Primo corso di perfezionamento:
Neurologia Cognitiva

International School
of Neurological Sciences

La teoria della mente e la cognizione sociale

Anna Rita Giovagnoli

annarita.giovagnoli@istituto-besta.it

FONDAZIONE I.R.C.C.S.
ISTITUTO NEUROLOGICO CARLO BESTA

Dipartimento di Diagnostica e Tecnologia Applicata
Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano

Le funzioni sociali

- Contatto psicofisico tra gli individui
- Co-patia, rende più omogenei gli stati emozionali tra individui e attenua conflitti
- Comunicazione verbale e non verbale
- Coordinazione di movimenti di gruppo
- Cooperazione
- Coesione del gruppo, senso di appartenenza
- Cognizione sociale

Social Relationships and Health

JAMES S. HOUSE, KARL R. LANDIS, DEBRA UMBERSON

Recent scientific work has established both a theoretical basis and strong empirical evidence for a causal impact of social relationships on health. Prospective studies, which control for baseline health status, consistently show increased risk of death among persons with a low quantity, and sometimes low quality, of social relationships. Experimental and quasi-experimental studies of humans and animals also suggest that social isolation is a major risk factor for mortality from widely varying causes. The mechanisms through which social relationships affect health and the factors that promote or inhibit the development and maintenance of social relationships remain to be explored.

Science 1988, vol 241

. . . my father told me of a careful observer, who certainly had heart-disease and died from it, and who positively stated that his pulse was habitually irregular to an extreme degree; yet to his great disappointment it invariably became regular as soon as my father entered the room.—Charles Darwin (*1*)

Maggiore integrazione sociale, minore mortalità

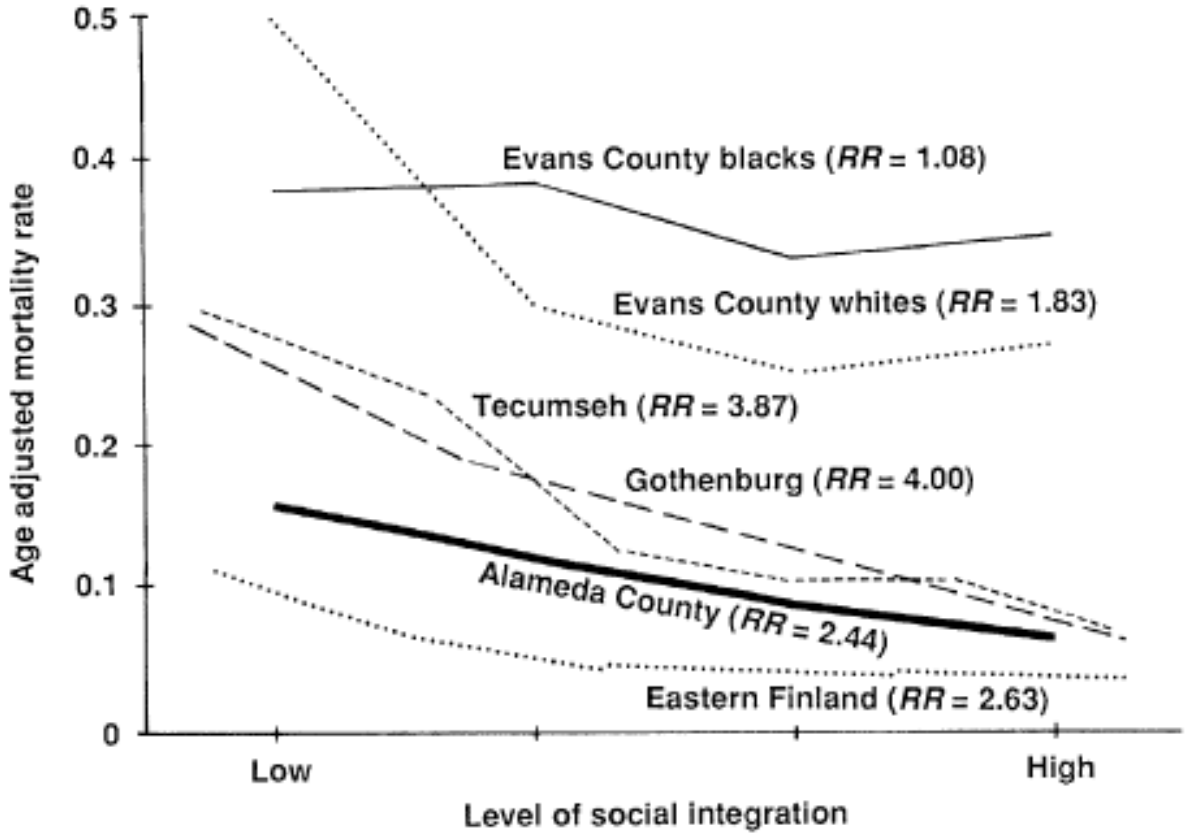


Fig. 1. Level of social integration and age-adjusted mortality for males in five prospective studies. *RR*, the relative risk ratio of mortality at the lowest versus highest level of social integration.

Does Rejection Hurt? An fMRI Study of Social Exclusion

Naomi I. Eisenberger,[1]* Matthew D. Lieberman,[1]
Kipling D. Williams[2]

10 OCTOBER 2003 VOL 302 SCIENCE

A neuroimaging study examined the neural correlates of social exclusion and tested the hypothesis that the brain bases of social pain are similar to those of physical pain. Participants were scanned while playing a virtual ball-tossing game in which they were ultimately excluded. Paralleling results from physical pain studies, the anterior cingulate cortex (ACC) was more active during exclusion than during inclusion and correlated positively with self-reported distress. Right ventral prefrontal cortex (RVPFC) was active during exclusion and correlated negatively with self-reported distress. ACC changes mediated the RVPFC-distress correlation, suggesting that RVPFC regulates the distress of social exclusion by disrupting ACC activity.

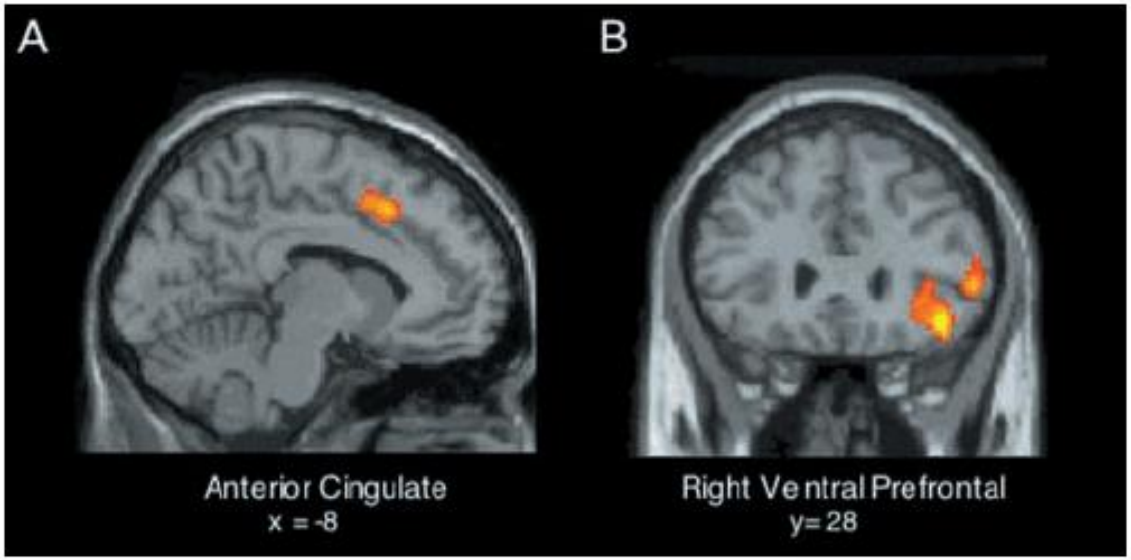


Fig. 1. (A) Increased activity in anterior cingulate cortex (ACC) during exclusion relative to inclusion. (B) Increased activity in right ventral prefrontal cortex (RVPFC) during exclusion relative to inclusion.

