy, 5 International Psychoanalytical Association, "Sapienza University of Rome", Rome, Italy

Abstract

Background: Eye Movement Desensitization and Reprocessing (EMDR) is a recognized first-line treatment for psychological trauma. However its neurobiological bases have yet to be fully disclosed.

Methods: Electroencephalography (EEG) was used to fully monitor neuronal activation throughout EMDR sessions including the autobiographical script. Ten patients with major psychological trauma were investigated during their first EMDR session (T0) and during the last one performed after processing the index trauma (T1). Neuropsychological tests were administered at the same time. Comparisons were performed between EEGs of patients at T0 and T1 and between EEGs of patients and 10 controls who underwent the same EMDR procedure at T0. Connectivity analyses were carried out by lagged phase synchronization.

Results: During bilateral ocular stimulation (BS) of EMDR sessions EEG showed a significantly higher activity on the orbito-frontal, prefrontal and anterior cingulate cortex in patients at T0 shifting towards left temporo-occipital regions at T1. A similar trend was found for autobiographical script with a higher firing in fronto-temporal limbic regions at T0 moving to right temporo-occipital cortex at T1. The comparisons between patients and controls confirmed the maximal activation in the limbic cortex of patients occurring before trauma processing. Connectivity analysis showed decreased pair-wise interactions between prefrontal and cingulate cortex during BS in patients as compared to controls and between fusiform gyrus and visual cortex during script listening in patients at T1 as compared to T0. These changes correlated significantly with those occurring in neuropsychological tests.

Conclusions: The ground-breaking methodology enabled our study to image for the first time the specific activations associated with the therapeutic actions typical of EMDR protocol. The findings suggest that traumatic events are processed at cognitive level following successful EMDR therapy, thus supporting the evidence of distinct neurobiological patterns of brain activations during BS associated with a significant relief from negative emotional experiences.

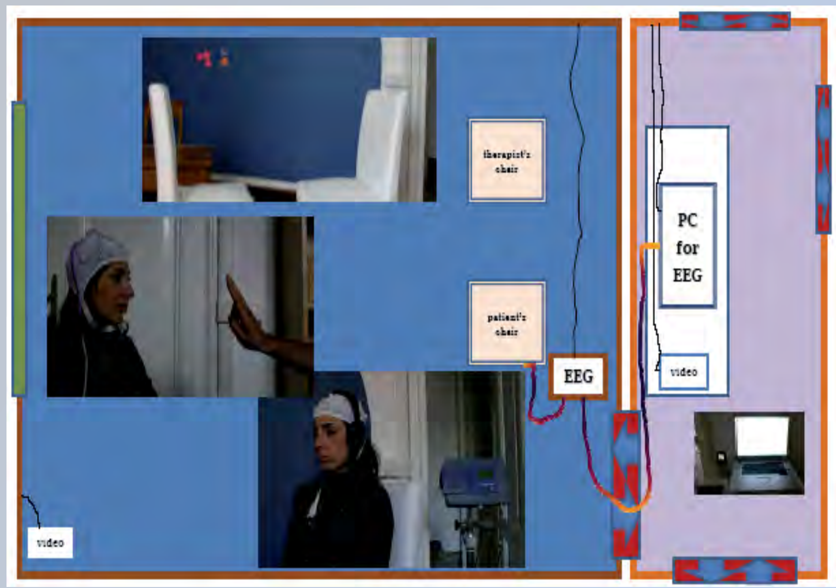
Citation: Pagani M, Di Lorenzo G, Verardo AR, Nicolais G, Monaco L, et al. (2012) Neurobiological Correlates of EMDR Monitoring – An EEG Study. PLoS ONE 7(9): e45753. doi:10.1371/journal.pone.0045753

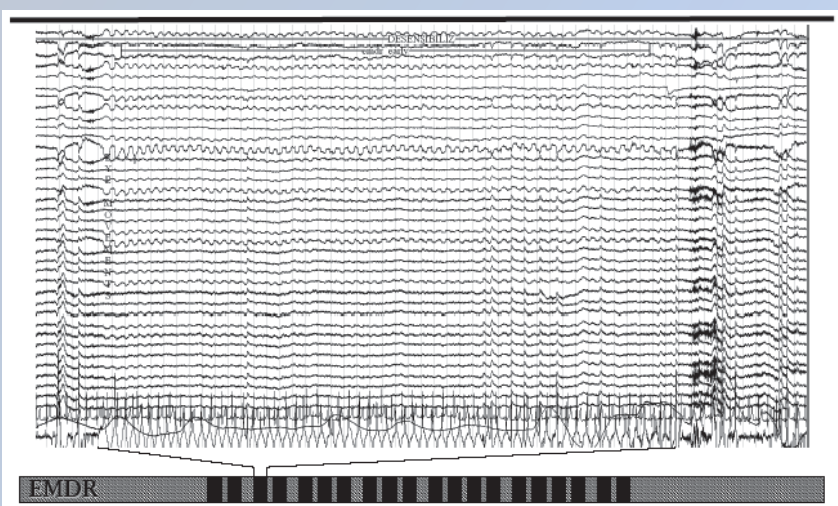
- To explore the technical feasibility of the on-line recording of whole EMDR sessions by means of EEG and data analyses
- To identify the regions activated during the bilateral ocular stimulation upon traumatic memory exposure

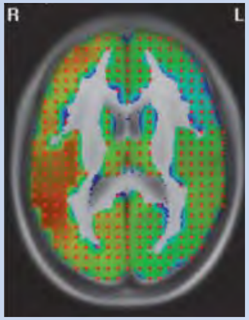
EMDR AND EEG

- Clients with psychological traumas consisting in sexual abuse, grief and loss trauma, abortion related trauma, severe physical abuse and natural catastrophies.
- Healthy subjects freely willing to participate served as controls undergoing the same therapeutic protocol and neuropsychological assessments
- In all control subjects the index trauma was chosen among the memories with the highest impact on their memories
- The major distinction between patients and controls was the lack of trauma-related symptoms in the latter

EMDR AND EEG


therapist's chair
patient's chair
EEG
PC for EEG
video
video


EMDR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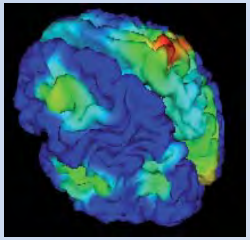
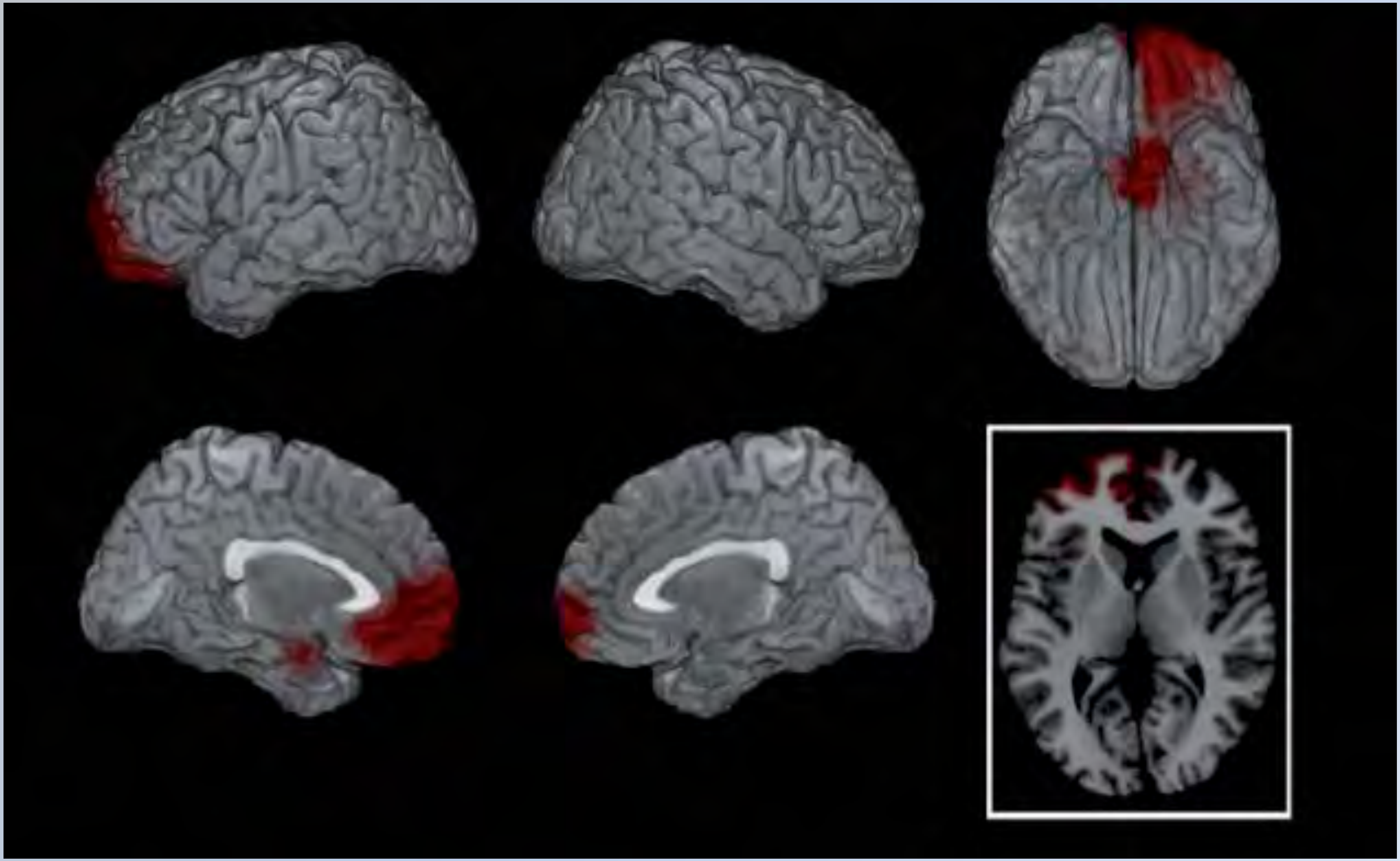


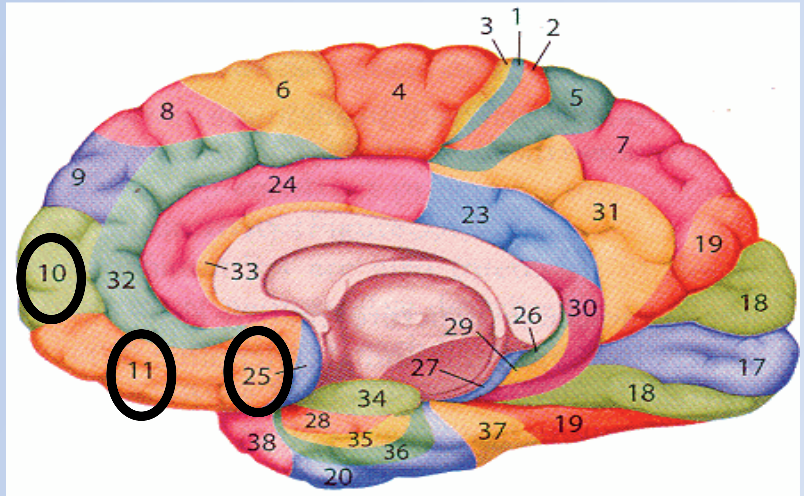
CLIENTS PRE-EMDR *vs* non-symptomatic CONTROLS DURING BILATERAL OCULAR STIMULATION



PREFRONTAL CORTEX

Symptomatic phase: PREFRONTAL ACTIVATION

- Evaluation of self-generated material
- Autobiographical/episodic memory retrieval
- Suppressing unwanted memories



Rostral PFC (OFC):

- In PTSD it is associated with activation in the amygdala during the recollection of personal traumatic events

