

III. Schizophrenia

III. Schizofrenia

- Bleuler (1911): l'autismo, un distacco dal mondo esterno, combinato con una predominanza della vita interiore, è uno dei sintomi definiti della schizofrenia
- Minkowski (1927): una mancanza del “contatto vitale con la realtà”, un’inabilità di risuonare con il mondo e di provare empatia per gli altri, causata da un deficit soggettivo nella sintonizzazione tra l’individuo e il suo mondo, riflette l’essenza della schizofrenia.

III. Schizofrenia

- **La schizofrenia come un disurbo dell'esperienza del Sé che trapela attraverso la sua sintomatologia, includendo problemi sociali** (Sass & Parnas 2003; Nelson et al. 2009; Henriksen et al. 2010)
- **Riconciliando queste idee: la schizofrenia come una trasformazione fondamentale della struttura della soggettività (ipseità, intenzionalità e intersoggettività)** (Parnas, Bovet & Zahavi 2002; Gallese 2003)

III. Schizofrenia

- E' stato proposto un ruolo cruciale del Sé soggettivo e la sua relazione con il mondo esterno nella schizofrenia.
- Le anomalie funzionali sottostanti i deficit sociali nella schizofrenia specificamente riguardano l'intersoggettività oppure hanno le loro radici nei disturbi del Sé?

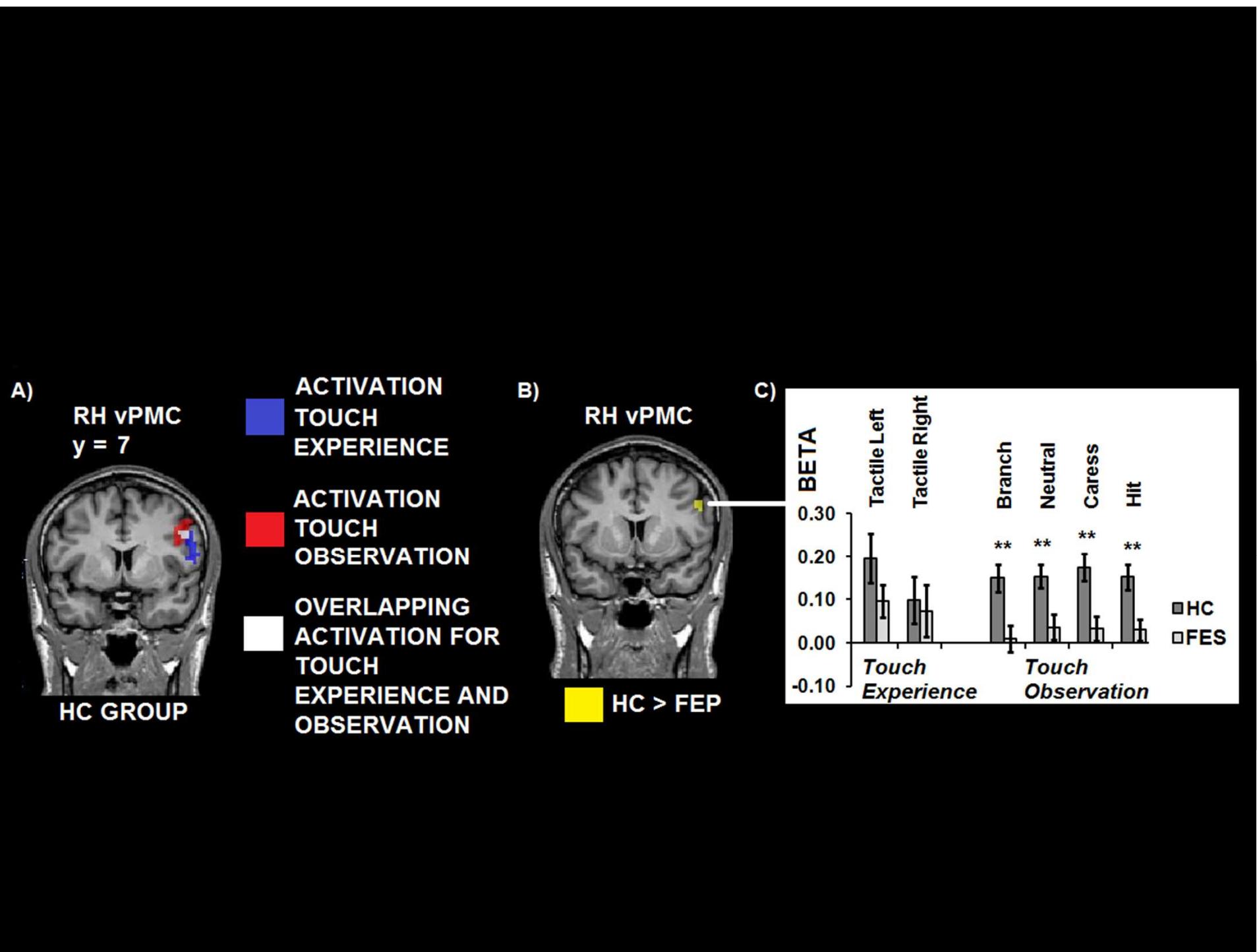
Out of touch with reality? Social perception in first-episode schizophrenia