LA COGNIZIONE SOCIALE

Modello di Brothers (1990)

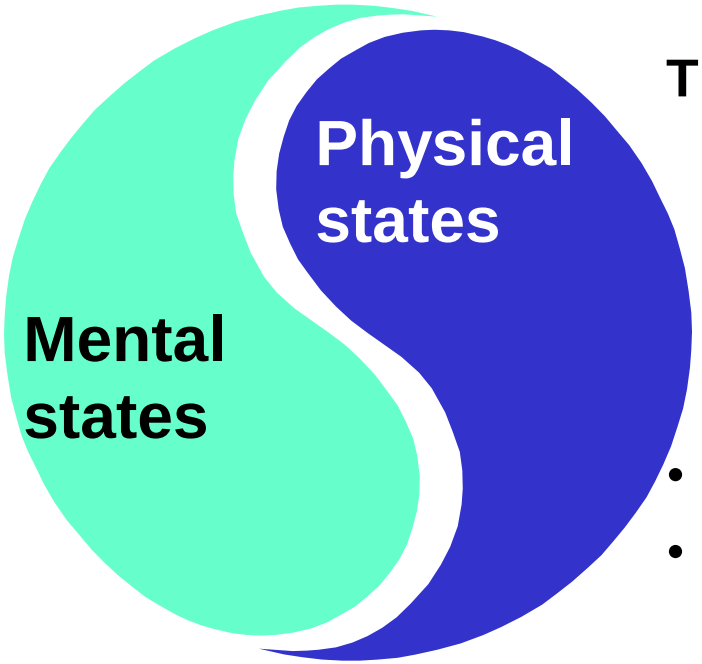
- Insieme delle operazioni mentali che sono alla base delle interazioni sociali, inclusa la capacità tipicamente umana di percepire le intenzioni e le disposizioni degli altri.
- Il modello di Brothers prevede l'esistenza di uno specifico sistema cerebrale predisposto alla cognizione sociale.
- Tre aree cerebrali coinvolte:
  - ❖Amigdala (informazioni emozionali e mimica facciale)
  - ❖Solco temporale superiore (percezione di volti)
  - ❖Corteccia orbitofrontale (interazioni sociali e modulazione dei comportamenti)

Modello quadrifattoriale di Blair e Cipollotti (2000)

- I° fattore: capacità di analizzare gli stati mentali altrui (Teoria della Mente)
- II° fattore: attribuzione di specifici stati emotivi
- III° fattore: identificazione di comportamenti adeguati e di violazioni
- IV° fattore: adesione alle regole sociali (regole morali e regole convenzionali)

Modello di Adolphs (2001)

Complesso di funzioni che costruiscono le rappresentazioni mentali delle relazioni sociali e usano adeguatamente per vivere in modo flessibile nell'ambiente sociale (assumere la prospettiva di un altro, avere empatia, apprezzare l'appropriatezza di un comportamento, comprendere le regole sociali).



Theory of mind is the most representative function of social cognition: Ability to attribute mental states to others or own-self, and to understand if such states correspond to reality or persuasion, lie, irony, metaphor, delusion.

- Cognitive Theory of mind
- Affective Theory of mind

Intentionality is the feature that sets completely apart mental states from physical states:

- Mental states (knowledge, beliefs, desires, affects, willing, intentions, thoughts, hopes, remembrances) point towards objects or states of affairs that **do not exist "here and now"**, that can be **true or false**, or even **paradoxical**.

- **Physical states** hold the property of having a **material** existence

AMYGDALA and ORBITAL CORTEX

Neuronal correlates of theory of mind and empathy: A functional magnetic resonance imaging study in a nonverbal task
Vollm et al., 2006, NeuroImage

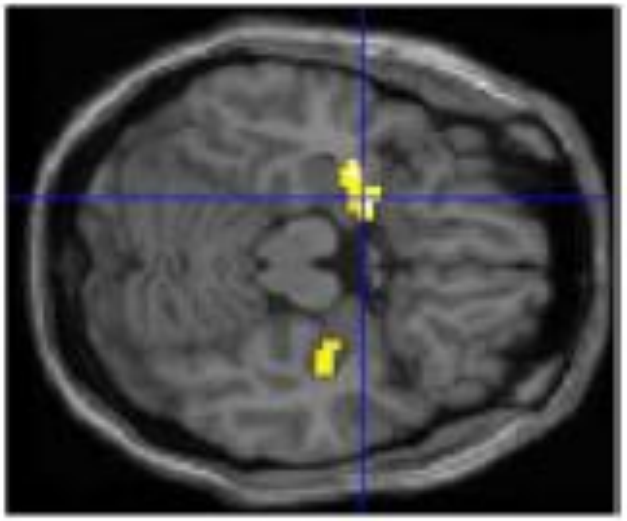


Fig. 4. Area of activation in the left amygdala in the contrast ('Emp' – 'Physical 2') – ('ToM' – 'Physical 1'). This area was activated to a greater extent when subjects were processing empathy stimuli than during ToM processing. Crosshairs at (–21; –1; –15).

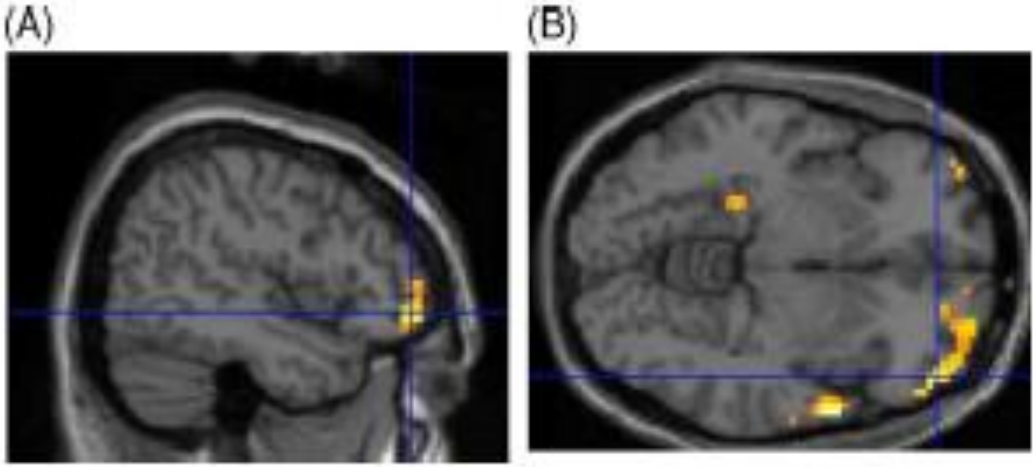


Fig. 3. Area of activation in the orbitofrontal cortex in the contrast ('ToM' – 'Physical 1') – ('Emp' – 'Physical 2'). This area was activated to a greater extent when subjects were processing ToM stimuli than during attending to empathy stimuli. (A) Sagittal view. (B) Transverse view. Crosshairs at (48; 48; –6).

TEMPOROPARIETAL JUNCTION

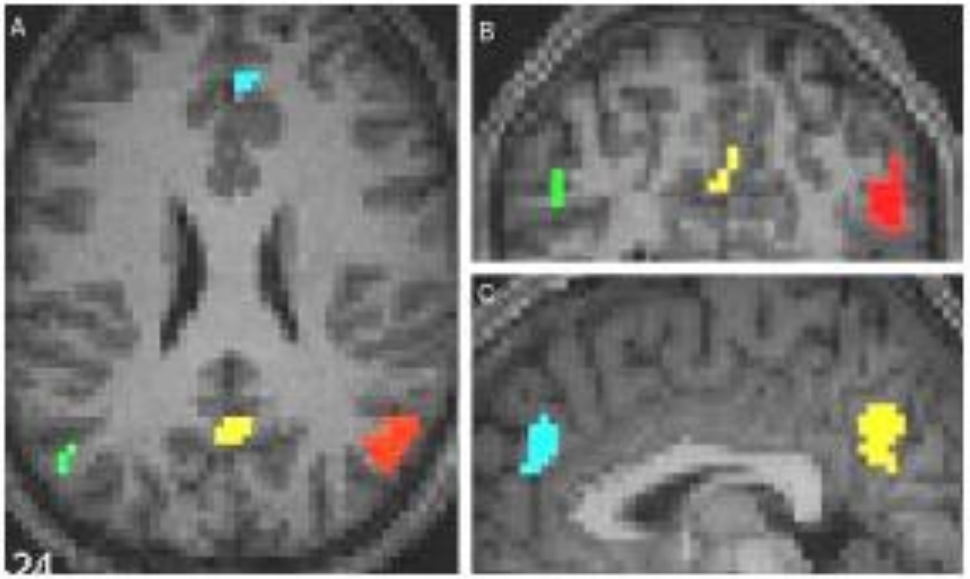


Fig. 1. Four 'Theory of Mind' regions of interest (ROIs) in a single representative subject. ROIs were defined as contiguous voxels in which the response was higher when subjects read stories about beliefs than when subjects read logically similar stories about photographs ($p < 0.0001$, uncorrected). Red = right temporo-parietal junction (RTPJ). Green = left TPJ. Cyan = medial prefrontal cortex (MPFC). Yellow = posterior cingulate (PC). (A) Axial slice, $z = 24$. (B) Coronal slice, $y = -60$. (C) Saggital slice, $x = 4$ (midline).