Amydgala

In PTSD, hyperresponsivity to threat-related stimuli

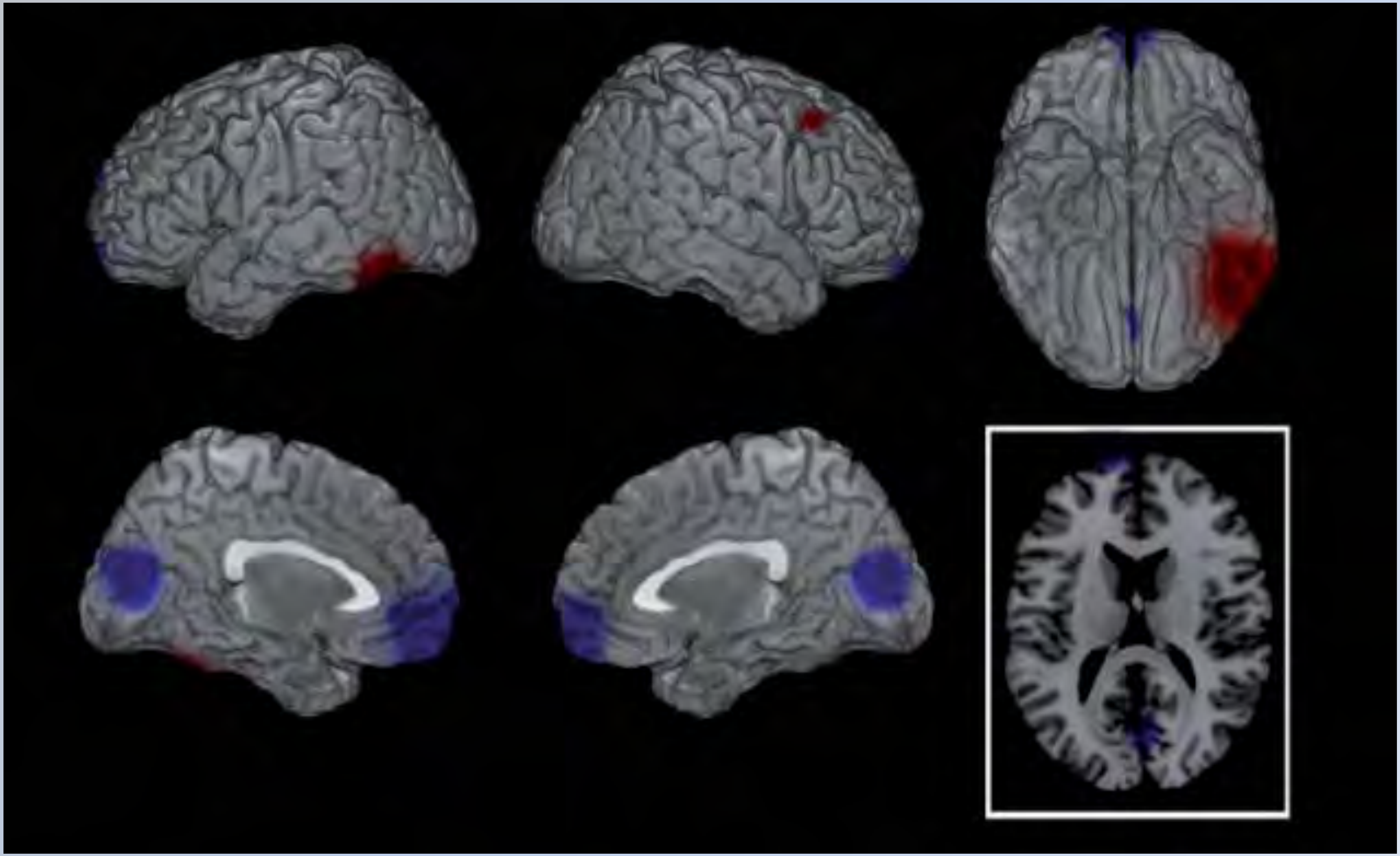
CLIENTS PRE-EMDR *vs* CLIENTS POST-EMDR

NEUROPSYCHOLOGICAL DATA

Table 2. Pre *vs* post EMDR treatment: mean (SD) and statistically significant differences in IES, BDI and SCL-90-R scores in patients

	Patients (N=10)	T	p
IES / pre / TOTAL *vs* IES / post / TOTAL	40.8 (15.9) *vs* 12.8 (12)	6.386	.000
IES /pre / intrusion *vs* IES / post / intrusion	21.1 (9.8) *vs* 6.6 (6.6)	5.7	.000
IES /pre / avoidance *vs* IES / post / avoidance	19.7 (7.7) *vs* 6.3 (5.9)	5.448	.000
BDI / pre / TOTAL *vs* BDI / post / TOTAL	23.9 (10.1) *vs* 9.5 (9.5)	4.003	.003
BDI / pre / cognitive *vs* BDI / post / cognitive	15.7 (8.1) *vs* 6.7 (7.1)	3.085	.013
BDI / pre / somatic *vs* BDI / post / somatic	8.2 (3.3) *vs* 2.8 (2.6)	4.92	.001
SCL / pre / PST *vs* SCL / post / PST	59.6 (20.2) *vs* 37.7 (19.7)	4.948	.001
SCL / pre / PSDI *vs* SCL / post / PSDI	2.11 (.53) vs 1.41 (.46)	3.625	.006
SCL / pre / GSI *vs* SCL / post / GSI	1.49 (.65) vs 0.66 (.52)	4.131	.003

CLIENTS PRE-EMDR *vs* CLIENTS POST-EMDR DURING BILATERAL OCULAR STIMULATION



EMDR AND EEG

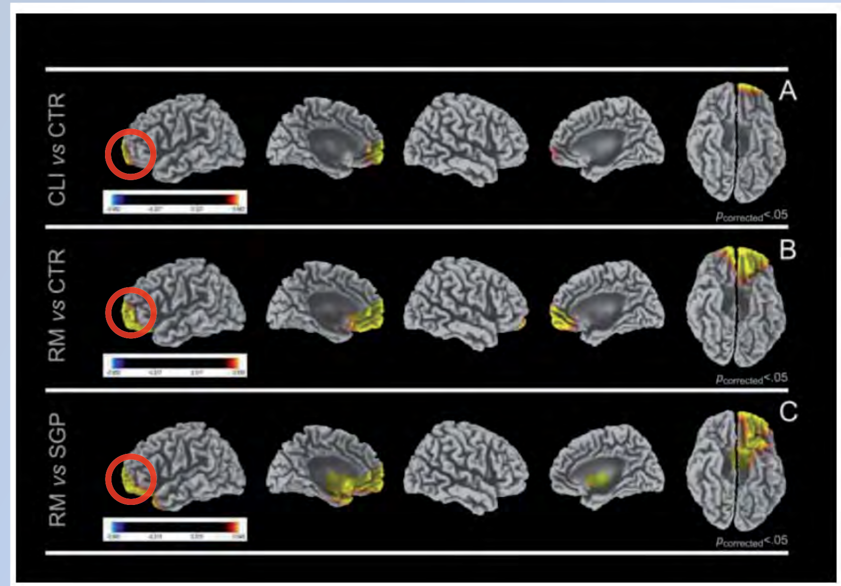
- For the first time, brain activations associated in real time with psychotherapy could be imaged and dynamically represented by functional imaging throughout its whole duration
- Our findings pointed to a highly significant activation shift following EMDR therapy from limbic regions with high emotional valence to cortical regions with higher cognitive and associative valence
- This suggested a strong neurobiological rationale of EMDR, thus supporting its efficacy as an evidenced based treatment for trauma

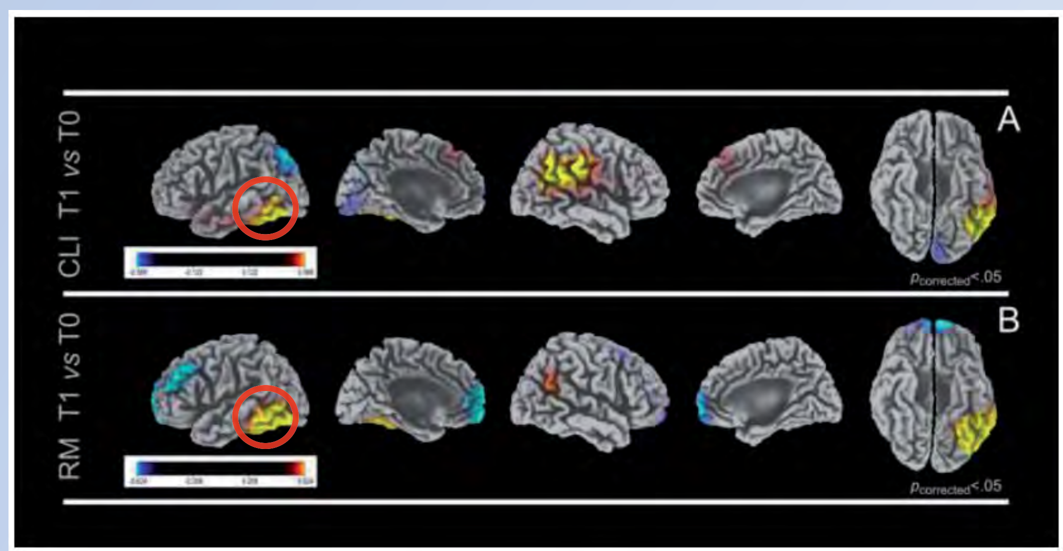
EMDR AND EEG

SAN GIULIANO DI PUGLIA EARTHQUAKE 2002

Marco Pagani; Giorgio Di Lorenzo; Leonardo Monaco; Andrea Daverio; Iannis Giannoudas; Patrizia La Porta; Anna Rita Verardo; Cinzia Niolu; Isabel Fernandez; Alberto Siracusano

In review Frontiers in Psychology - Psychology for Clinical settings





EMDR AND EEG

- We monitored by EEG EMDR psychotherapy sessions in two groups of clients
- In the symptomatic phase trauma exposure caused prevalent prefrontal activation
- After symptoms disappearance the activation shifted to cognitive associative areas
- In chronically exposed clients the neurobiological response was similar to that in healthy controls
- The social context impacts on the neurobiological response to trauma exposure
- The second arm of the study will reveal the differences in neurobological response between EMDR and tf-CBT

MEMORY MECHANISMS

frontiers in
HUMAN NEUROSCIENCE
ORIGINAL RESEARCH ARTICLE
published: 14 August 2014
doi: 10.3389/fnhum.2014.00629

Age-related alterations of brain network underlying the retrieval of emotional autobiographical memories: an fMRI study using independent component analysis

*Ruiyang Ge[1,2,3], Yan Fu[4,5], Dahua Wang[4], Li Yao[1,2,3] and Zhiying Long[1,2]**

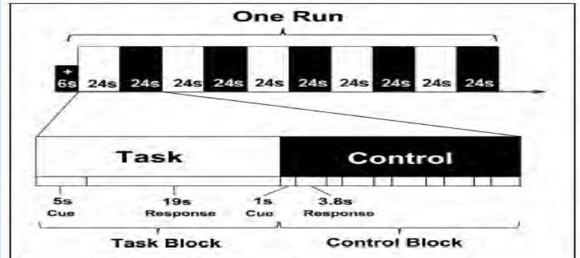


FIGURE 1 | fMRI experimental paradigm.