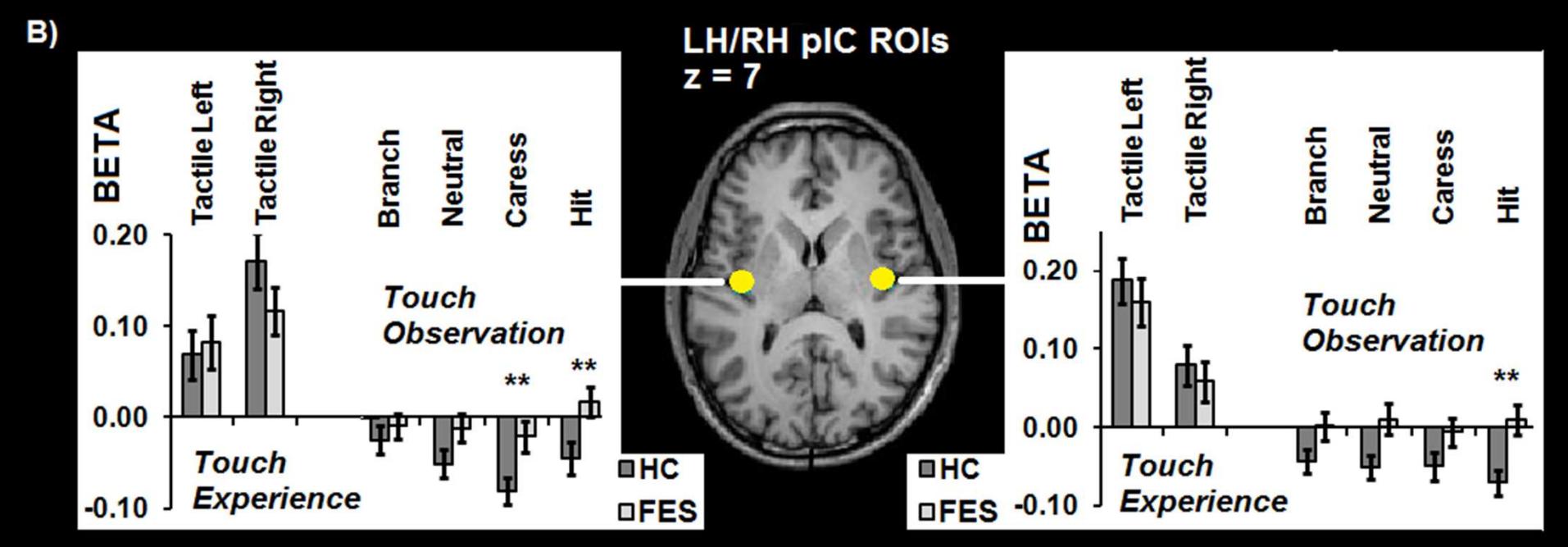
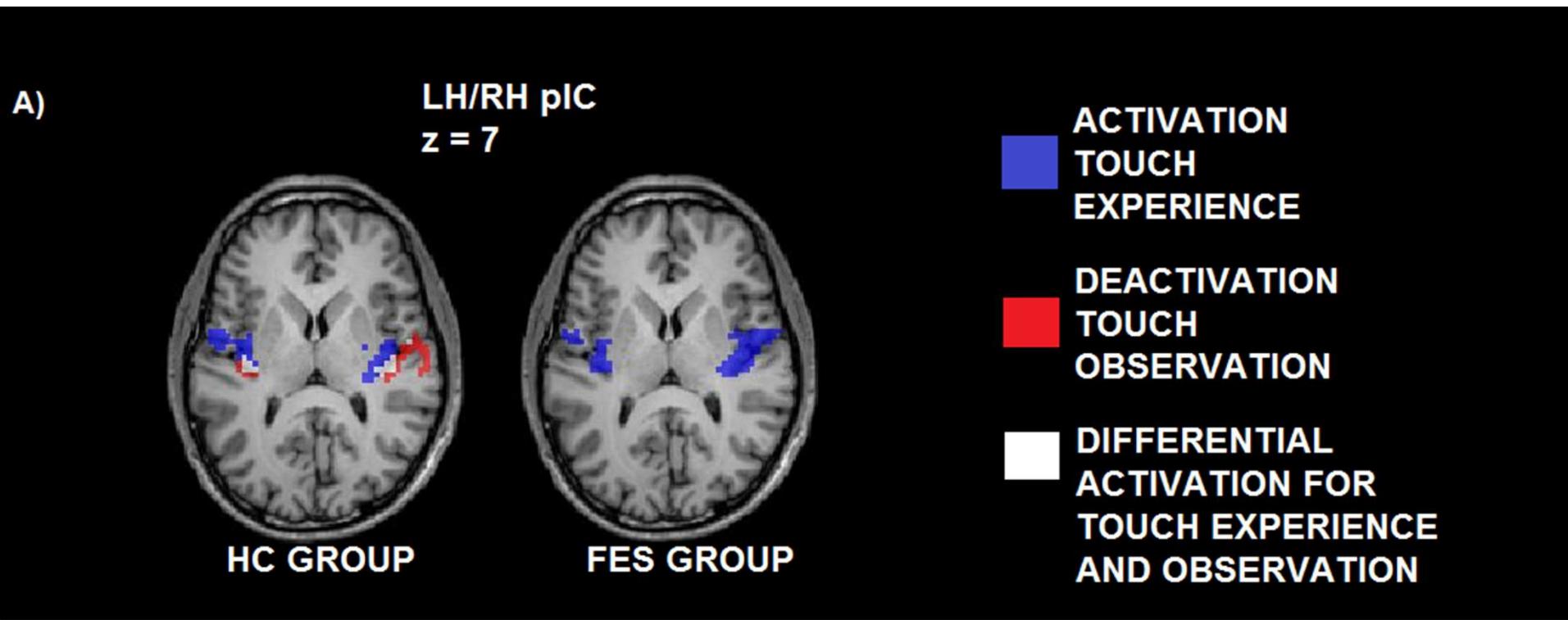
SCAN (2012)

Sjoerd J. H. Ebisch,^{1,2} Anatolia Salone,^{1,3} Francesca Ferri,⁴ Domenico De Berardis,^{5,3} Gian Luca Romani,^{1,2} Filippo M. Ferro,^{1,3} and Vittorio Gallese^{4,6}

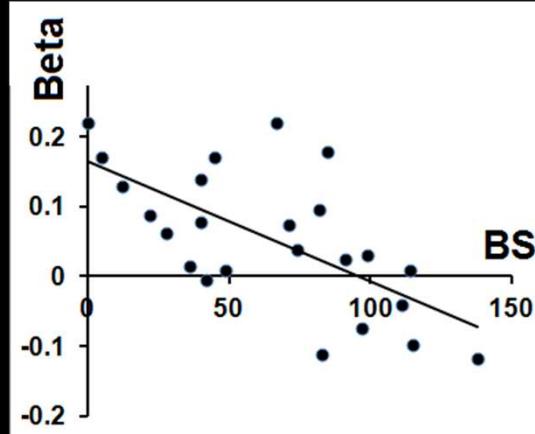
- **Do patients with schizophrenia show altered vicarious neural activations (e.g. *somatosensory cortex, anterior insula, ...*)**
- **or rather aberrant neural processes underlying multisensory integration and differentiation between self and others' bodily experiences during social perception (e.g. *posterior insula, premotor cortex, intraparietal cortex, ...*)?**

- 24 patients with first-episode schizophrenia (FES), a first manifestation of schizophrenia and an important condition to study primary aspects of the pathology without chronicity-related confounds, and 22 matched healthy control (HC) participants underwent fMRI scanning during a social perception task.
- FES patients were evaluated for the presence of Basic symptoms (BS) (Klosterkötter et al., 2001) by means of the Schizophrenia Proneness Instrument (SPI-A) (c et al., 2011):
(sub-clinical) subjective disturbances of self-experience in the domains of cognition, perception, bodily experience, action, and emotion (Huber, 1983; Klosterkotter, 1992).
- BS, appearing more or less continuously even many years before psychosis onset, possibly are related to a predisposition and reflect the first changes in experience that set off the development of schizophrenic psychotic (positive/negative) symptoms (Parnas 1999; Klosterkötter et al., 2001; Schultze-Lutter 2009).