MEDIAL PREFRONTAL CORTEX

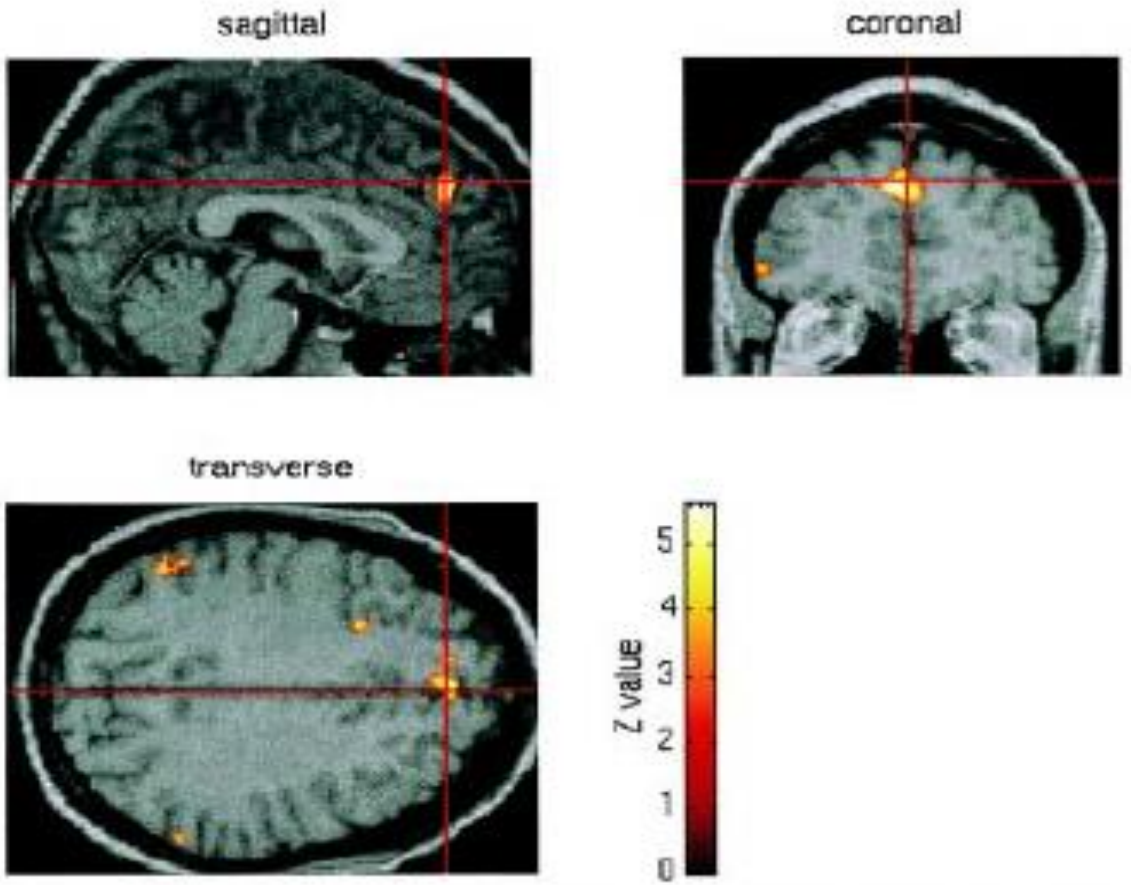


Fig. 4. Area of activation in the medial frontal cortex of a single subject elicited by theory of mind stories and cartoons. Co-registration of functional and structural scans for this subject show that the activation lies in the paracingulate cortex.

Stereotyped developmental sequence

- 18 months: joint attention.
- 2 years: distinction between pretend and reality, understanding others' desires and relating desires to emotions.
- 3-4 years: understanding first-order false beliefs, distinction between ones own and others' mental states, predicting others' behavior on the basis of their mental states.
- 5 years: understanding if a mental representation corresponds to a real situation.
- 6-7 years: understanding second-order false beliefs.
- 9-11 years: recognizing faux pas.
- 13 years: reading the mind in the eyes.

L'esame neuropsicologico della teoria della mente utilizza test di difficoltà crescente che corrispondono a diverse categorie di stati mentali e diverse fasi dello sviluppo:

False convinzioni di primo e secondo ordine: è la "cartina al tornasole" della teoria della mente! capacità di comprendere che una persona può avere convinzioni diverse dalle proprie e dalla realtà.

Inganno: capacità di comprendere che gli stati mentali derivano da ciò che si è sentito o osservato, pertanto possono essere manipolati.

Linguaggio non letterale o figurato (metafora, ironia, sarcasmo, allusione): capacità di comprendere la vera implicita comunicazione.

Gaffe: capacità di comprendere che non è intenzionale (deriva dalla incompleta conoscenza della realtà) e che ferisce un'altra persona.

Espressione degli occhi

The “classic” ToM Paradigm (False Belief): the Sally-Ann task (Baron-Cohen et al, 1985)

Representation of the reality...

Change of reality…

Reading Sally’s mind: “When she is back, where will she look for her marble?”

Representation of a mental state that is different from reality: Sally has a false belief (out-of-date representation)

Impaired on-line ToM performances

PERGAMON

Neuropsychologia 41 (2003) 209–220

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

Acquired theory of mind impairments in individuals with bilateral amygdala lesions

Valerie E. Stone[a,*], Simon Baron-Cohen[b], Andrew Calder[c], Jill Keane[c], Andrew Young[d]

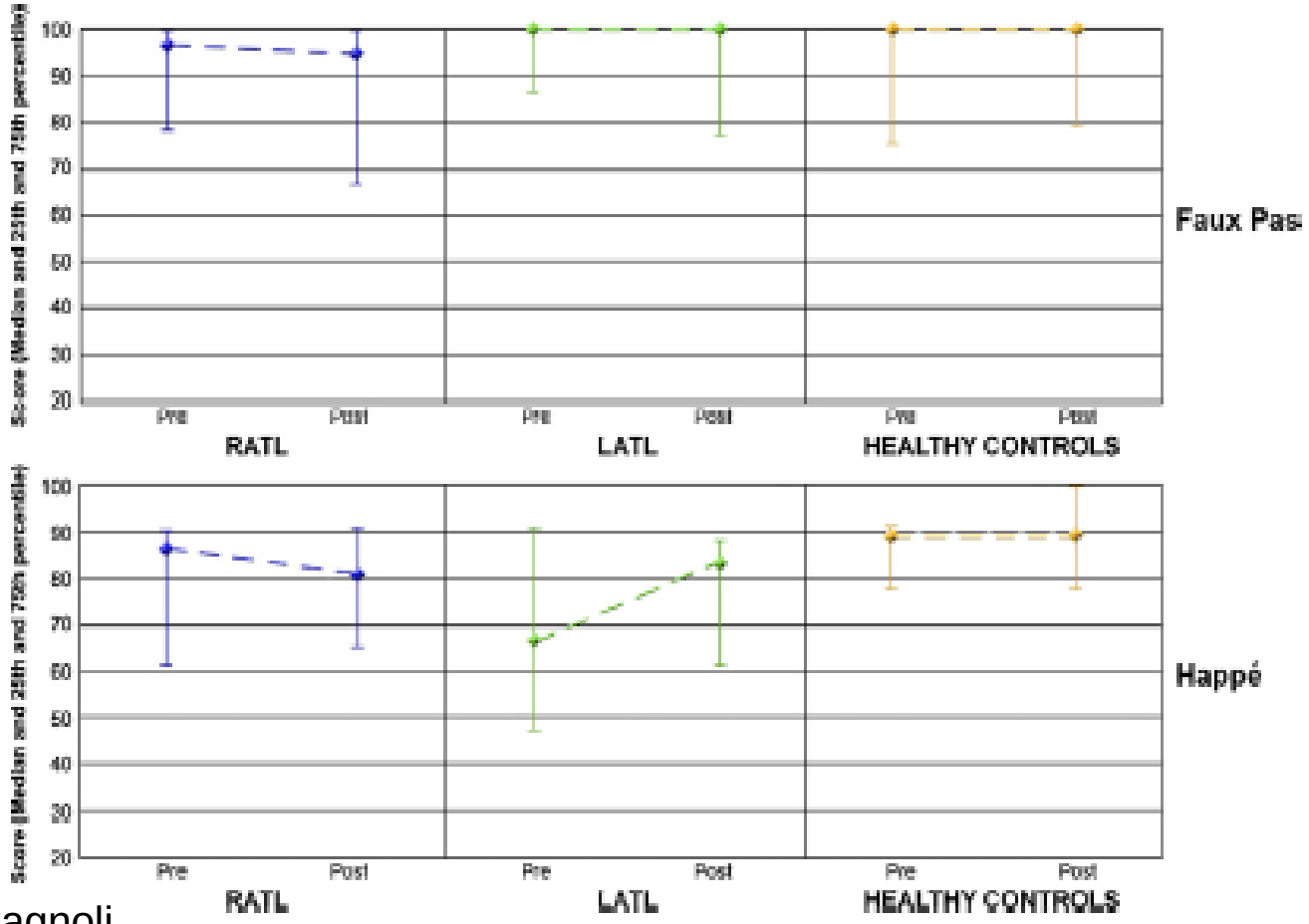
Two patients with bilateral amygdala damage acquired in adulthood: amygdalectomy for drug-resistant seizures
herpetic encephalitis