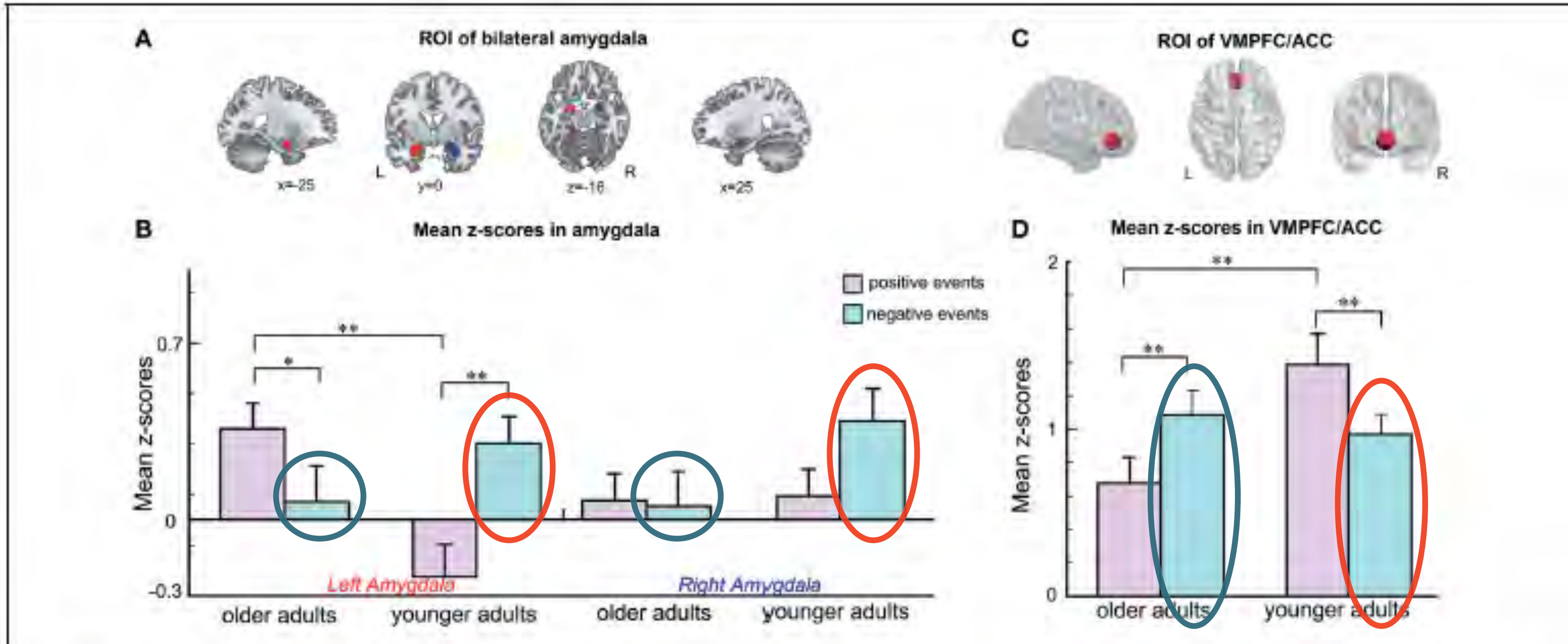
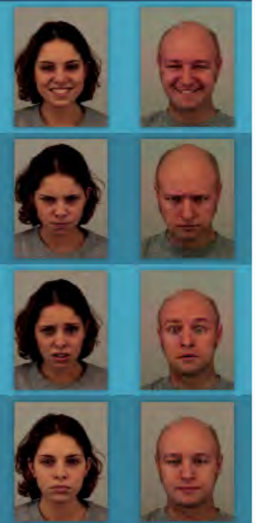


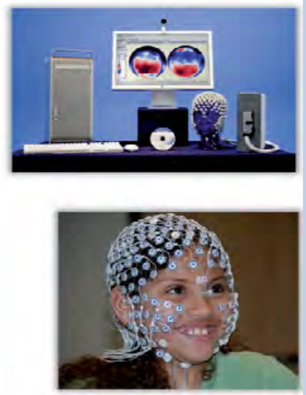
FIGURE 2 | Results of the ROI analyses for the region of the amygdala and the ventromedial prefrontal/anterior cingulate cortex. (A) Coronal, axial and sagittal views showing the anatomically defined ROIs of the left (red) and right (blue) amygdala. **(B)** Average z-scores within the bilateral amygdala of the two groups during the positive and negative memory retrieval. **(C)** Coronal, axial and sagittal views showing the selected ROI of the VMPFC/ACC. **(D)** Average z-scores within the VMPFC/ACC of the two groups during the positive and negative memory retrieval. Error bars represent standard error values. **$p < 0.05$; *$0.05 < p < 0.1$.

EMDR IN CHILDREN
EEG

STIMOLI	Donne	Uomini	Totale
Happy	20	20	40
Angry	20	20	40
Afraid	20	20	40
Neutral	20	20	40
Totale	80	80	160



256-channel Geodesic Sensor



Sample description		
Custodial caregiver		– Both parents (N=1) – Father (N=1) – Mother (N=6) – Maternal aunt (N=1)
Traumatic seperations from primary caregiver		– None (N=3) – From 1 to 6 months (N=4) – From 6 to 12 months (N=2)
Abuse	Gravity	– Severe (N=9)
	Main typology	– Sexual (N=1) – Neglect (N=1) – Witnessed domestic violence (N=3) – Mixed abuse (witnessed domestic violence, physical maltreatment, sexual abuse, neglect) (N=4)
	Abusing perpetrator	– Mother (N=2) – Father (N=5) – Grandfather (N=1) – Neighbour (N=1)

Trentini C, Fania P, Pagani M, Speranza A.M, Nicolais G, Sibilia A, Verardo AR, Inguscio L, Fernandez i, Ammaniti M

Submitted Frontiers in Psychology 2015

- During passive viewing paradigm, pictures are presented in randomized order, and remain on-screen for 1500-ms, with inter-stimulus interval (ISI) of 1000 ms.
- Pictures are all frontal head shots of adult amateur actors (50% men and 50% women), taken from the **Karolinska Directed Emotional Faces Series** (**KDEF**, Lundqvist et al., 1998).

EMDR IN CHILDREN
EEG

BEFORE EMDR:

ACTIVATION IN:

- mPFC
- LIMBIC FRONTO-TEMPORAL CORTEX

EMDR IN CHILDREN
EEG

AFTER EMDR:

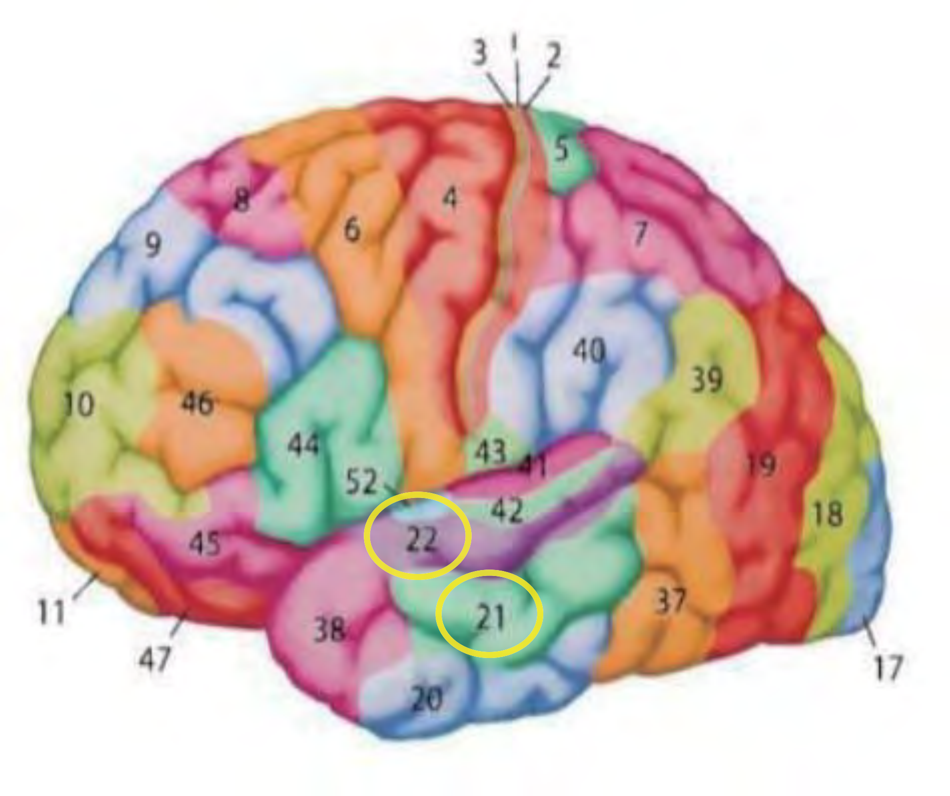
ACTIVATION IN:

- TEMPORO-MEDIAL SUPERIOR CORTEX

MEDIAL AND SUPERIOR TEMPORAL GIRI

Key role in *social cognition*:

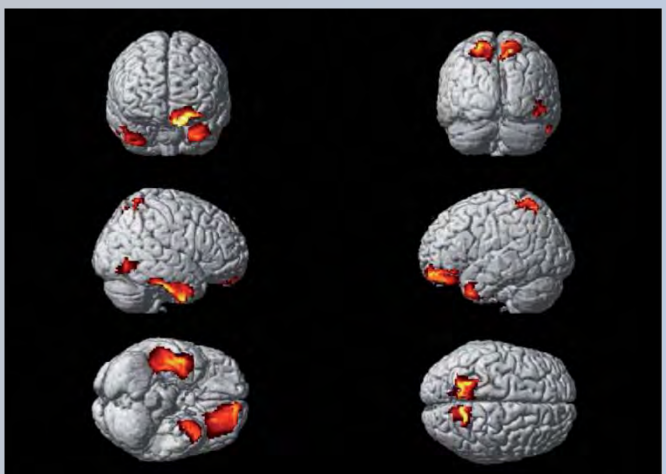
- Decode and retrieve autobiographical memories
- Process social and affective concepts
- Associate highly emotive content informations within personal semantic memory
- Modulate emotional processes involved in response to threatening stimuli



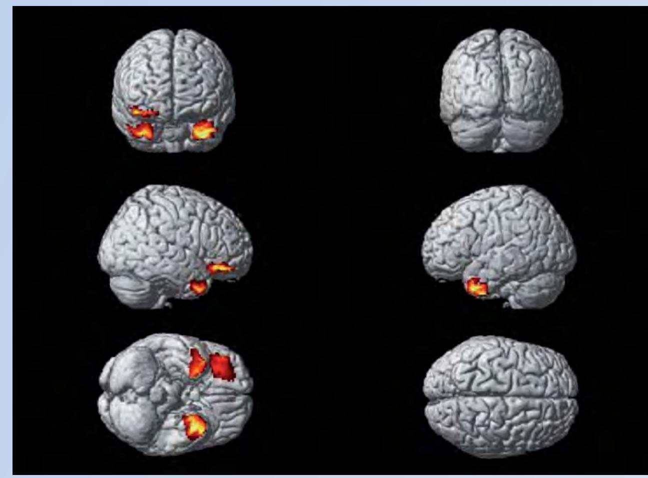
EMDR IN CHILDREN
EEG

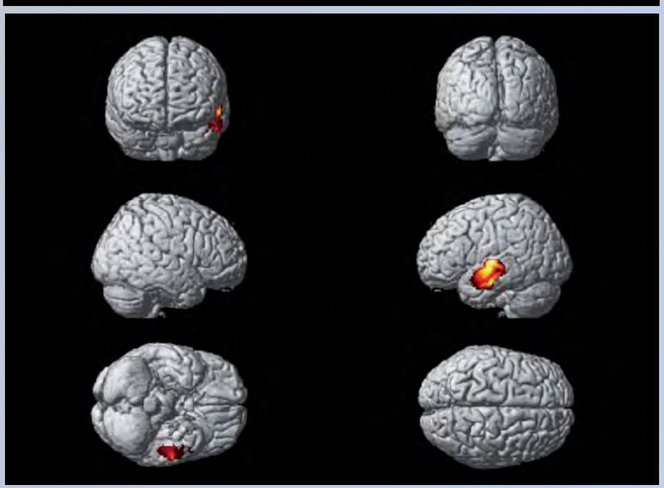
Correlations with
Trauma Symptom Checklist
for Children