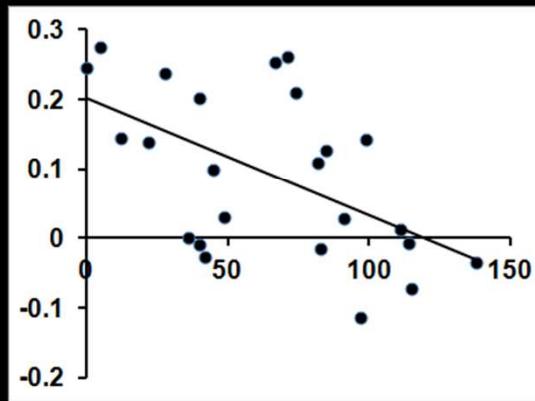




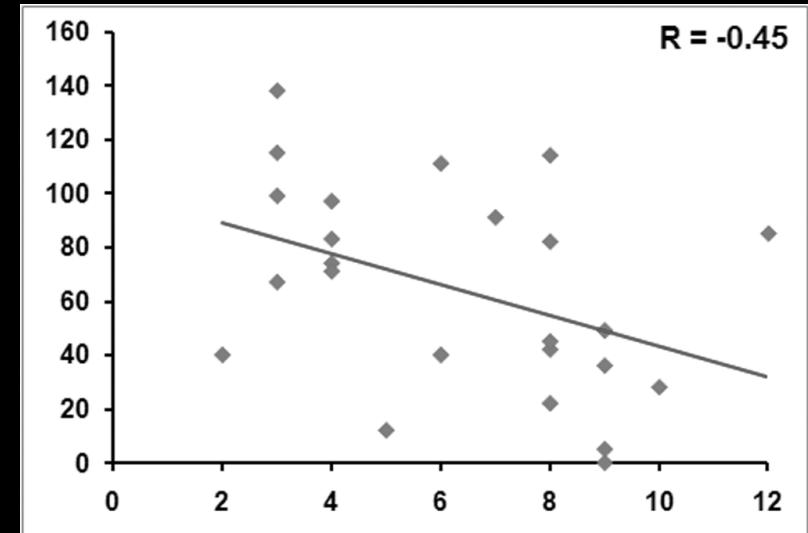
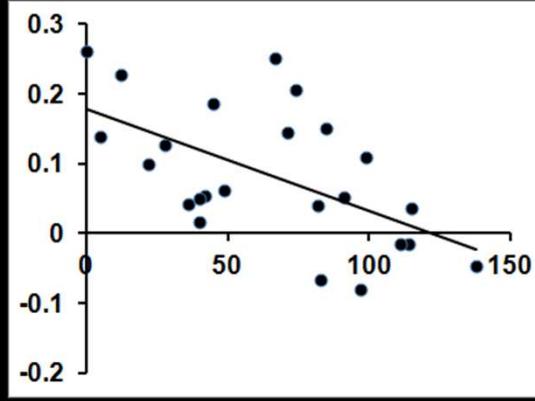
vPMC (54, 1, 32)
NEUTRAL - BS



vPMC (53, -1, 32)
CARESS - BS



vPMC (53, -1, 33)
HIT - BS



- **vPMC is the putative human homologue of monkey premotor area F4, integrating multisensory information from vision, touch and proprioception onto the motor representations of different body-parts, peripersonal space** (Bremmer et al. *Neuron* 2001; Gallese et al. *Curr Opin Neurobiol* 2002; Serino et al. *J Cogn Neurosci* 2011)
 - Altered BOLD in FES: disruption of an automatic multisensory representation of the bodily self
 - BS: close link between impaired multisensory representations in vPMC (F4) and a disrupted sense of a coherent self in everyday life
- **pIC: Interoception, self-awareness, self-other distinction based on pre-reflective suppression of self-oriented arousal**
 - Absent BOLD suppression in pIC: an impaired differentiation between self and other conditions during social perception in FES.

- Social perception at a pre-reflective level in FEP may be primarily characterized by altered neural activation patterns underlying self-disturbances
 - * self-other distinction
 - * multimodal representation of bodily self-experience
- Ipseity disturbances in schizophrenia may not be restricted to the realm of the self, but extend to the social domain
(Blankenburg 1971; Parnas et al. 2002; Gallese 2003; Nelson et al. 2009)

Altered Brain Long-Range Functional Interactions Underlying the Link Between Aberrant Self-experience and Self-other Relationship in First-Episode Schizophrenia