Deficits at the Faux pas and Reading the mind in the eyes tests

Amygdala is important to normal on-line ToM in adults, not just in the development

Normal ToM in temporal lobe epilepsy Shaw et al., 2007

19 TLE patients before and after temporal lobectomy including the amygdala.
19 healthy controls.
Faux pas task: detection score (recognition+question 1), epistemic ToM score (question 2), affective score ToM (question 4).
Happè' Strange stories. No correlation between ToM and executive functions scores.



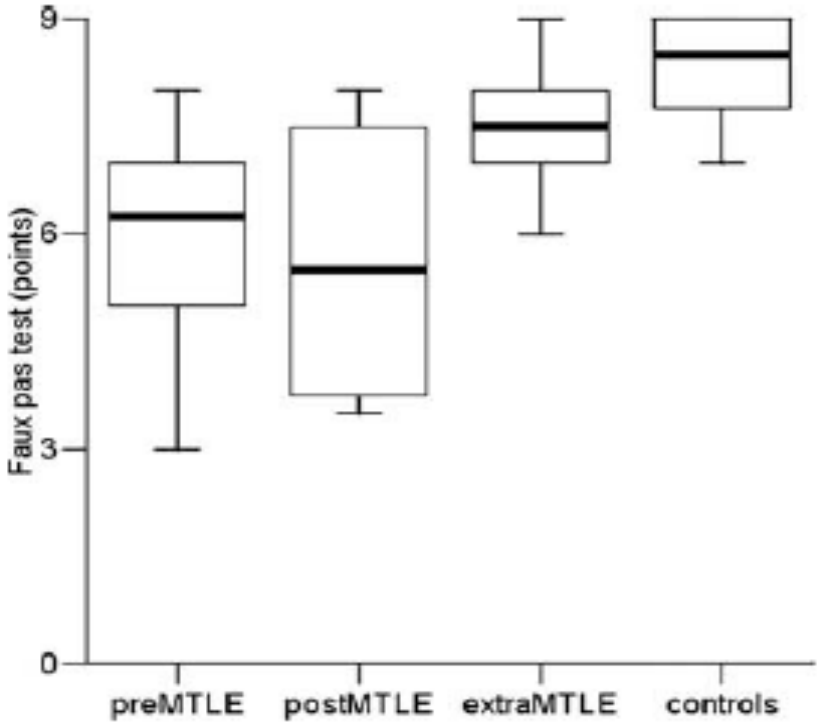
Impaired on-line ToM performances

Epilepsia, 47(12):2141–2146, 2006
Blackwell Publishing, Inc.

Mesial Temporal Lobe Epilepsy Impairs Advanced Social Cognition

Martina Schacher, Rebecca Winkler, Thomas Grunwald, Guenter Kraemer, Martin Kurthen, Victoria Reed, and Hennric Jokeit

Swiss Epilepsy Center, Zurich, Switzerland



- 27 pts. with MTLE (20 HS, 7 other lesions). 27 pts. with extra-MTLE (partial, generalized; no FLE).
- 12 healthy controls.
- 3 Faux pas stories.
- Detection score (recognition + 1-2-3 question scores), Factual comprehension score, Emotion recognition score, Control score.
- Lower scores in MTLE in extra-medial TLE patients and controls.
- No relationships to onset age, epilepsy duration, IQ, executive functions.

Impairment related to early amygdala damage

DOI: 10.1093/brain/awh168 *Brain* (2004), **127**, 1535–1548

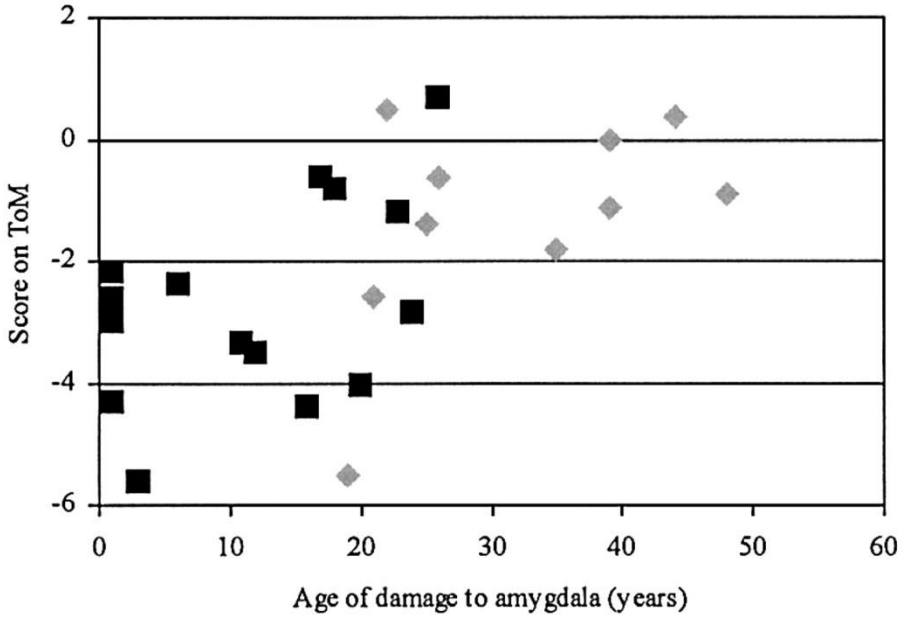
The impact of early and late damage to the human amygdala on 'theory of mind' reasoning

P. Shaw,[1] E. J. Lawrence,[1] C. Radbourne,[1] J. Bramham,[2] C. E. Polkey[3] and A. S. David[1]

[1]*Section of Cognitive Neuropsychiatry, Department of Psychological Medicine,* [2]*Neuropsychology Unit, Institute of Psychiatry and* [3]*Academic Neurosurgery, Centre for Neuroscience Research, King's College London, UK*

Correspondence to: Dr P. Shaw, Section of Cognitive Neuropsychiatry, Department of Psychological Medicine, 103 Denmark Hill, London SE5 8AF, UK
E-mail: p.shaw@iop.kcl.ac.uk

15 pts. with early amygdala lesions (DNET) onset age = age of seizure onset
11 pts. with late amygdala lesions (anterior temporal lobectomy)
age of onset = age at surgery
Controls: 14 lesions in other sites
38 healthy subjects



1° and 2° order false beliefs
(Baron-Cohen et al., 1985, 1989)
Happè Strange stories
(Happé, 1994; Snowden et al., 2003)
Metaphor and irony (Happé, 1993)
Faux pas (Stone et al., 1998; 9 stories)
Conflicting belief and emotion task
IQ, WMS
Hayling test (interference inhibition)
Brixton (shifting)

Tasks	Early	Late	Other
1° order beliefs			
Stange stories (p<0.001)	<other lesions		
Irony (p=0.012)	<healthy		
Metaphor			
Faux pas (9FP stories) Total score (p=0.01) **Epistemic score (2° question, p=0.001)**	 <healthy <healthy	<healthy	
Conflicting task 2°order false beliefs, p=0.01 **emotions, p<0.001**	<healthy <healthy & other	<healthy	<healthy

Impaired ToM in cryptogenic TLE

Epilepsy Research (2009) 84, 217–223

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

The neuropsychological pattern of Unverricht–Lundborg disease

Anna R. Giovagnoli[a,*], Laura Canafoglia[b], Fabiola Reati[a], Federico Raviglione[b], Silvana Franceschetti[b]

Table 3 Mean neuropsychological test scores of the ULD patients, cryptogenic TLE patients, and the healthy subjects.