Correlations with
Aggressive behavior (CBCL)

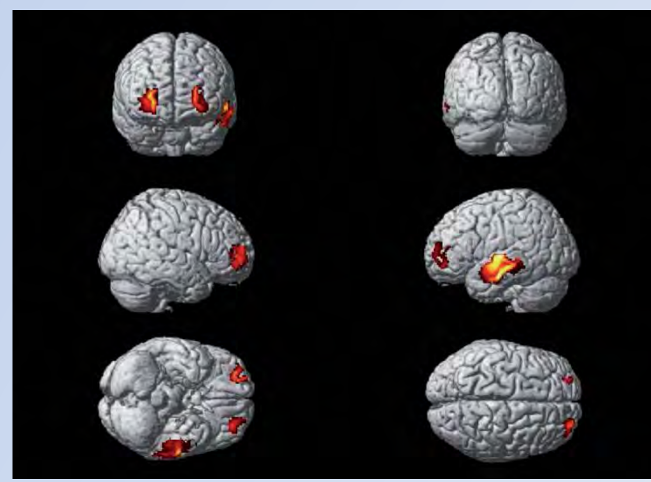


Positive correlation





Negative correlation



EMDR IN CHILDREN
EEG

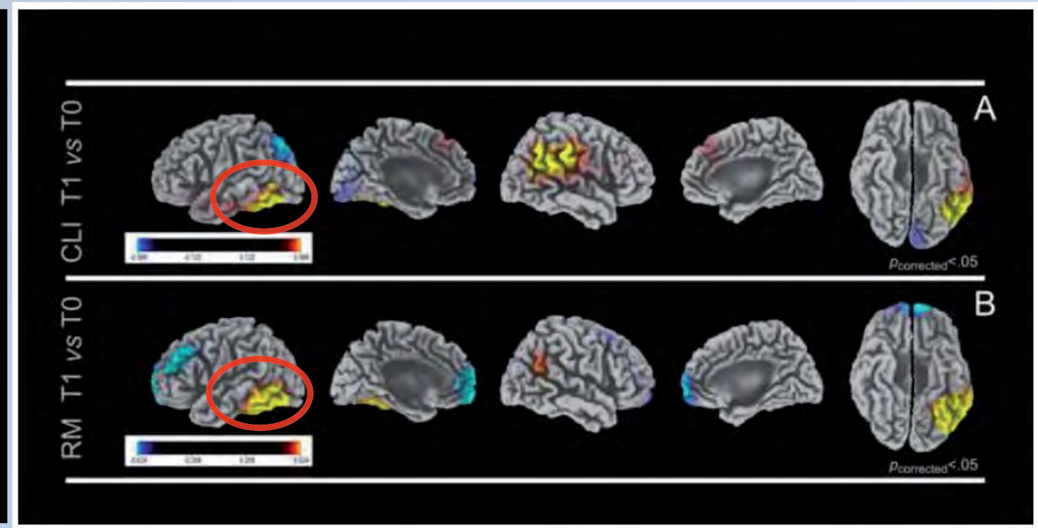
In children a cognitive associative processing of the traumatic event following successful EMDR therapy, coupled to a significant restraint of negative emotional experiences

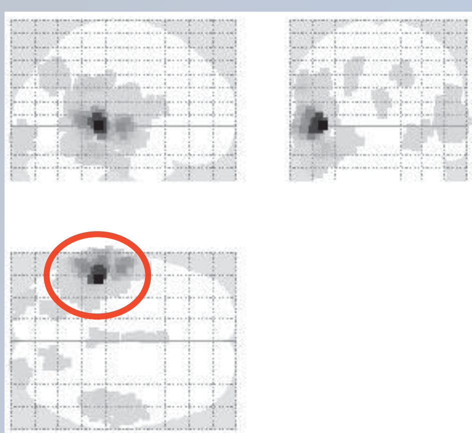
Neuropsychological scores correlated with cortical activity in the same activated regions confirming their appropriateness as symptoms probes

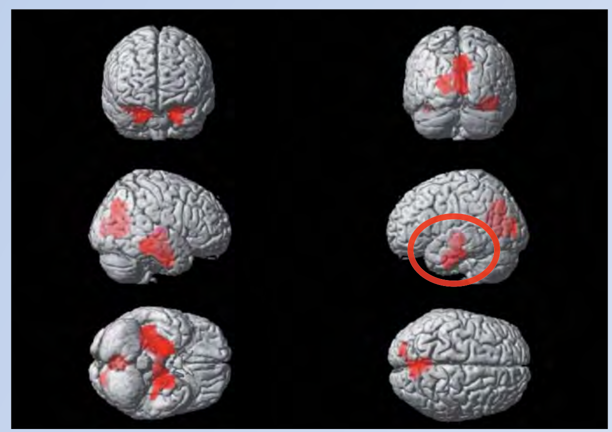
The similar pre-therapy response to all kinds of stimuli can be interpreted in two ways:

- all faces as belonging to adults cause a similar traumatic response
- also happy and neutral faces might make the kids remembering circumstances in which adults were smiling or serious before abusing them

EMDR NEUROBIOLOGICAL HALLMARK?







WHY EMDR?

BEYOND PTSD

PUTATIVE MECHANISM OF ACTION

WHY EMDR?

BEYOND PTSD

PUTATIVE MECHANISM OF ACTION

EMDR AND BIPOLAR DISORDER


Contents lists available at ScienceDirect

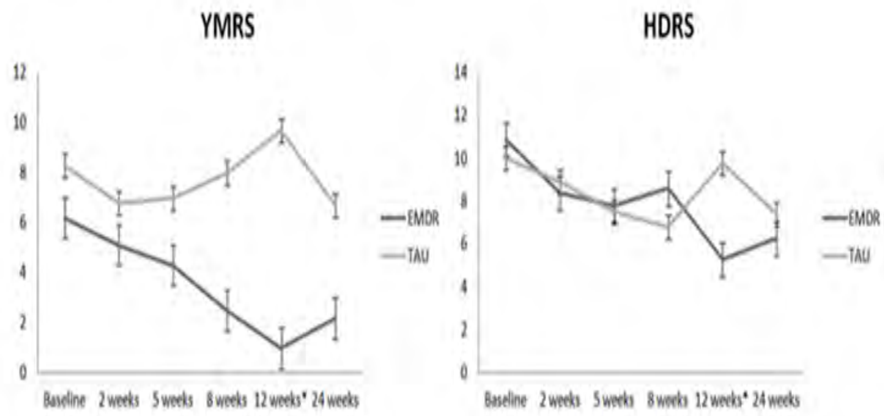
Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Eye movement desensitization and reprocessing therapy in subsyndromal bipolar patients with a history of traumatic events: A randomized, controlled pilot-study

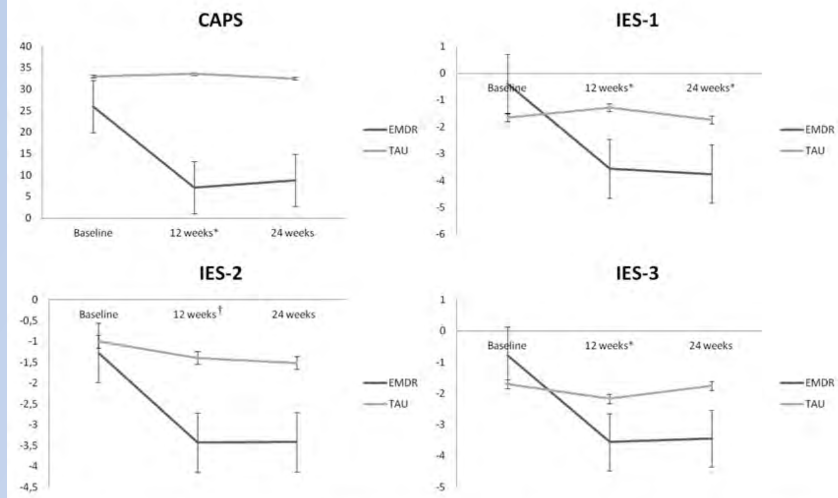
Patricia Novo [a,b], Ramon Landin-Romero [a,c], Joaquim Radua [a,c], Victor Vicens [a,c], Isabel Fernandez [d], Francisca Garcia [e], Edith Pomarol-Clotet [a,c], Peter J. McKenna [a,c], Francine Shapiro [f], Benedikt L. Amann [a,c,*]

Figure 1. Evolution of clinical scores with LOCF and intention-to-treat in the mood symptoms between the EMDR (n = 10) and TAU (n = 10) groups



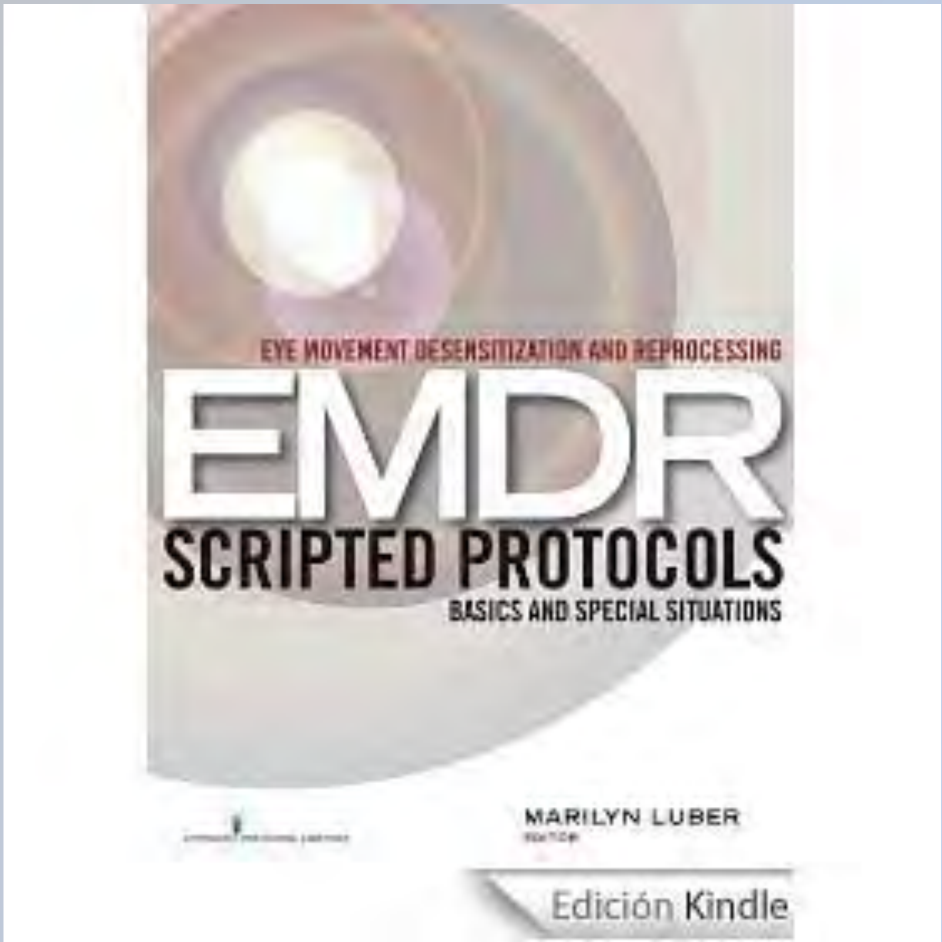
LOCF: Last Observation Carried Forward; EMDR: Eye Movement Desensitization Reprocessing; TAU: Treatment as Usual; YMRS: Young Mania Rating Scale; HDRS: Hamilton Depression Rating Scale; CGI-m: Clinical Global Impression-mania; CGI-d: Clinical Global Impression-depression; * Significant differences between groups

Figure 2. Evolution of clinical scores with LOCF intention-to-treat in the trauma symptoms were significant differences were found between the EMDR (n = 10) and TAU (n = 10) groups



LOCF: Last Observation Carried Forward; EMDR: Eye Movement Desensitization Reprocessing; TAU: Treatment as Usual; CAPS: Clinician Administered PTSD Scale; IES-1: Impact of Event Scale 1; IES-2: Impact of Event Scale 2; IES-3: Impact of Event Scale 3; * Significant differences between groups, †Trend level statistical significance

EMDR AND BIPOLAR DISORDER



10

The EMDR Protocol for Bipolar Disorder (EPBD)

Barcelona EMDR Research Group: Benedikt L. Amann, Roser Batalla, Vicky Blanch, Dolors Capellades, Maria José Carvajal, Isabel Fernández, Francisca García, Walter Lupo, Marian Ponte, Maria José Sánchez, Jesús Sanfiz and Antonia Santed, with Marilyn Luber

2014

Sánchez, J., Sanfiz, J. Santed, A. with Luber, M. (Manuscript in preparation). EMDR and Patients with Bipolar Disorder. In M. Luber (Ed.), *Eye Movement Desensitization and Reprocessing (EMDR) Scripted Protocols and Summary Sheets: Anxiety, Depression and Medical Related Issues*. New York: Springer.