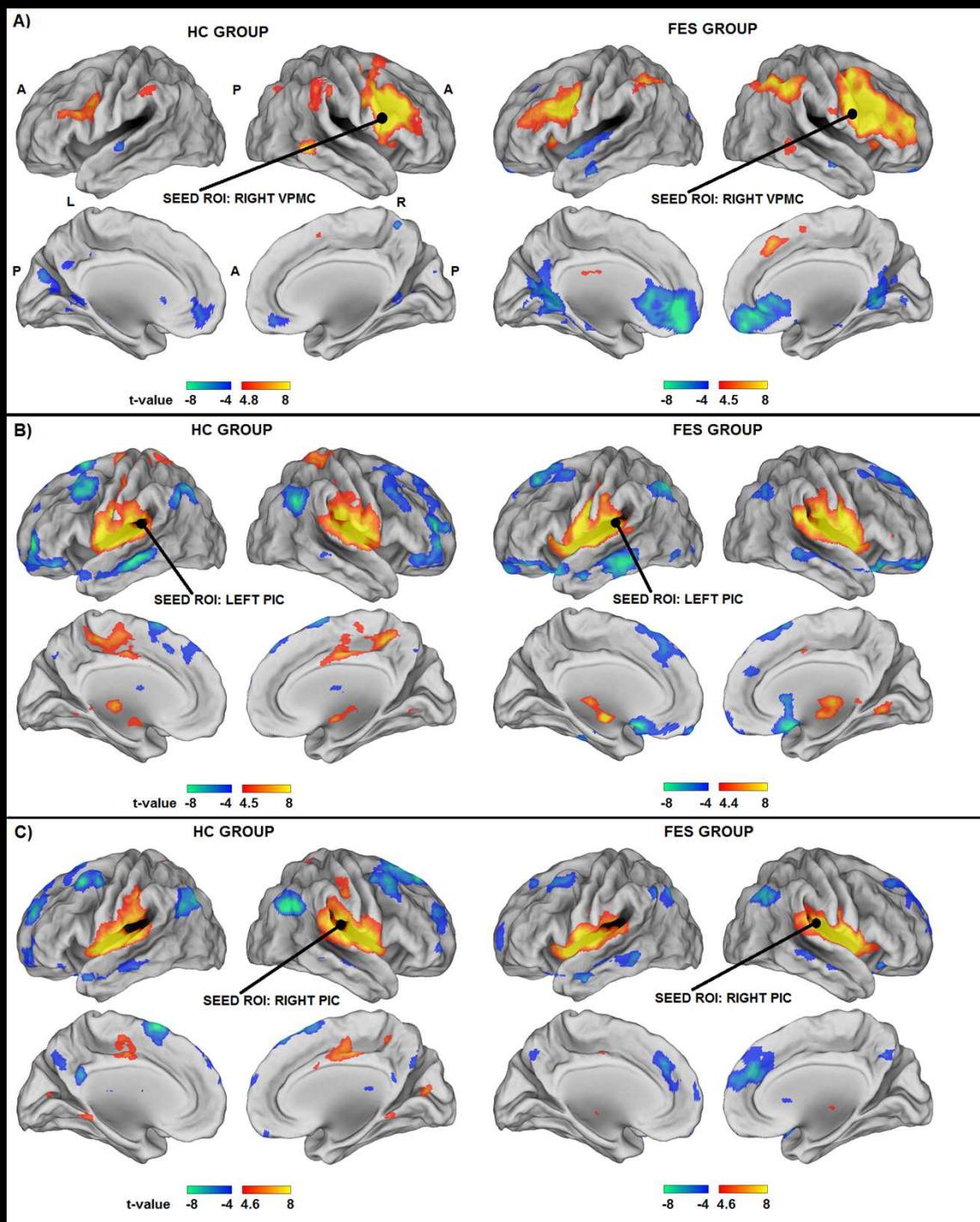
Schizophrenia Bulletin 2013

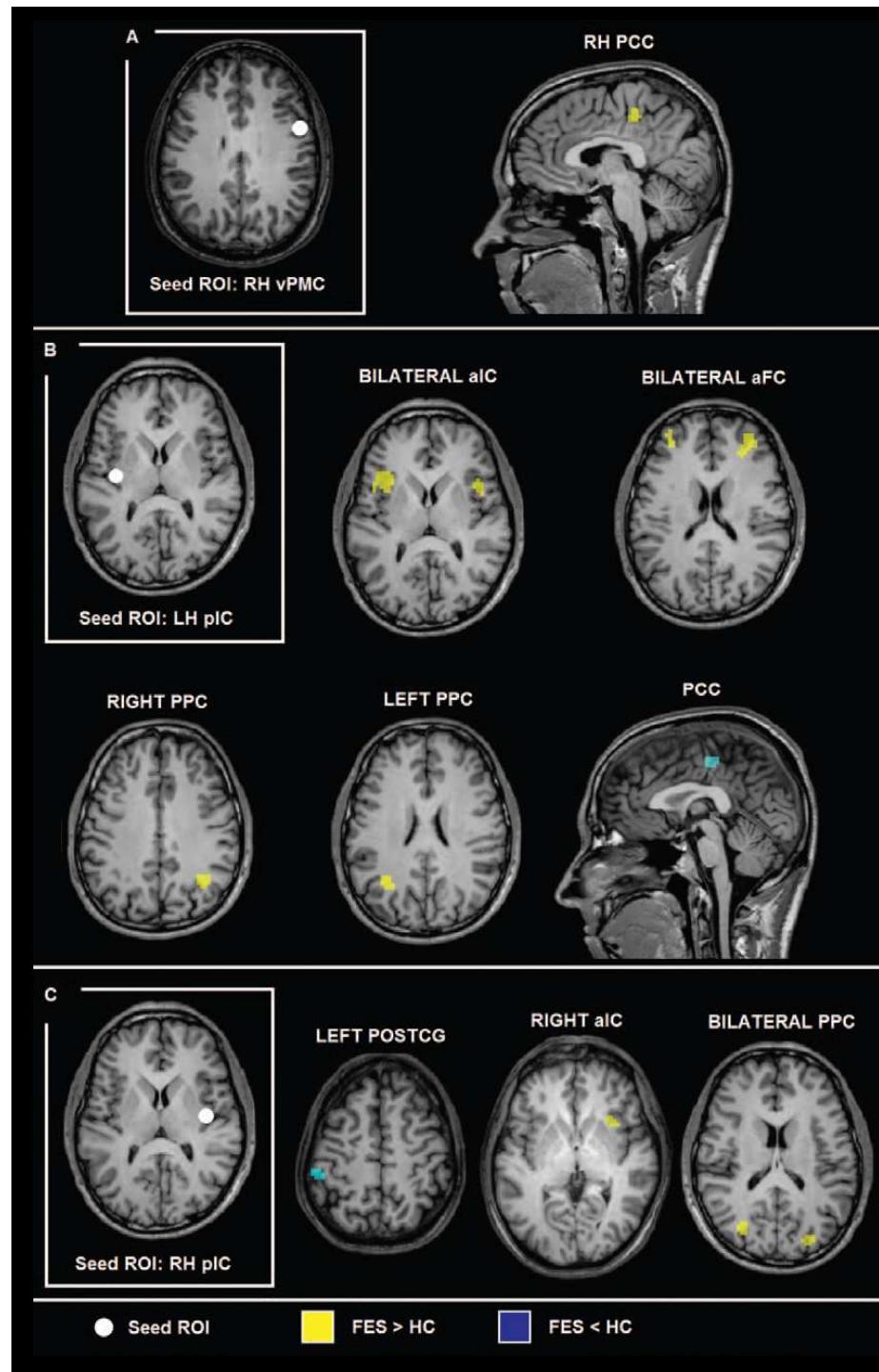
Sjoerd J. H. Ebisch ^{*,1,2}, Dante Mantini^{3,4}, Georg Northoff⁵, Anatolia Salone^{1,6}, Domenico De Berardis⁷, Francesca Ferri⁵, Filippo M. Ferro^{1,6}, Massimo Di Giannantonio^{1,6}, Gian L. Romani^{1,2}, and Vittorio Gallese^{8,9}

Framing focal brain dysfunction within a network perspective:

- How can impairments in self-other relationship in schizophrenia be related to altered functional interaction patterns?
 - can vPMC and pIC be characterized by altered neuro-functional interactions,
 - can these provide information complementary to task-evoked activation patterns,
 - can they be related to symptomatology?