	ULD patients	Cryptogenic TLE patients	Healthy subjects
Raven's coloured progressive matrices	23.86 ± 7.67	31.05 ± 4.80	31.48 ± 4.52
Token test	30.00 ± 5.56	33.62 ± 2.35	34.57 ± 1.39
Rey's figure copying	25.12 ± 11.44	34.67 ± 1.77	33.60 ± 2.85
Imitating gestures	18.57 ± 4.34	19.62 ± 0.66	20.00 ± 0.00
Imitating facial expressions	18.05 ± 4.32	19.52 ± 0.75	19.81 ± 0.51
Weigl's sorting test	9.14 ± 4.57	11.52 ± 2.63	11.52 ± 2.42
Boston naming test	41.86 ± 8.48	47.43 ± 6.96	53.19 ± 4.30
Word fluency on phonemic cues	18.52 ± 10.09	30.24 ± 10.59	35.33 ± 12.03
Word fluency on semantic cues	25.57 ± 7.97	35.52 ± 10.36	39.33 ± 8.59
Digit span	4.57 ± 1.24	5.86 ± 1.27	5.67 ± 1.35
Corsi's blocks span	3.86 ± 1.35	5.67 ± 1.35	5.57 ± 0.92
Short story	11.57 ± 6.00	10.83 ± 4.89	15.03 ± 4.81
Rey's figure delayed reproduction	11.10 ± 8.81	14.74 ± 6.13	20.52 ± 5.90
Word list learning	177.43 ± 43.16	99.52 ± 50.11	122.06 ± 38.11
Corsi's blocks learning	15.11 ± 5.40	21.35 ± 5.22	24.09 ± 3.17
Attention matrices	37.48 ± 16.58	53.14 ± 7.76	53.52 ± 6.52
Trail making test A	110.95 ± 76.23	50.67 ± 30.93	44.14 ± 19.57
Trail making test B	253.57 ± 125.38	130.33 ± 74.44	125.05 ± 73.57
Street's completion test	6.48 ± 2.94	7.38 ± 2.47	8.67 ± 2.19
Tower of London	14.38 ± 7.22	24.33 ± 3.90	27.43 ± 5.70
Faux pas recognitions	9.10 ± 1.09	8.90 ± 1.54	9.67 ± 0.73
Faux pas rejections	9.05 ± 0.80	9.90 ± 0.30	9.32 ± 1.04

Partial ToM deficits in frontal lobe epilepsy patients

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Available online at www.sciencedirect.com
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Epilepsy & Behavior 7 (2005) 506–516

Epilepsy & Behavior

www.elsevier.com/locate/yebeh

Social cognition in frontal lobe epilepsy

Annette Farrant [a], Robin G. Morris [a,b,*], Tamara Russell [c], Robert Elwes [d,e], Nozomi Akanuma [d,f], Gonzalo Alarcón [d,e], Michael Koutroumanidis [f]

14 FLE patients, 14 healthy controls.
Happé Strange stories, Faux pas recognition, Humor appreciation
Reading the eyes in the mind, Recognition of facial emotion expression.

FLE patients with normal intellective and memory functions have significant impairments in humor appreciation, emotion recognition and reading the mind in the eyes (no relevant difficulties at a Faux pas task and Strange stories).
No correlation between theory of mind and executive functions.

ToM impairments in adult patients with FLE or TLE

Diagnosis of TLE or FLE based on seizure symptoms and EEG.

MRI-detected focal lesions congruent with the epileptic zone.

No psychiatric disorders, intellective deficits, or different neurological disturbances.

	Left TLE N=62	**Right TLE N=47**	**FLE N=29**	**Controls N=69**
Females/males	38/24	27/20	18/11	40/29
Schooling (years)	12 ± 4	11 ± 3	12 ± 3	11 ± 4
Age (older controls, p<0.001)	36 ± 12	38 ± 11	36 ± 12	52 ± 17
Disease duration (longer in TLE, p=0.03)	15 ± 13	16 ± 15	8 ± 8	-
Age of seizure onset	21 ± 15	22 ± 14	27 ± 14	-
Monthly seizure frequency (in the previous year)	9 ± 18	9 ± 16	8 ± 8	-
Focal non-progressive lesions	24 cryptogenic 24 MTLS 6 medial non-MTLS 9 lateral temporal lesions (dysplasia, cavernoma, ganglioglioma)	16 cryptogenic 19 MTLS 5 medial non-MTLS 6 lateral temporal lesions (dysplasia, cavernoma, ganglioglioma)	22 cryptogenic 7 lesions (dysplasia, injury, cavernoma, ganglioglioma)	

Giovagnoli et al. 2011

Riconoscimento di gaffée
(Stone et al., 1998)

Compito del test:

Riconoscimento e comprensione di stati mentali epistemici e affettivi

Giulia ha appena traslocato in un nuovo appartamento. Ha acquistato nuove tende per la camera da letto.
Ha appena finito di sistemare l'appartamento che la sua migliore amica, Elisa, arriva e dice: "Oh, queste tende sono orribili! Spero che ne le comprerai nuove".
Giulia risponde: "Vuoi vedere il resto della casa?"

Riconoscimento *"Qualcuno ha detto qualcosa che non avrebbe dovuto dire?"*

Comprensione (se risponde sì):

"Chi l'ha detto?"

"Perchè non avrebbe dovuto dirlo?"

"Perchè l'ha detto?"

"Come si è sentita Giulia"

Controllo: *"Che cosa aveva comprato Giulia?"*

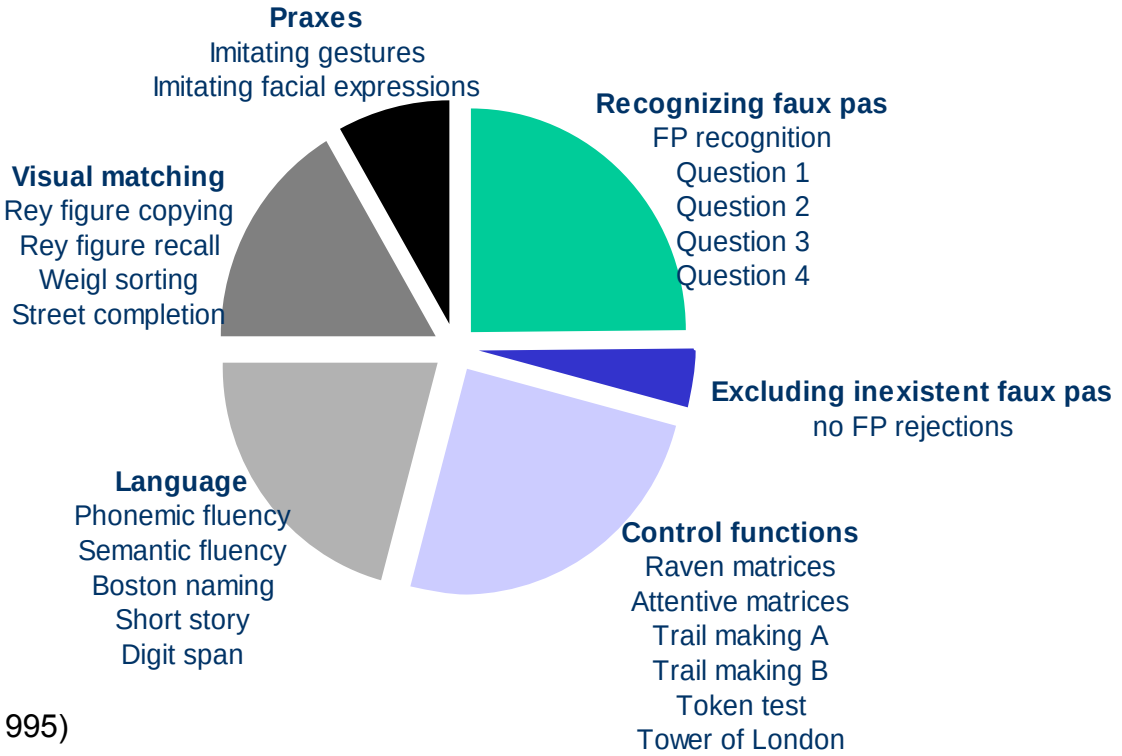
Punteggi

Riconoscimento (0-10)
Comprensione totale (0-40)
Comprensione singole domande (0-10)
Controllo (0-10)