EMDR AND VIOLENCE

BRAIN STRUCTURES AND NEUROTRANSMITTERS REGULATING AGGRESSION IN CATS: IMPLICATIONS FOR HUMAN AGGRESSION

THOMAS R. GREGG[1] AND ALLAN SIEGEL[1,2]

Prog. Neuro-Psychopharmacol. & Biol. Psychiat. 2001, Vol. 25, pp. 91–140

1. Violence and aggression are major public health problems.
2. The authors have used techniques of electrical brain stimulation, anatomical-immunohistochemical techniques, and behavioral pharmacology to investigate the neural systems and circuits underlying aggressive behavior in the cat.
3. The medial hypothalamus and midbrain periaqueductal gray are the most important structures mediating defensive rage behavior, and the perifornical lateral hypothalamus clearly mediates predatory attack behavior. The hippocampus, amygdala, bed nucleus of the stria terminalis, septal area, cingulate gyrus, and prefrontal cortex project to these structures directly or indirectly and thus can modulate the intensity of attack and rage.

Defensive rage behavior occurs in response to a real or perceived threat (reactive aggression) it lacks planning and is highly impulsive in its nature.
It is associated with a massive attivation of sympathetic system resulting in a minimal cortical involement

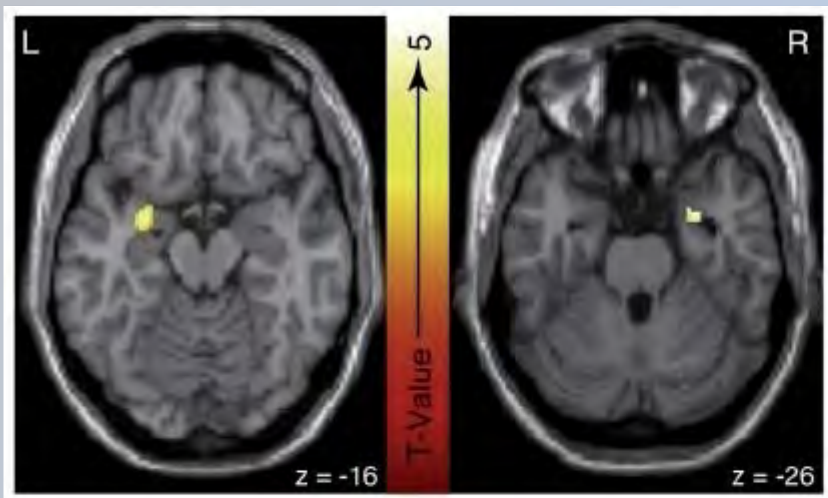
Predatory attack behavior (proactive aggression) is highly directed to the prey object and requires planning and strategies to be employed in the attack, suggesting that that the cerebral cortex is typically employed in the attack sequence

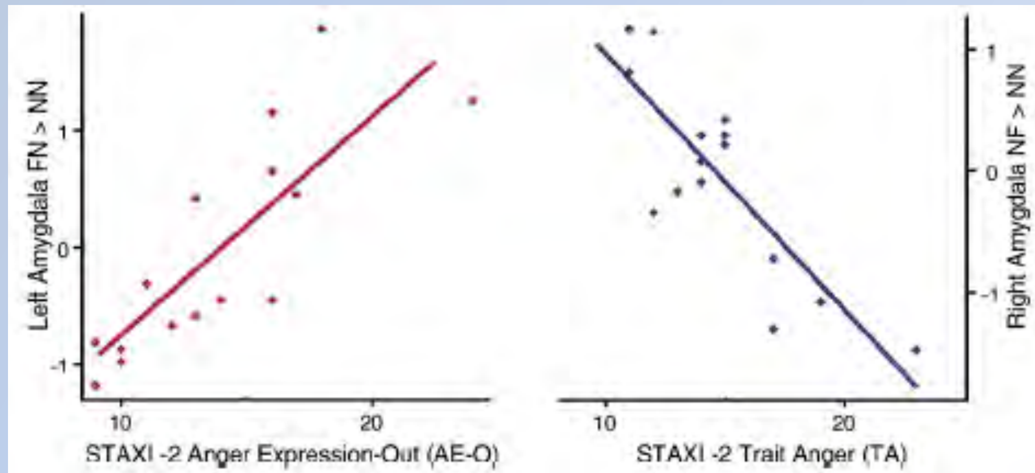
Limbic system controls both such behaviors

EMDR AND VIOLENCE

Blind rage? Heightened anger is associated with altered amygdala responses to masked and unmasked fearful faces

Joshua Michael Carlson*, Tsafrir Greenberg, Lilianne R. Mujica-Parodi





Hyperactive left (approach-related behaviors) amygdala in individuals with higher levels of anger expression may reflect a mechanism that triggers aggressive responses (defensive rage)

Hypoactive right (withdrawal behaviors) amygdala may reflect deficits in fearful face processing leading to “blind rage” or aggressive behavior without appropriate distress processing

EMDR AND VIOLENCE

Violence as any other mind/brain process has neurobiological bases

Altered amygdalar response in present in both violence sufferers and perpetrators

Aggressive behaviors are under the control of limbic system and potentially regulated by cognitive stimuli

EMDR may play a role in integrating violence triggers into cognitive components

EMDR AND ONCOLOGY

Hippocampal and Amygdalar Volumes in Breast Cancer Survivors with Posttraumatic Stress Disorder

Eriko Hara, M.D.
Yutaka Matsuoka, M.D., Ph.D.
Yuko Hakamata, Ph.D.
Mitsue Nagamine, D.Sc., Ph.D.
Masatoshi Inagaki, M.D., Ph.D.
Shigeru Imoto, M.D., Ph.D.
Koji Murakami, M.D., Ph.D.
Yoshiharu Kim, M.D., Ph.D.
Yosuke Uchitomi, M.D., Ph.D.

(The Journal of Neuropsychiatry and Clinical Neurosciences 2008; 20:302–308)

Reduced hippocampal volume and verbal memory performance associated with interleukin-6 and tumor necrosis factor-alpha levels in chemotherapy-treated breast cancer survivors

Shelli Kesler[a,*], Michelle Janelsins[b], Della Koovakkattu[a], Oxana Palesh[a], Karen Mustian[b], Gary Morrow[b], and Firdaus S. Dhabhar[a]

[a] Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305, United States

Brain Behav Immun. 2013 March ; 30(0): S109–S116

TABLE 3. Partial Correlations between Normalized Hippocampal or Amygdalar Volume and IES Scores in Cancer Survivors with PTSD (n = 15)

	Left Hippocampus		Right Hippocampus		Left Amygdala		Right Amygdala	
Characteristics	r	p	r	p	r	p	r	p
IES intrusion	–0.665	0.013*	–0.555	0.049*	–0.380	0.200	–0.425	0.147
IES avoidance	0.138	0.652	[illegible]	0.326	0.224	0.462	0.007	0.981
Total	–0.313	0.298	–0.115	0.708	–0.061	0.842	–0.266	0.380

PTSD = posttraumatic stress disorder; IES = Impact of Event Scale
*p<0.050
Covariated: alcohol, age

Total brain and hippocampal volumes (cubic centimeters).

	Breast cancer	Controls	F	*p*
N	42	35		
Total brain	1170 (97)	1184 (101)	0.159	0.69
Left hippocampus	4.37 (0.40)	4.68 (0.49)	6.88	0.01
Right hippocampus	4.36 (0.41)	4.61 (0.53)	3.35	0.07

Data are shown as marginal means after removing the effects of covariates and (standard deviation).

EMDR AND ONCOLOGY

Prefrontal Cortex and Amygdala Volume in First Minor or Major Depressive Episode After Cancer Diagnosis

Eisho Yoshikawa, Yutaka Matsuoka, Hidenori Yamasue, Masatoshi Inagaki, Tomohito Nakano, Tatsuo Akechi, Makoto Kobayakawa, Maiko Fujimori, Naoki Nakaya, Nobuya Akizuki, Shigeru Imoto, Koji Murakami, Kiyoto Kasai, and Yosuke Uchitomi

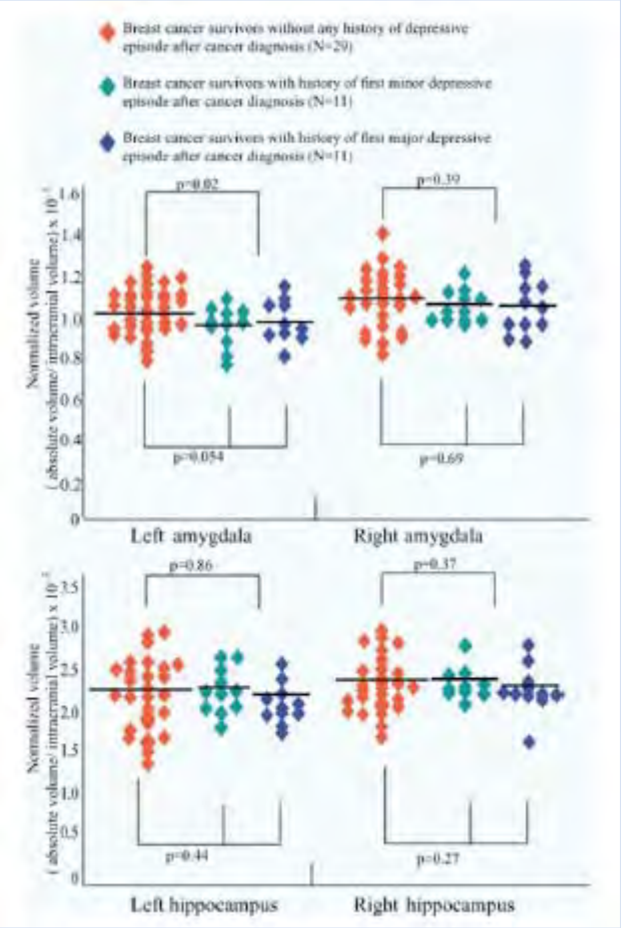
BIOL PSYCHIATRY 2006;59:707–712

Table 2. Amygdala and Hippocampal Volume in Breast Cancer Survivors with No History of Any Depressive Episodes After Cancer Diagnosis, a History of First Minor Depressive Episode, and a History of First Major Depressive Episode

Normalized Volume × 10^{-3} (Absolute Volume/Intracranial Volume)	History of First Depressive Episode After Cancer Diagnosis: None Mean (SD)	Minor Mean (SD)	Major Mean (SD)	F^a	p
Amygdala					
Left	1.05 (.11)	.97 (.09)	.99 (.10)	3.12	.054
Right	1.09 (.14)	1.06 (.07)	1.06 (.12)	.37	.69
Hippocampus					
Left	2.32 (.31)	2.38 (.24)	2.23 (.21)	.84	.44
Right	2.45 (.28)	2.45 (.15)	2.31 (.22)	1.36	.27

	None Mean (SD)	Minor and/or Major Mean (SD)		
Amygdala				
Left	1.05 (.11)	.98 (.09)	6.17	.02
Right	1.09 (.14)	1.06 (.99)	.75	.39
Hippocampus				
Left	2.32 (.31)	2.30 (.23)	.03	.86
Right	2.45 (.28)	2.38 (.20)	.81	.37

ANOVA, analysis of variance.
[a]Differences were analyzed by ANOVA.