- **Seed-based analysis of long-range functional interactions was performed identifying temporally correlated patterns of brain activity across brain regions** (Van Dijk et al. 2010; Fox & Raichle 2007; Fair et al. 2007; Power et al. 2012)
- **Voxel-wise, whole brain analyses for the 3 seed regions of interest (spheres, 6-mm radius):**
 - **right vPMC (Talairach coordinates: 50, 7, 32)**
 - **right pIC (Talairach coordinates: 38, -12, 7)**
 - **left pIC (Talairach coordinates: -38, -10, 7).**





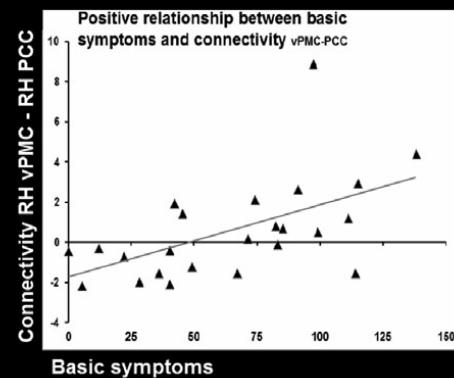
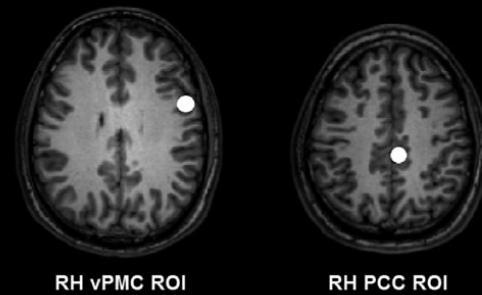
PCC

Black: 2/3 consensus
(seed-ROIs in right vPMC & left pIC)

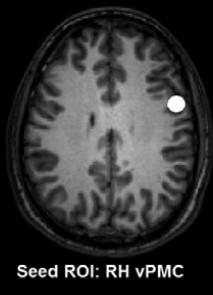
White: 3/3 consensus
(seed-ROIs in right vPMC and
bilateral pIC)



RESULTS OF ROI BASED APPROACH

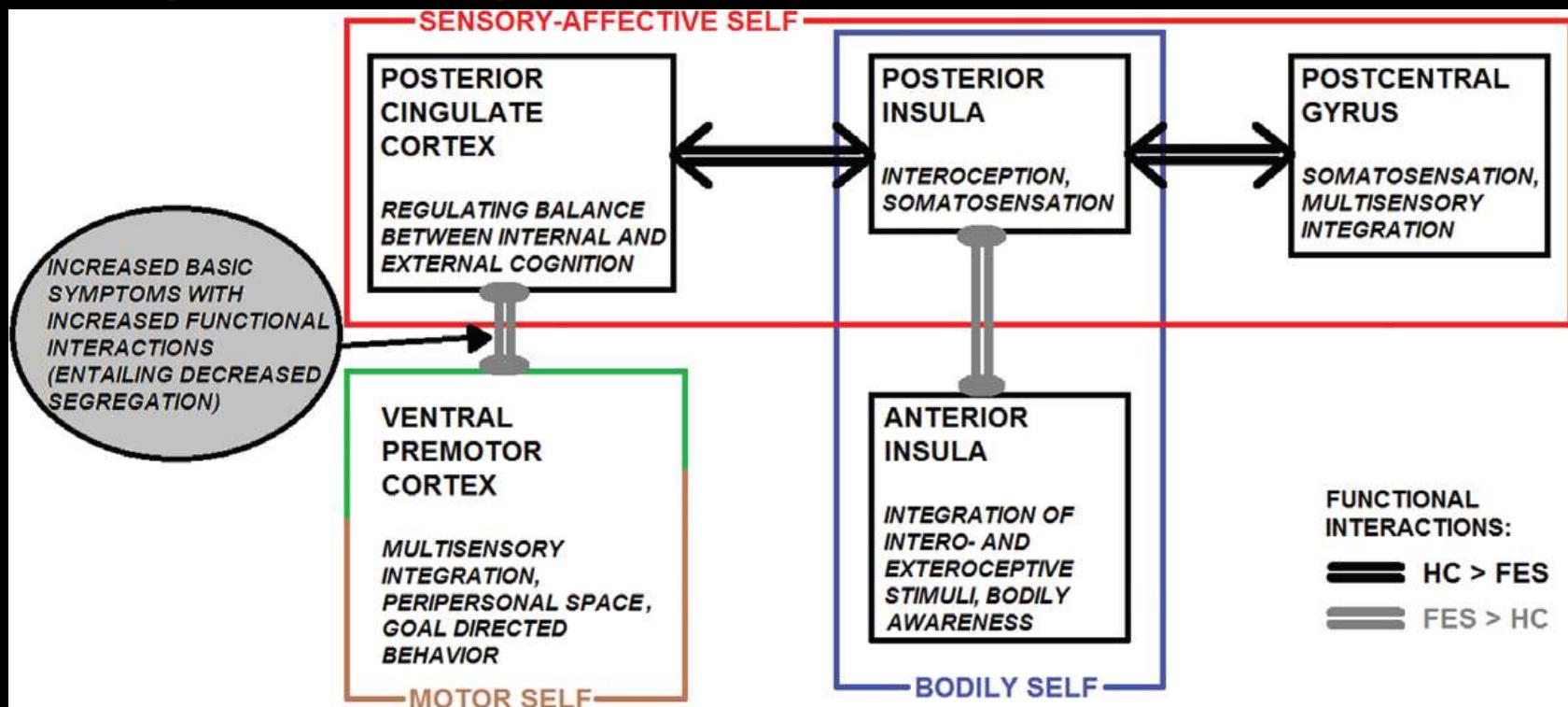


RESULTS OF VOXEL-WISE APPROACH



PCC voxels showing a significant correlation between RH vPMC connectivity and basic symptoms

First-episode schizophrenia



III. Schizofrenia

- **Un meccanismo neurale sottostante un'interazione deregolata tra un Sé sensoriale/affettivo afflitto e il suo ambiente (sociale) nella schizofrenia.**
- **Questi dati empirici nei pazienti cominciano a chiarire in modo originale le alterazioni cerebrali alla base di uno sbilanciamento nell'elaborazione di informazioni guidate internamente ed esternamente e l'integrazione anormale con l'esperienza del Sé.**
- **Questo sbilanciamento può essere mediato da PCC ed è strettamente legato all'esperienza del Sé anomalo nella schizofrenia.**

IV. Al comportamento sociale

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Come possiamo capire la mente di un altro e usare quelle informazioni per interagire in modo sociale con gli altri?