Factor structure of the battery

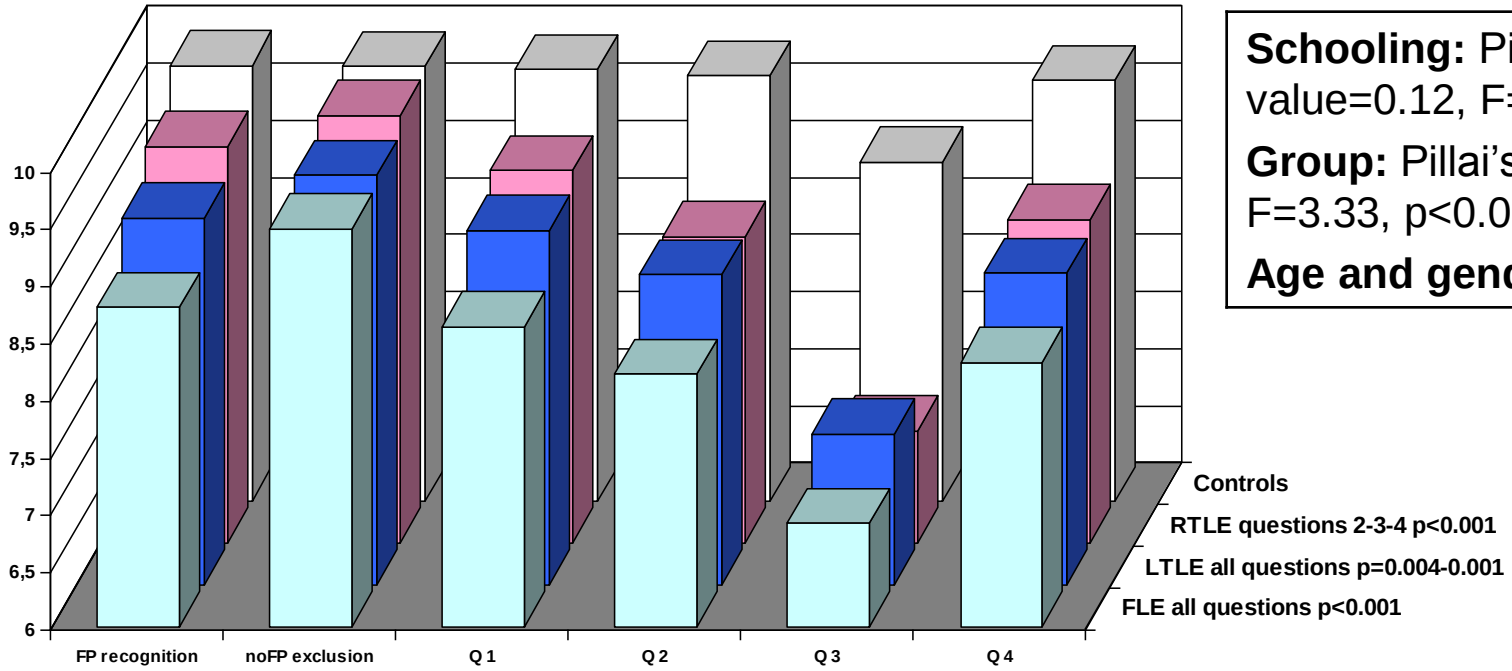
FACTOR LOADINGS > 0.5

Total explained variance 72%



- **MEMORY:** Short story (Novelli et al., 1986)
  Rey's complex figure recall (Lezak, 1995)
  Digit span (Spinnler & Tognoni, 1987)
  Corsi blocks span (Lezak, 1995)
- **EXECUTIVE FUNCTIONS:** Tower of London (Shallice & McCarthy, 1982)
  Weigl completion test (Weigl, 1933)
  Word fluency on phonemic cue (Novelli et al., 1987)
  Trail making test (Lezak, 1995)
  Attentive Matrices (Spinnler & Tognoni, 1987)
  Raven's colored matrices (Basso et al., 1987)
- **PRAXIS:** Imitating gestures (Spinnler & Tognoni, 1987)
  Imitating facial expressions (Spinnler & Tognoni, 1987)
  Rey complex figure copying (Lezak, 1995)
- **LANGUAGE:** Token test (De Renzi & Vignolo, 1963)
  Word fluency on semantic cue (Novelli et al., 1986)
  Boston naming Test
- **VISUAL PERCEPTION:** Street completion test (Street, 1993)

Epilepsy patients vs Healthy Controls
(demographic covariates)



Schooling: Pillai's value=0.12, F=4.47 p<0.001

Group: Pillai's value=0.28, F=3.33, p<0.001

Age and gender: no effect

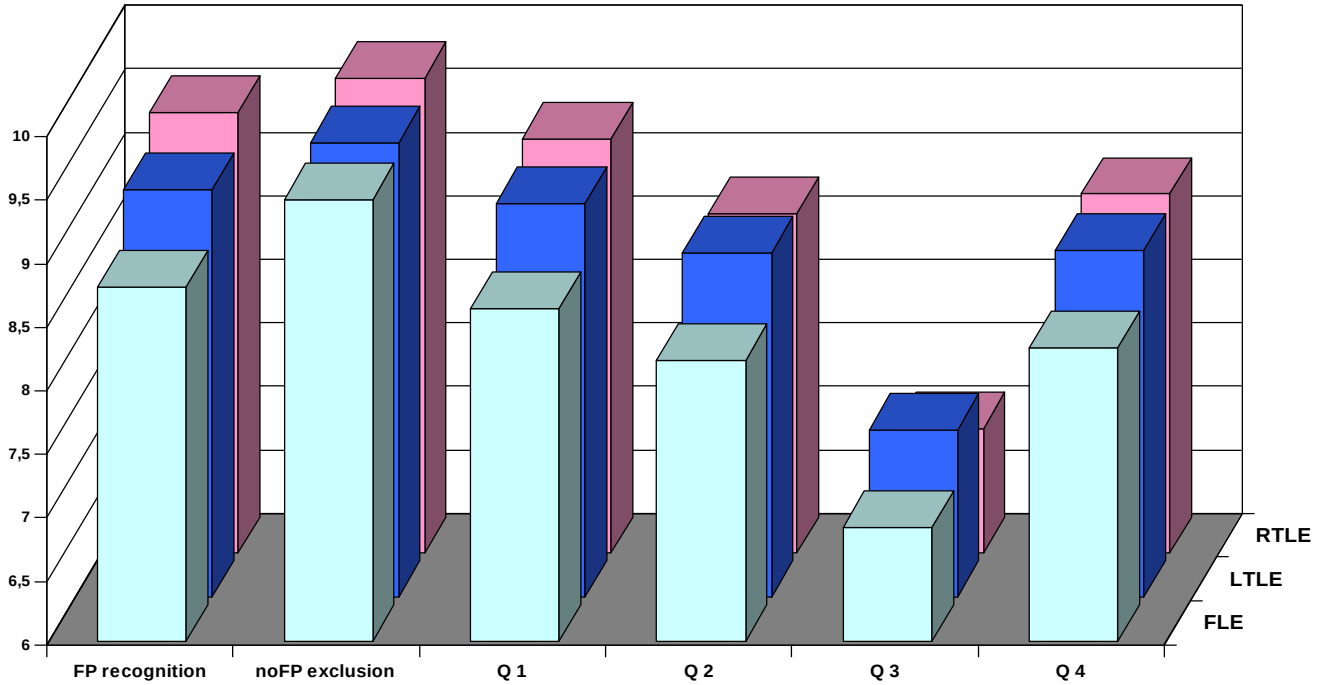
FLE and TLE < Controls

FLE < RTLE FP recognition and intentions comprehension

No-FP exclusion: no difference

Site of epilepsy by Age of seizure onset

(epilepsy-related and neuropsychological covariates)