EMDR AND ONCOLOGY

EMDR and CBT for Cancer Patients: Comparative Study of Effects on PTSD, Anxiety, and Depression

Liuva Capezzani
Psychiatry Department and Area di Supporto alla Persona, Regina Elena National Cancer Institute, Rome, Italy

Luca Ostacoli
Marco Cavallo
Sara Carletto
Department of Mental Health, "San Luigi Gonzaga" Hospital Medical School, University of Turin, ASL TO3, Orbassano, Italy

Isabel Fernandez
EMDR Italy Association, Bovisio Masciago (MI), Italy

Roger Solomon
Buffalo Center for Trauma and Loss, Buffalo, NY

Marco Pagani
Institute of Cognitive Sciences and Technologies, CNR, Rome, Italy

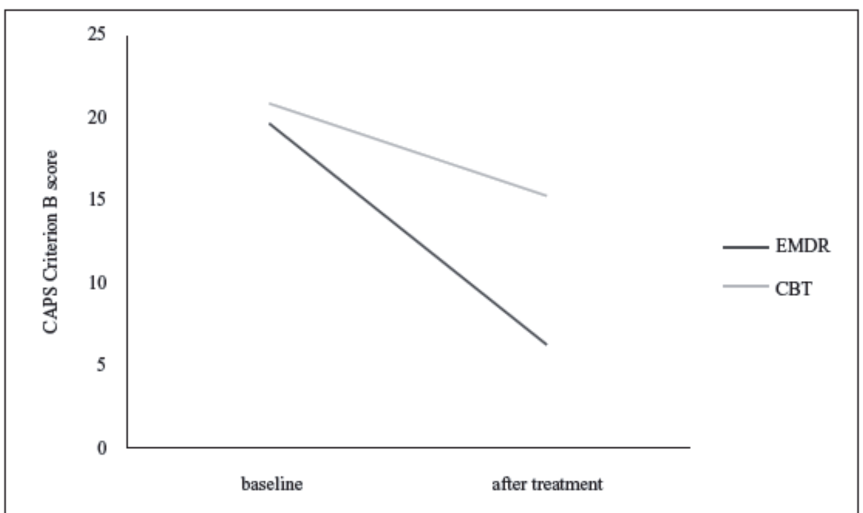


FIGURE 2. Interaction between time and treatment for CAPS Criterion B score.

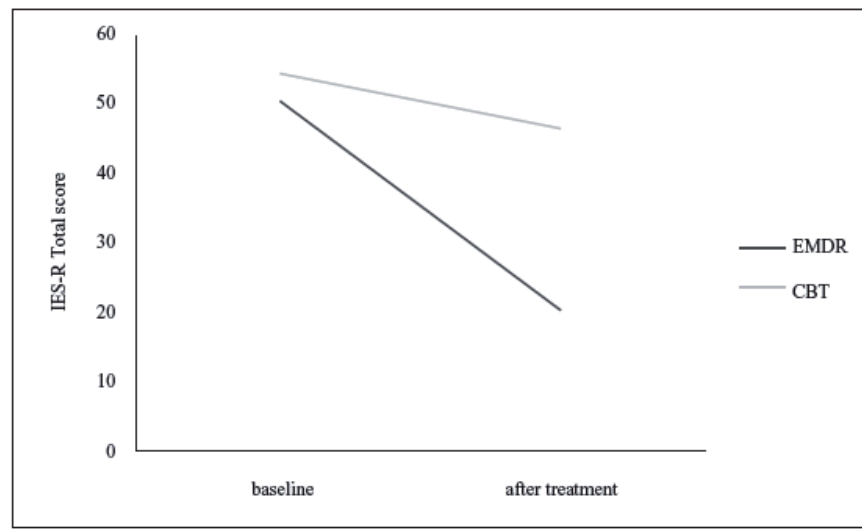


FIGURE 1. Interaction between time and treatment for IES-R total score.

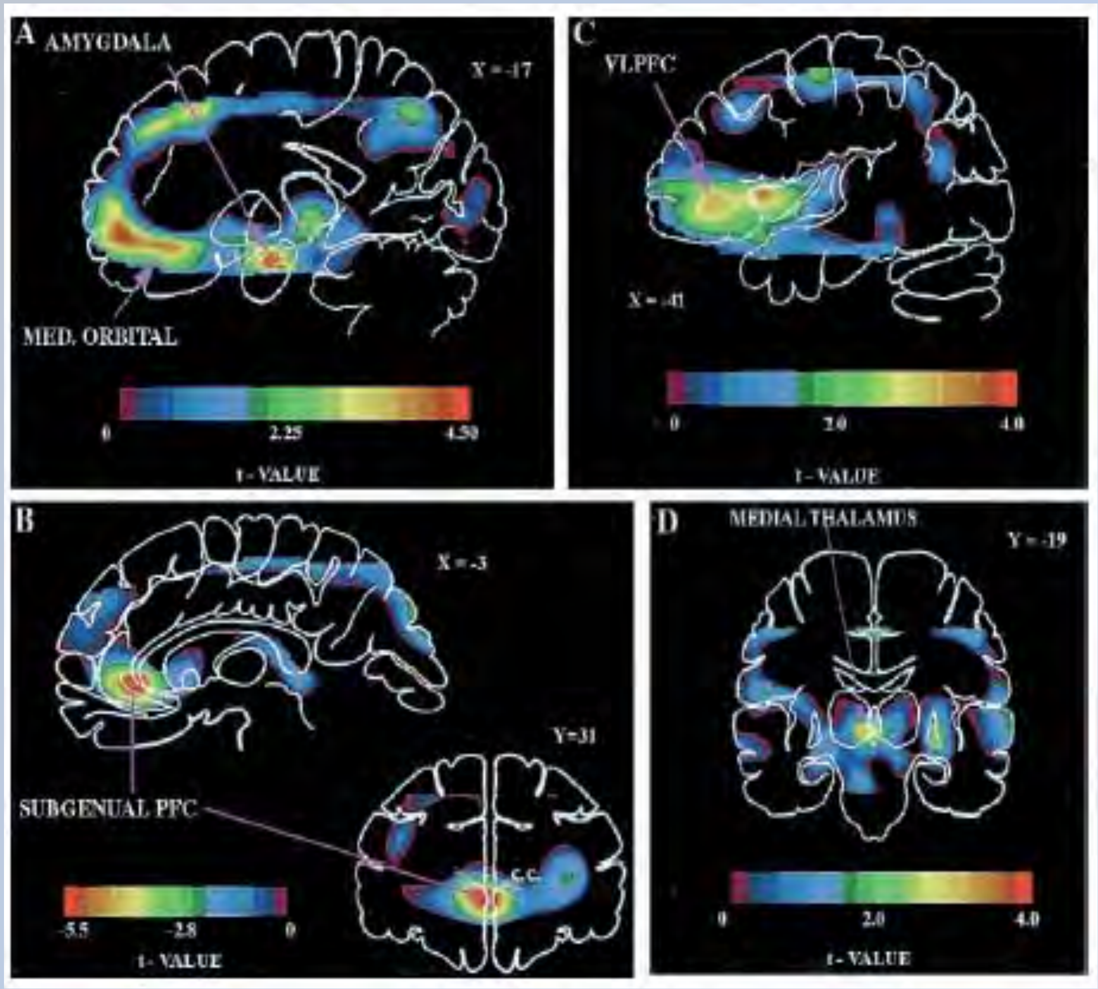
EMDR AND ONCOLOGY

Neurobiological features and response to EMDR treatment of PTSD in breast cancer patients

20 patients treated with EMDR
20 patients not treated

MONTHS 1-4	PATIENTS SELECTION AND RECRUITMENT
MONTHS 5-12	NEUROPSYCHIATRIC AND NEUROPSYCHOLOGICAL ASSESSMENTS. FIRST SET OF EEGs AND EMDR SESSIONS FOR PATIENTS AND CONTROLS
MONTHS 13-18	SECOND SET OF EMDR SESSIONS, NEUROPSYCHIATRIC AND NEUROPSYCHOLOGICAL ASSESSMENTS AND FINAL EEGs FOR PATIENTS DATA ANALYSIS

EMDR AND DEPRESSION

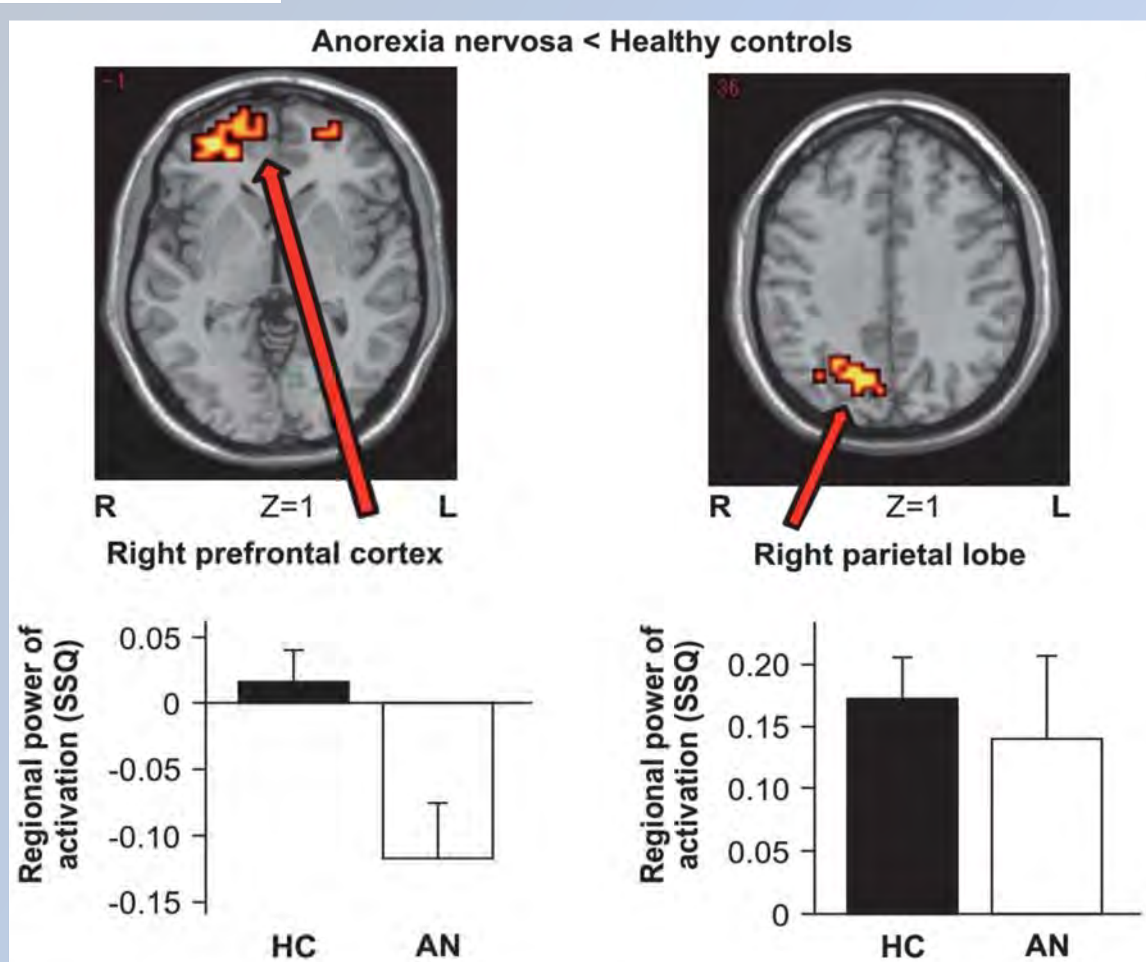


Drevets et al. Biol Psychiatry 2000;48:813–829

EMDR AND EATING DISORDERS

Neuroimmagini e neurobiologia dei disturbi alimentari

Marco Pagani, Marco Cavallo



Suda M ET AL PLoS ONE2014;9: e97998

WHY EMDR?