Qual è la rilevanza funzionale dei sistemi cerebrali che sono stati associati con percezioni personali e sociali di esperienze corporee per come ci comportiamo nelle interazioni con gli altri?

Reach Out and Touch Someone: Anticipatory Sensorimotor Processes of Active Interpersonal Touch

2014. Journal of Cognitive Neuroscience 26:9 , pp. 2171–2185

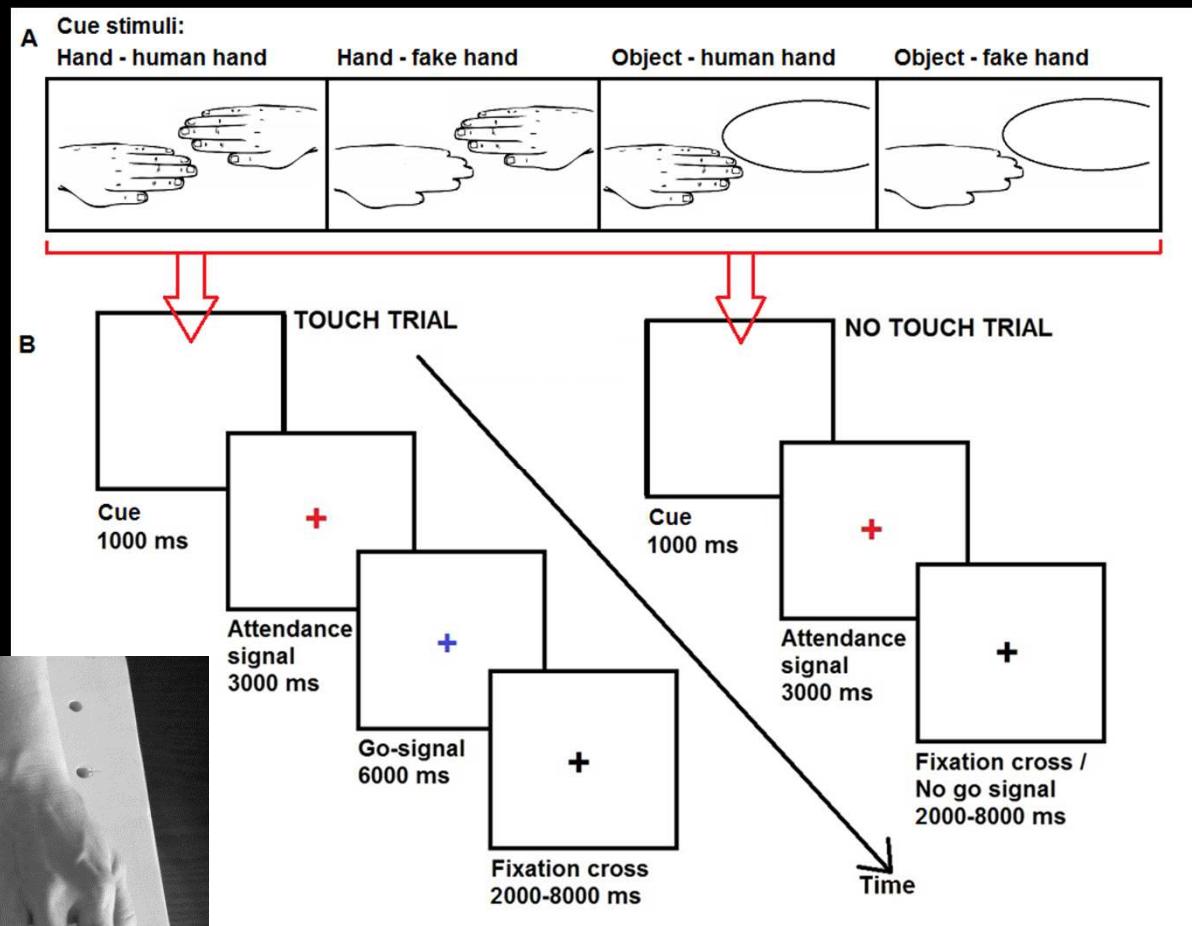
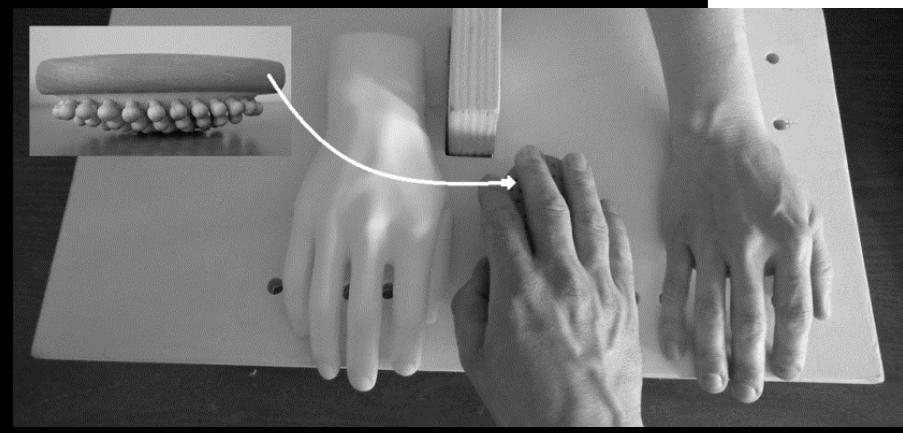
Sjoerd J. H. Ebisch¹, Francesca Ferri^{2,3}, Gian Luca Romani¹,
and Vittorio Gallese²

- **Social behavior requires appropriate motor coordination to obtain the intended consequences for other individuals** (Sebanz et al. 2006)
- **Social interaction: predicting both one's own personal sensorimotor experiences and others' behavior and experiences.**
- **Active interpersonal touch: intensity, velocity, and fine motor skills are regulated based on the expected sensation of both oneself and the other.**
- **Do sensorimotor brain circuits involved in the processing of first-person tactile experiences contribute to active interpersonal touch by anticipating not only one's own, but also others' experiences?**