Site of focus:
Pillai's=0.10, F=2.13
p=0.05

Age of seizure onset:
Pillai's=0.13, F=2.64,
p=0.02

Onset x site:
Pillai's=0.13, F=2.72,
p=0.017

Control functions:
Pillai's=0.43, F=6.20,
p<0.001

FLE < TLE: FP recognition, F=3.76, p=0.03

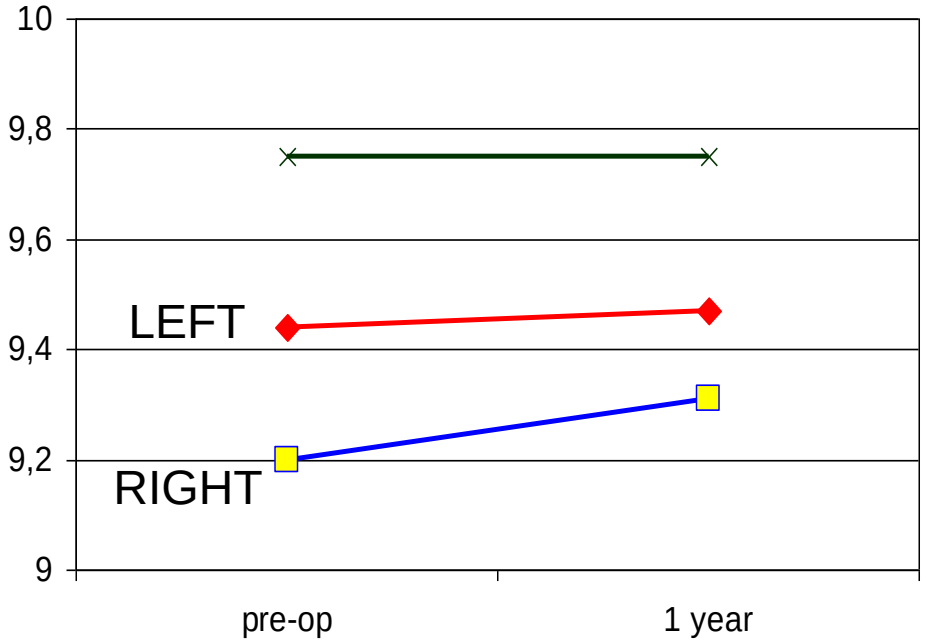
Early onset TLE < late onset TLE: emotional states comprehension, F=6.28, p=0.01

Pts. with lower Control functions: lower intentions comprehension F=9.59, p=0.003

Seizure frequency (in the last year) and anti-epileptic drugs: no effect

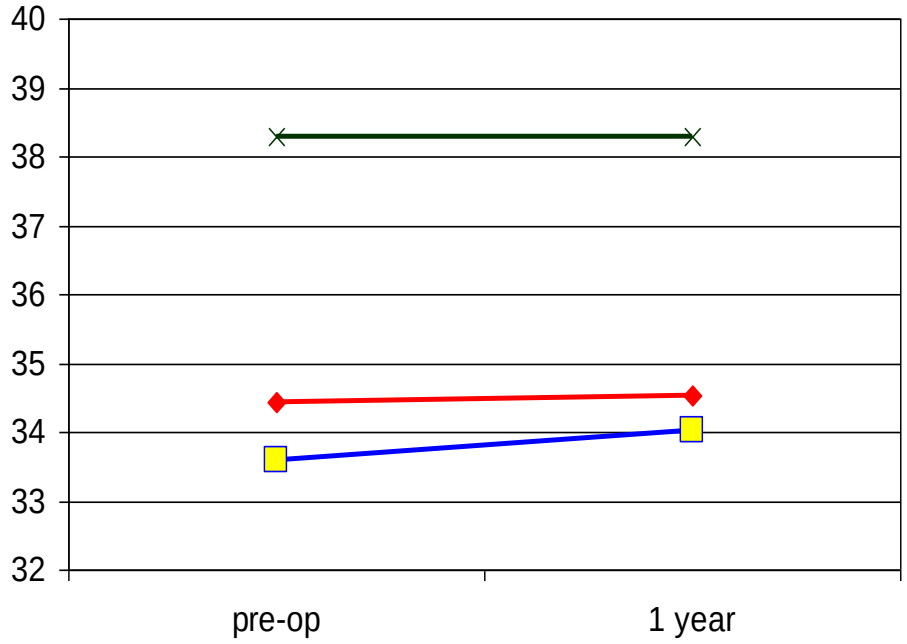
Recognition and comprehension of faux pas after ATL

Recognition



Schooling p=0.014

Comprehension



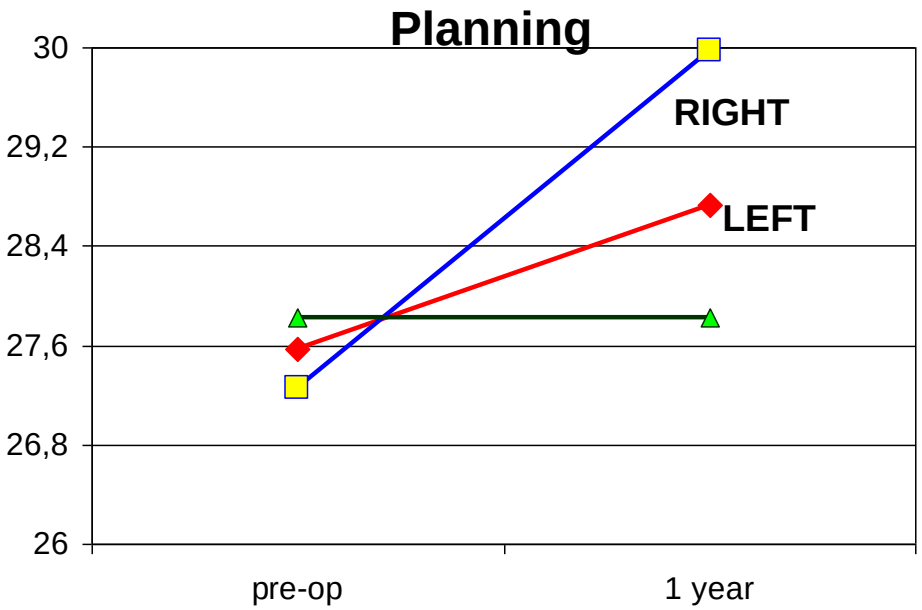
Schooling p=0.001

Mild improvement

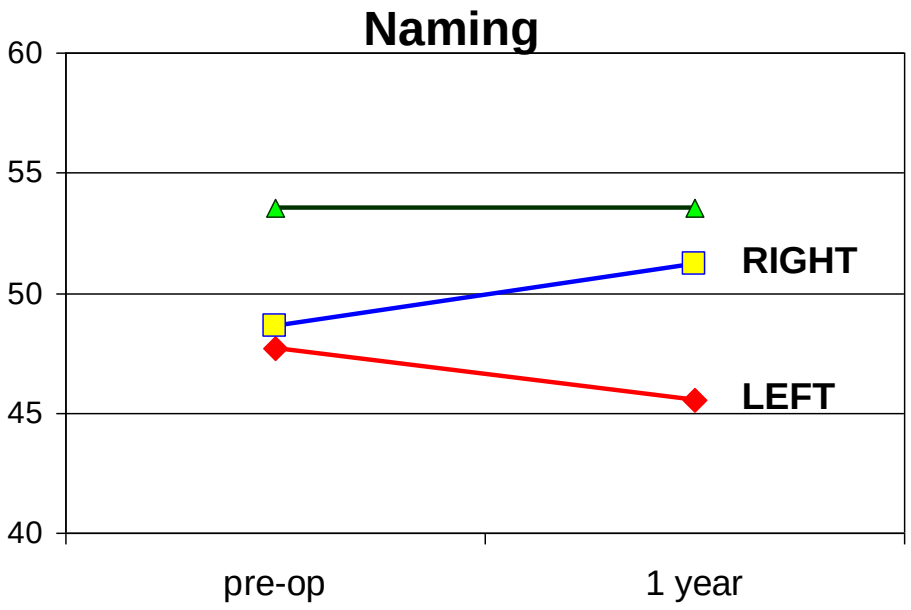
Time NS - Side of surgery NS – Time by Side of surgery NS