BEYOND PTSD

PUTATIVE MECHANISM OF ACTION

MECHANISM OF ACTION

Behavioural and Cognitive Psychotherapy, 2013, 41, 290–300
First published online 29 October 2012 doi:10.1017/S1352465812000793

What is the Role of Eye Movements in Eye Movement Desensitization and Reprocessing (EMDR) for Post-Traumatic Stress Disorder (PTSD)? A Review

Fiona W. Jeffries and Paul Davis

University of Surrey, Guildford, UK

component of EMDR, further research is needed. It should be noted that it is not unusual to be uncertain about how any psychotherapy works, not just EMDR (Gunter, 2009). Whilst it may feel uncomfortable to some clinicians to practise EMDR without knowing exactly how it works, the growing research base will aid us in our search for answers.

MECHANISM OF ACTION

The mechanism by which EMDR exerts its effect in PTSD is poorly understood

Controversies continue to exist regarding how EMDR works

EMDR has generated considerable debate around the mechanism responsible for its effectiveness

Conflicting account remain as to the mechanism of action of EMDR

KEY QUESTION

Does anybody know the neurobiological mechanism of CBT?

CBT-CENTRIC TOLEMAIC SYSTEM

MECHANISM OF ACTION

- Eye Movements (EM) increase inter-hemispheric connectivity (Christman et al., 2003; Parker et al., 2008)
  - Not supported in EEG studies (Samara et al., 2011, Propper et al., 2007)
- Taxing working memory reduces vividness of stored memories (Van der Hout et al., 2001; Kemps & Tiggerman 2007;Andrade et al., 2007)
  - EM produces a reduction in the memory span
- Modulation of the Default Mode Network (Landin-Romero et al., 2013)

In review by Landin-Romero et al 2015

EM provokes physiological changes similar to REM-sleep (Stickgold 2002; Barrowcliff et al., 2004; Sack et al. 2008)

MEMORY AND SLEEP

PTSD AND SLEEP

Sleep disturbances are main features of PTSD

In DSM-5 nightmares are considered intrusive symptoms (cluster B) and insomnia among excitation and hyperreactivity symptoms (cluster E)

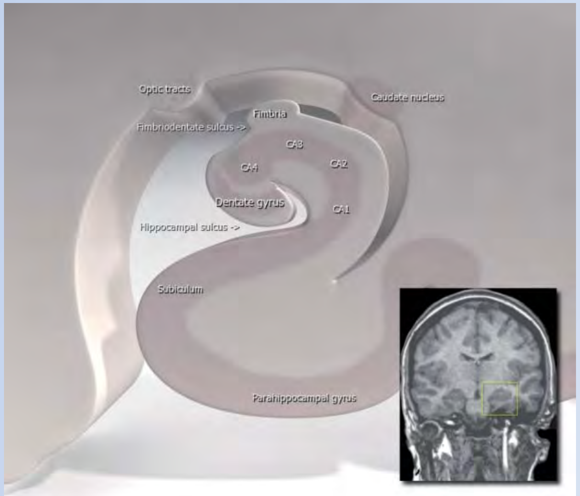
Both impact on general health and cause also cognitive and memory deficits

PTSD AND SLEEP

Sleep has a bracing function and facilitates emotional processes

Sleep disturbances as a powerful stressing factor enhance and prolong daytime PTSD symptoms worsening the capability to recover.

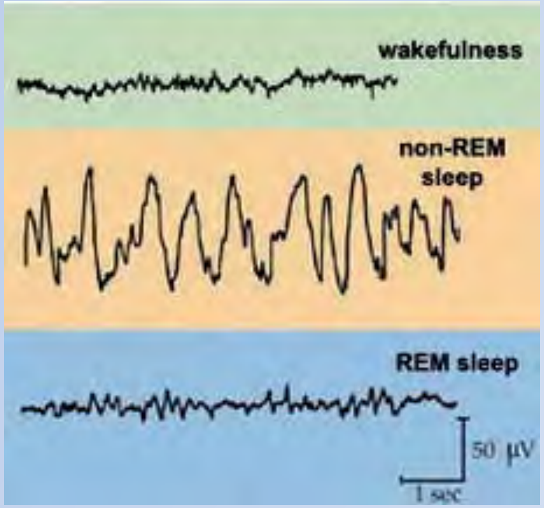
Chronic insomnia and relative chronic stress cause reduction of hippocampal volume and neurogenesis



SLEEP AND MEMORY

Converging evidence supports the significance of sleep in learning and memory reprocessing

Non-REM sleep (slow-wave-sleep, SWS) appears to have a key role in memory consolidation



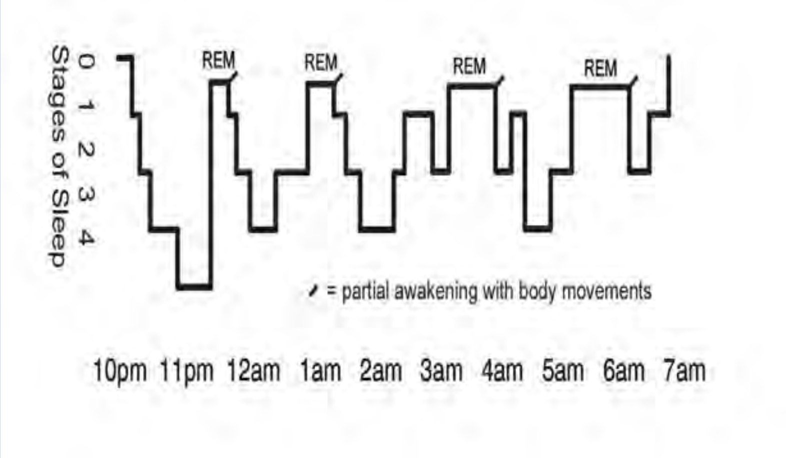
SWS also facilitates information transfer from hippocampus to neocortex and the reorganization of distant functional networks

SLEEP AND MEMORY

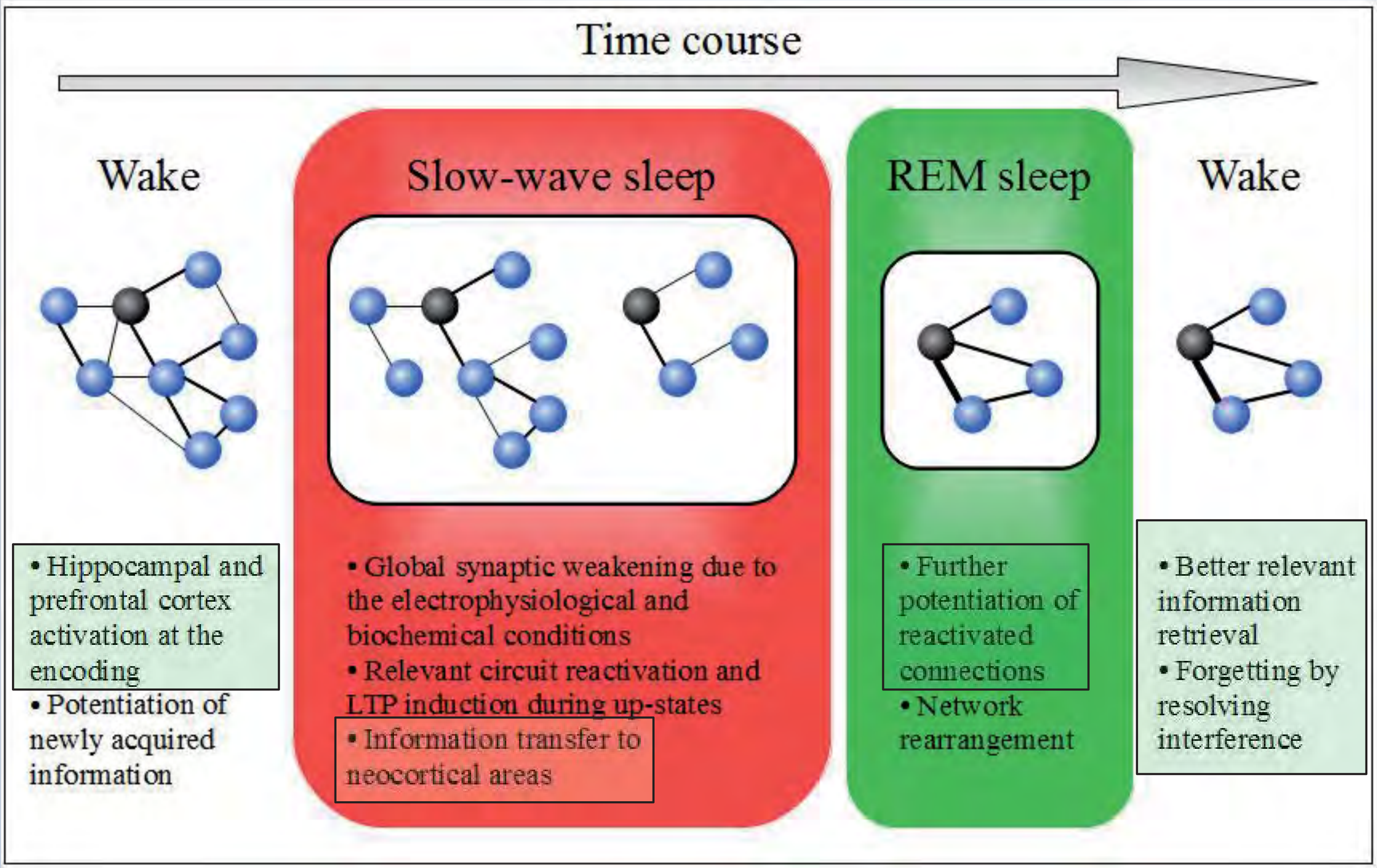
The “dialog” between hippocampus and neo-cortex favors memory encoding

During Rapid Eye Movement (REM) sleep there is a decreased activity from hippocampus to neo-cortex suggesting a more intense memory consolidation

In this phase new associations of emotional events mediated by limbic structures take place



SLEEP AND MEMORY



MECHANISM OF ACTION

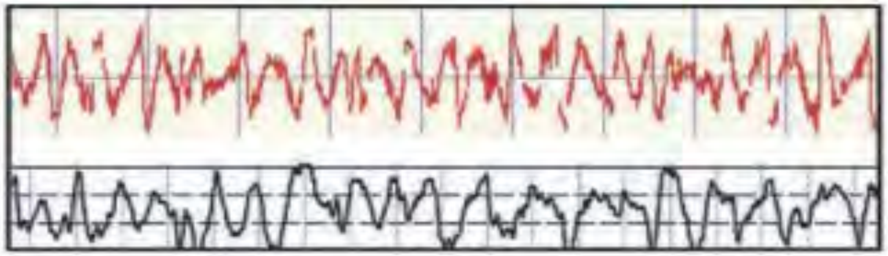


Figure 7. Illustration of similarity of EEG data recorded during BBS (upper) and slow wave sleep (lower).
NOTE: Data for upper waveform is from Participant 1; bottom waveform is from Rétey et al. (2005). Copyright 2005 National Academy of Sciences, USA, used with permission. Width of section: 20 seconds.