- **Somatosensation:**
 - **elementary component of action consequences** (Blakemore & Sirigu, 2003) **and social cognition** (Gallese & Ebisch, 2013; Keysers, Kaas, & Gazzola, 2010).
 - **Sensory prediction for motor control** (Blakemore et al. 2001; Jackson et al. 2011)
 - **Predictive coding of others' peripheral sensations** (Bosbach et al. 2005; Ramsay et al. 2012; Morrison et al. 2012)

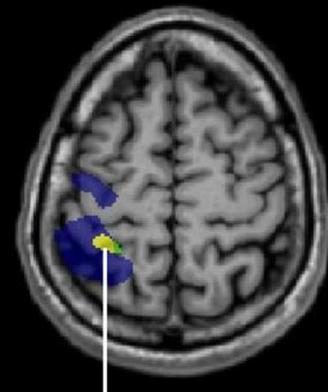
- **BA 2 and SII: direct reciprocal connections with multisensory integration areas intraparietal sulcus and aIPL** (Ishida et al. 2010, Keysers et al. 2010; Rozzi et al. 2006; Bremmer et al. 2001)
- **BA 2 projects to primary motor cortex** (Caria et al. 1997; Kaneko et al. 1994) **for motor control during haptic behavior** (Freund, 2003; Iwamura & Tanaka, 1996; Hikosaka et al. 1985).
- **aIPL** (PF/PFG, Caspers et al. 2006/2008):
 - **somatosensory and proprioceptive neurons discharging in association with movements - goal-directed motor acts** (Gallese et al. 2002; Hyvärinen 1982);
 - **transformation of sensory information into a motor format** (Rozzi et al., 2008);
 - **final goal of a performed action from the early phase of action unfolding** (Bonini et al., 2011);
 - **mirror neurons** (Fogassi et al. 2005; Bonini et al. 2010);
 - **touch observation and prediction** (Ebisch et al. 2008; Morrison et al. 2012).
- **aIPL - ventral premotor cortex connections: sensorimotor coupling underlying the integration of multisensory information with motor representations** (Rozzi et al. 2006; Gallese et al. 2002)

16 healthy participants (8 males, 8 females, age 20-32) underwent functional magnetic resonance imaging scanning at 3T (Philips Achieva) at the ITAB, Chieti.

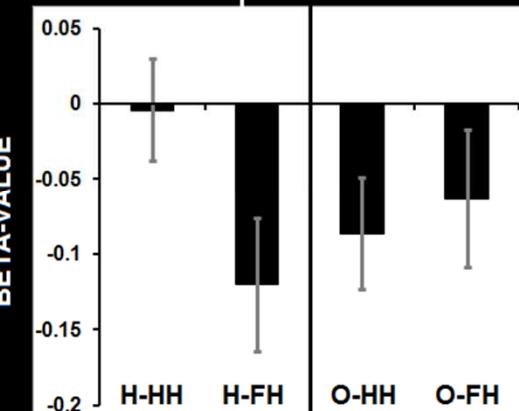


CONTRAST:
 $[(\text{HAND/HUMAN HAND} > \text{HAND/FAKE HAND}) - (\text{OBJECT/HUMAN HAND} > \text{OBJECT/FAKE HAND})]$

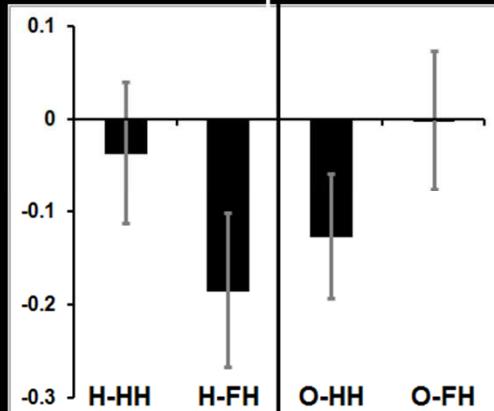
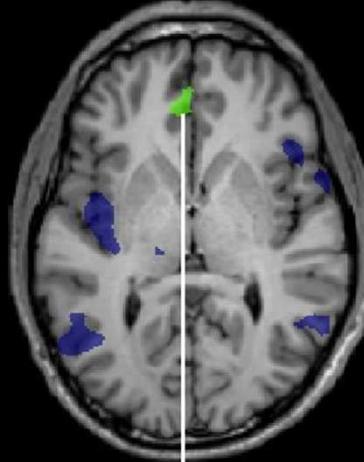
LEFT SI/BA2



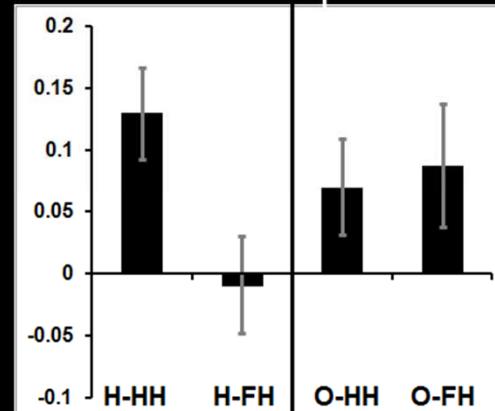
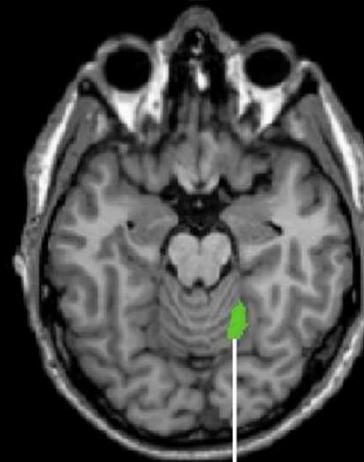
BETA-VALUE



LEFT MPFC



RIGHT CEREBELLUM



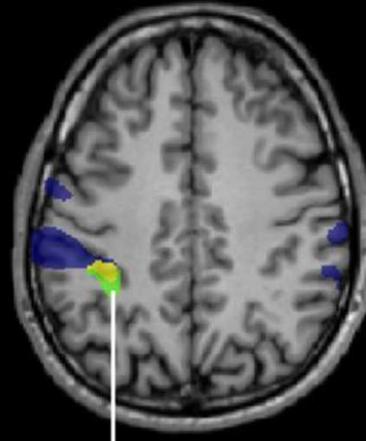
[█ BOLD MODULATION DUE TO A DIFFERENT TARGET (HUMAN HAND > FAKE HAND) OUTSIDE TACTILE LOCALIZER MASK