Age of epilepsy onset NS – Seizure outcome NS

(Giovagnoli et al., 2014)

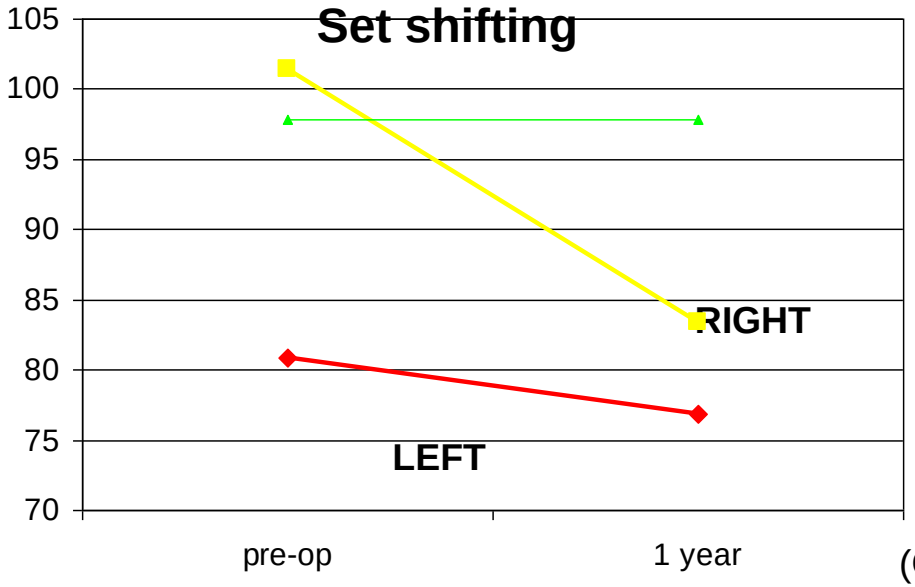


Improvement after RATL or LATL
Time, Schooling, and Side: NS
Time by Side NS



Improvement after RATL, Worsening after LATL
Time NS - Schooling p<0.001 - Side p=0.04
Time by Side p<0.001

Improvement after RATL
Time p=0.06
Schooling p<0.001
Side of surgery NS
Time by Side p=0.028



(Giovagnoli et al., 2014)

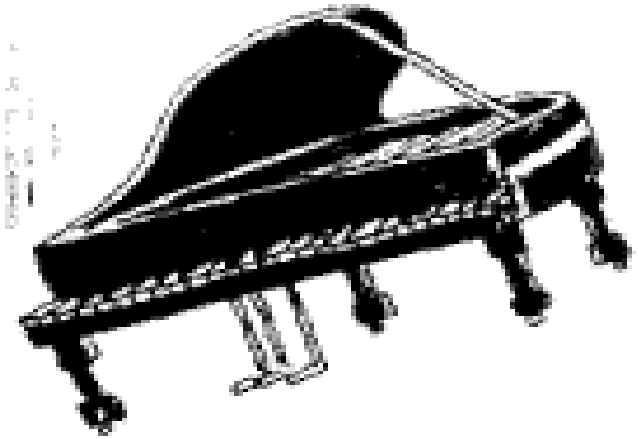
Eziopatogenesi dei deficit di teoria della mente e cognizione sociale nell'epilessia

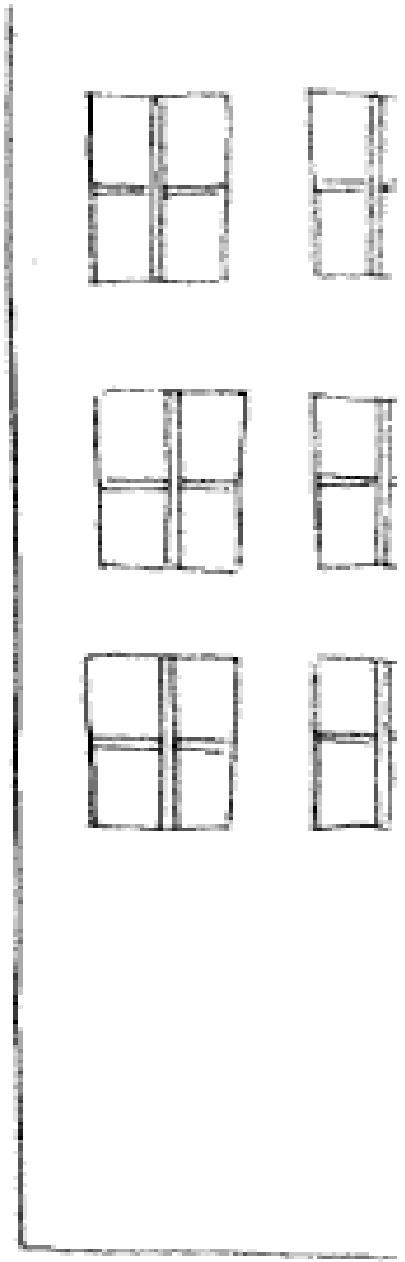
Clinico-patologiche:

- Lesione o disfunzione di strutture e connessioni del circuito neurale (temporomesiale, frontoorbitaria/mediale)
- Lunga durata di malattia
- Anomalo sviluppo neuromotorio nei casi ad esordio precoce
- Ridotta acquisizione di comportamenti sociali nell'età dello sviluppo a causa di crisi frequenti
- Ridotta analisi degli stimoli sociali/ambientali secondaria a difetto di working memory e attenzione causato dai farmaci antiepilettici

Psicosociali:

- Isolamento sociale secondario a stigmate, scarsa autostima o eccessiva protezione da parte dei familiari
- Basso livello scolastico e culturale
- Disoccupazione o sottoccupazione
- Difficoltà ad avviare una vita di coppia e formare una famiglia
- Vulnerabilità socioeconomica accentuata dall'età e dalla presenza di comorbidità





Implicazioni cliniche:

I deficit di ToM si associano a peggiore qualità della vita, minori interazioni sociali e minore capacità di adattamento

(Giovagnoli et al., 2013)

Raccomandazioni cliniche

Valutare la teoria della mente e la cognizione sociale nei pazienti che:

- mostrano disturbi del comportamento e delle funzioni sociali:
- sono affetti da epilessia temporomesiale o frontale
- sono candidati all'intervento chirurgico
- sono in fase di cambiamento della terapia antiepilettica

Batteria neuropsicologica:

- test di adeguata complessità che valutano:
  - le principali componenti della cognizione sociale
  - le funzioni che possono interferire con la teoria della mente (funzioni esecutive, ragionamento astratto, memoria, linguaggio)

Valutare il profilo psicopatologico e comportamentale:

- ansia, depressione, coping, autostima, personalità, ecc.

Trattamento:

- tener conto della teoria della mente e cognizione sociale nei pazienti cadidati al training cognitivo o alla psicoterapia

Raccomandazioni per la ricerca

Analizzare i correlati neurali della teoria della mente e della cognizione sociale nei pazienti con epilessia focale o generalizzata, mediante imaging strutturale e funzionale

Esaminare la connettività cerebrale associata a modificazioni della teoria della mente (EEG, MEG, neuroimaging)

Esaminare l'impatto dei farmaci antiepilettici e dell'intervento chirurgico sulla teoria della mente e sulla cognizione sociale, a breve e lungo termine

Esaminare le interazioni tra teoria della mente e funzioni esecutive, memoria e linguaggio

Elaborare batterie neuropsicologiche in grado di discriminare livelli diversi di compromissione che tengano conto del normale sviluppo neurale e delle componenti della cognizione sociale

Sviluppare studi transculturali