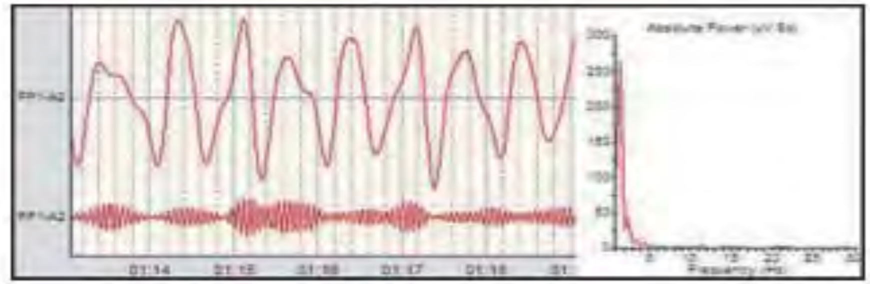
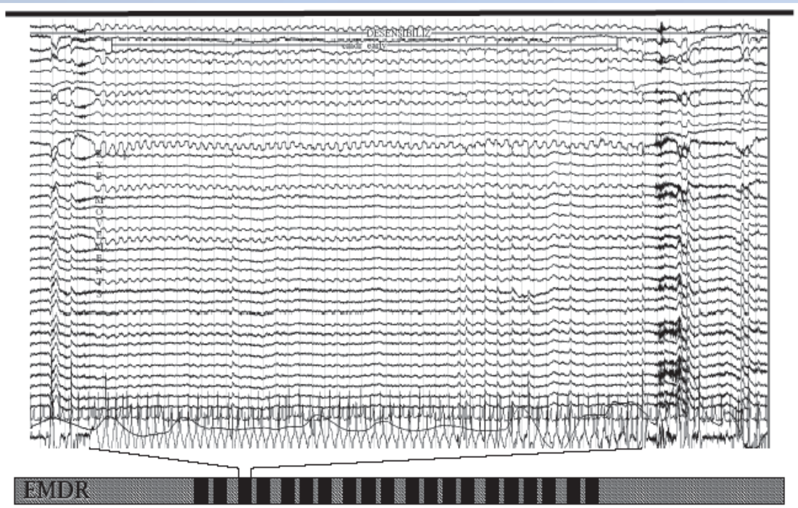


Figure 8. Comparison of BBS input with EEG output.
NOTE: Input was BBS using 1 Hz lateral eye movements, Participant 1. The evoked response shown here consists of 1.5 Hz delta waves and 13.5 Hz beta spindles paced by the delta waves. Delta and low beta bandpass filters applied; width of section is 6 seconds.

Harper et al. 2009 – Traumatology 15:81-95



Pagani et al. 2012 – PLOS ONE Volume 7 | Issue 9 | e457535

MECHANISM OF ACTION

Sleep, Learning, and Dreams: Off-line Memory Reprocessing

R. Stickgold,[1*] J. A. Hobson,[1] R. Fosse,[1,2] M. Fosse[1]

2 NOVEMBER 2001 VOL 294 SCIENCE

Table 1. Brain physiology shifts across sleep states. Human sleep is divided into REM and NREM, with NREM further subdivided into sleep onset (stage 1 sleep), light NREM (stage 2), and SWS (stages 3 and 4). The physiological parameters listed here are characterized by robust state-dependent changes that are thought to be linked to sleep-dependent learning and memory reprocessing. Arrow represents changes in activity relative to waking. See text for explanations.

Physiological correlates of sleep stages	REM	Stage 2 NREM	SWS
Synchronous brain electrical activity	4 to 6 Hz	12 to 14 Hz	0.5 to 4 Hz
Eye movements	⇈	⇊	⇊
Muscle tone	⇊	↓	↓
External inputs	⇊	↓	↓
Hippocampal-neocortical dialog (HC-NC)	NC→HC	?	HC→NC
Cholinergic modulation (ACh)	⇈	↓	↓
Aminergic modulation (NE and 5-HT)	⇊	↓	↓
Glucocorticoids (GC)	(↓)	–	(↑)
Frontal activation (DLPFC)	⇊	?	↓
Limbic activation (e.g., anterior cingulate cortex)	↑	?	↓
Sensory cortices	↑	?	↓

MECHANISM OF ACTION

INTEGRATION OF MEMORIES (Stickgold 2002)

Fragmented episodic and traumatic memories are stored in hippocampus or amigdala without contextual integration

Memory integration needs the encoding in association cortex to create an understanding in a larger context

Hippocampal-amygdala complex memories are transferred to neocortex, replayed, consolidated into semantic associative memory networks and information integrated to create meaning and "learn from the event"

MECHANISM OF ACTION

INTEGRATION OF MEMORIES (Stickgold 2002)

The transfer might occur during slow-wave-sleep (1-3 Hz) and definitive memory consolidation during REM sleep (about 4-6 Hz)

The traumatic episodic memory is weakened and then removed from hippocampus. If this does not happen the lack of free space may lead to memory and cognitive deficits (3° PTSD criterium)

Bilateral stumulation during EMDR reproduces the neurophysiological conditions favorable for episodic memory integration in associative neocortex

MECHANISM OF ACTION

INTEGRATION OF MEMORIES (Stickgold 2002)

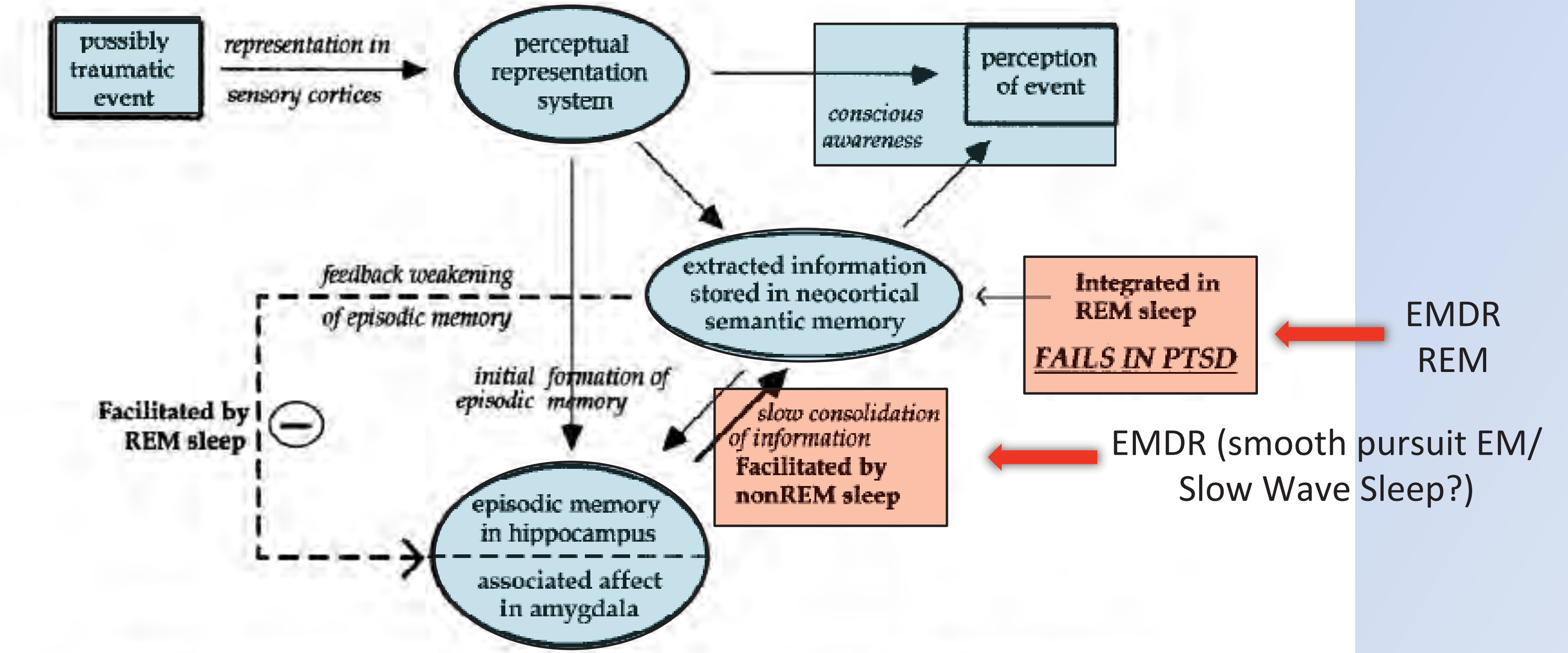
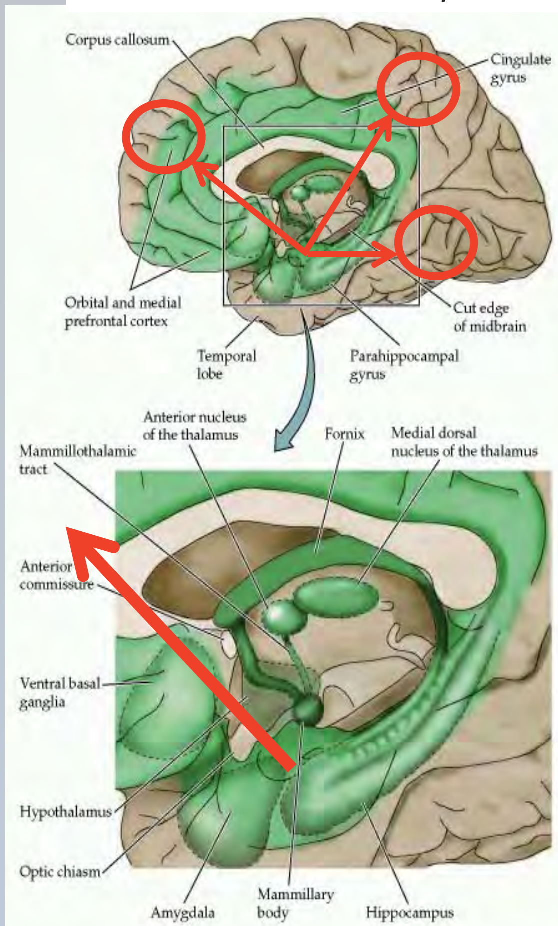


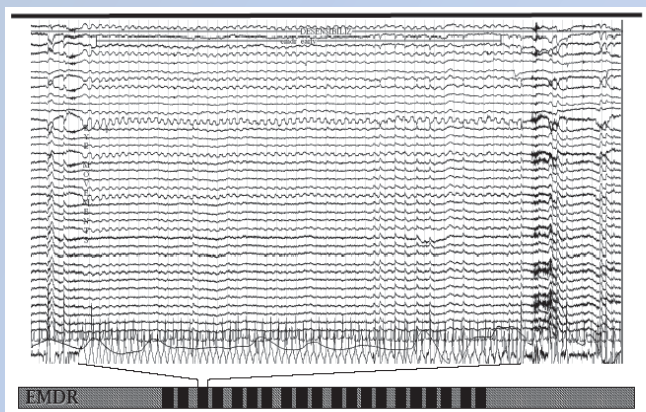
Figure 1. General model for sleep-dependent transfer and integration of episodic memories.

MECHANISM OF ACTION

Semantic memory



Episodic memory
Emotional implications



MECHANISM OF ACTION

INTEGRATION OF MEMORIES (Stickgold 2002)

We are not claiming that we have solid evidence for all of the links and interpretations in the train of logic presented here

Our goal is to demonstrate that there is a reasonable explanation of how EMDR works, which is consonant with modern neurobiology and cognitive neuroscience

Stickgold, Journal of Clinical Psychology 2002; 58: 61-75

PHYLOSOPHY AND (NEURO)SCIENCE

A theory is clear, decisive, and positive, but it is believed by no one exept the man who created it

On the other hand experimental findings are messy and inexact but are believed by everyone except the man who did that work

H. Shapley, 1969

THANKS

marco.pagani@istc.cnr.it