[█ BOLD MODULATION DUE TO A DIFFERENT TARGET (HUMAN HAND > FAKE HAND) INSIDE TACTILE LOCALIZER MASK

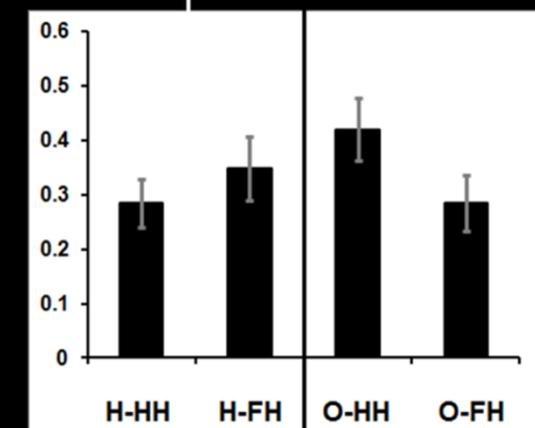
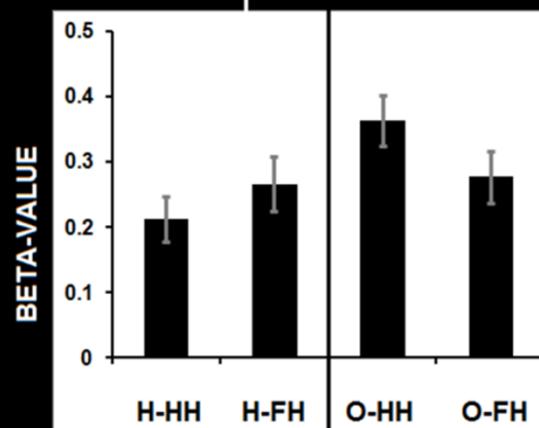
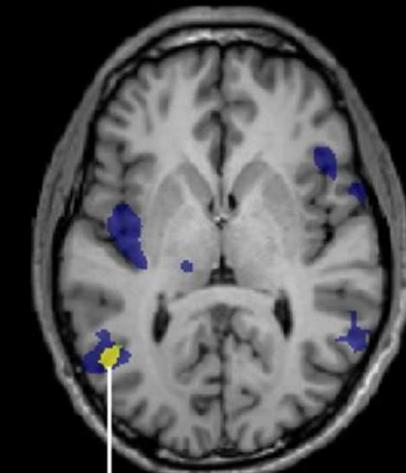
[█ TACTILE LOCALIZER MASK

CONTRAST:
[(OBJECT/HUMAN HAND > OBJECT/FAKE HAND) -
(HAND/HUMAN HAND > HAND/FAKE HAND)]

LEFT aIPL/PostCS



LEFT IOT



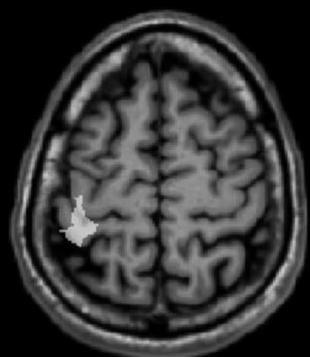
■ BOLD MODULATION DUE TO A DIFFERENT TARGET (HUMAN HAND > FAKE HAND)
OUTSIDE TACTILE LOCALIZER MASK

■ BOLD MODULATION DUE TO A DIFFERENT TARGET (HUMAN HAND > FAKE HAND)
OUTSIDE TACTILE LOCALIZER MASK

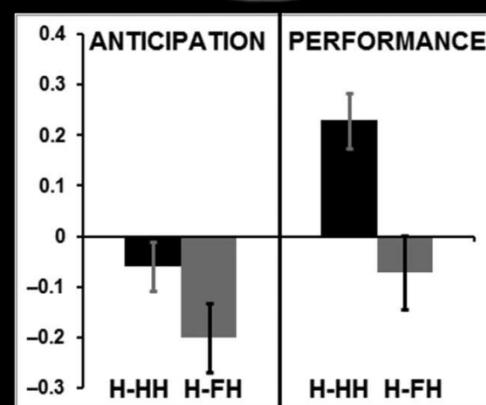
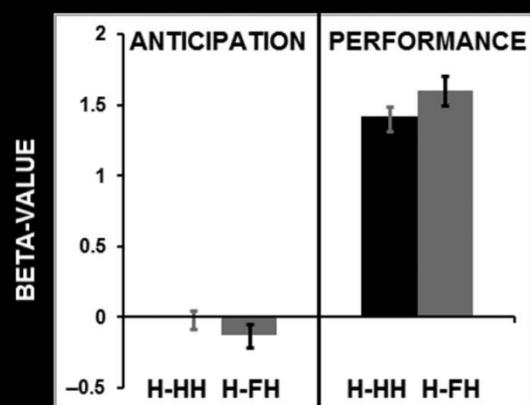
■ TACTILE LOCALIZER MASK

CONJUNCTION CONTRAST:
[(HAND/HUMAN HAND > HAND/FAKE HAND) ANTICIPATION
 \cap
(HAND/HUMAN HAND > HAND/FAKE HAND) PERFORMANCE]

LEFT SI/BA 2



LEFT MPFC



- **Cerebellum: altering the perception of the effect of one's action by providing predictions about the sensory consequences of motor commands** (Hughes et al. 2013; Blakemore, et al. 2000; Wolpert et al. 1998).
- **Effects in both SI and cerebellum are in line with sensory prediction in the cerebellum modulating activity in somatosensory cortices when tactile stimuli are self-generated** (Blakemore et al. 1999; Bastian 2006; Wolpert et al. 1998): **amplifying/attenuating sensory consequences.**
- **Stronger deactivation in MPFC for inanimate touch anticipation: anticipatory suppression of social reasoning processes** (Schippers et al. 2010; Gilbert et al. 2007)

- **Multisensory regions associated with social perception of touch - aIPL, PostCS and IOT - activate in anticipation of active interpersonal touch without the need for any sensory input.**
 - **Incorporation of the predicted sensory experiences of the person who is going to be touched by mapping them onto the somatosensory representation of our own tactile experiences** (Keysers et al., 2010, Gallese & Eibisch 2013).
- **Others' predicted somatosensory experiences could be integrated with motor programs in aIPL/PostCS, supporting action coordination when individuals interact** (Sebanz et al., 2006), like the regulation of active interpersonal touch.