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Abstract

Tactile perception on one's own face is enhanced when viewing a fearful face being touched – as opposed to just approached – by fingers, compared to viewing other expressions, a phenomenon known as the emotional modulation of Visual Remapping of Touch (eVRT). This effect seems to be related to a preferential activation of the somatosensory system in response to threat. To test the contribution of the amygdala to this mechanism, a group of patients with unilateral lesions to the amygdala, a control group of patients with lesions in the extra-temporal regions and a group of healthy participants completed an eVRT paradigm. They were required to detect bilateral tactile stimulation on their own cheeks, while viewing fearful, happy or neutral faces being touched or just approached by fingers. Healthy participants and control patients confirmed that viewing a neutral face being touched -as opposed to just approached- by fingers increases tactile detection on one's own face (i.e., the typical VRT effect) and that this effect is enhanced for fearful faces, compared to neutral and happy faces. However, in patients with amygdala lesion, although the standard VRT effect was preserved for neutral faces, this was disrupted for fearful faces. This result indicates that the preferential activation of the somatosensory cortices in response to threat relies on structural integrity of the amygdala.

1. Introduction

Facial expressions represent a powerful nonverbal display of emotion, signaling valuable information about other people's intentions and inner states, in order to provide appropriate responses in social interactions. Understanding others' emotions is thought to involve a mechanism of internal representation, where the emotional state of the other is simulated in one's own sensory system (Gallese & Sinigaglia, 2011; Goldman & Sripada, 2005; Niedenthal, 2007; Niedenthal, Augustinova, & Rychlowska, 2010). This embodied emotion simulation relies on the activation of a distributed sensorimotor network, involving premotor, somatosensory, insular and anterior cingulate cortices and the amygdalae (Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003; Jabbi, Swart, & Keysers, 2007; Singer et al., 2004; Wicker et al., 2003).

In particular, the somatosensory cortices appear to actively participate in the processing of emotional facial expressions, as revealed by fMRI (Winston, O'Doherty, & Dolan, 2003) and lesional studies (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000). Crucially, it has been demonstrated that disrupting the somatic simulation of emotions by targeting the right somatosensory cortex with repetitive transcranial magnetic stimulation (rTMS) compromise the ability of recognizing several visually presented emotional expressions (Pitcher, Garrido, Walsh, & Duchaine, 2008). However, the level of internal somatic representation in somatosensory cortices for the processing of emotional faces might vary in response to different emotional expressions (Hussey & Safford, 2009). Indeed, Pourtois et al. (2004) showed that single pulse TMS to the right somatosensory cortex selectively interferes only with recognition of fearful expressions, suggesting a preferential involvement of the somatosensory cortex in processing fear. Since fearful faces represent a highly arousing emotional signal, such preferential activation in the somatosensory cortex might represent an evolutionary adaptive feature, critical for survival. Indeed, the presence of a fearful face might signal a potential threat in the environment requiring a rapid and appropriate defensive response.

In relation to this, the preferential activation of somatosensory cortices in response to fearful faces might depend on modulatory ascending signals conveyed through long-range connections from the amygdala to the cortex (Abivardi & Bach, 2017). In keeping, because of its broad connectivity with cortical sensory and prefrontal cortices (Amaral, Pitkanen, & Carmichael, 1992; Young, Scannell, Burns, & Blakemore, 1994), the amygdala represents a subcortical structure ideally situated to influence cognitive functions in reaction to emotional stimuli (Phelps, 2006). More specifically, the amygdala has been widely reported to be a core-face selective region (Mende-Siedlecki, Verosky, Turk-Browne, & Todorov, 2013; Todorov, 2012), responding to a variety of emotional facial traits and expressions (Anderson, Christoff, Panitz, De Rosa, & Gabrieli, 2003). Indeed, amygdala responses have been shown to track the arousal, the valence and the predictive uncertainty of facial expression (Whalen et al., 2013; Kim et al., 2003; Kim et al., 2017). Moreover, since pioneering physiological studies on animals (Kapp, Frysinger, Gallagher, & Haselton, 1979; Kapp, Whalen, Supple, & Pascoe, 1992), the amygdala has been suggested to be a necessary component of the neural circuits mediating responses to fear (for recent reviews: Adolphs, 2013; LeDoux, 2014). Notably, neuro-imaging meta-analysis (Fusar-Poli et al., 2009; Phan, Wager, Taylor, & Liberzon, 2002; Vytal & Hamann, 2010), animal models (Davis, 1994), single-unit recordings (Maren, 2001) and lesional studies (Adolphs, Tranel, Damasio, & Damasio, 1994) have suggested a prominent role of the amygdala in processing threat-related faces.

Based on these premises, to test the contribution of the amygdala to the preferential activation of the somatosensory cortices in response to threat, a group of patients with unilateral lesions to the amygdala following temporal lobectomy, a control group of patients with lesions in the extratemporal regions and a group of healthy participants were tested in a multisensory paradigm called Visual Remapping of Touch (VRT; Serino, Pizzoferrato, & Làdavas, 2008). In VRT, viewing a face being touched - as opposed to merely approached - by fingers increases the detection of near-threshold tactile stimuli on one's own face. This visually evoked tactile enhancement relies on an increased activity in a fronto-parietal network of pre-motor cortices and somatosensory cortices

(SI/SII; Cardini et al., 2011), responsible for processing tactile information (Macaluso, 2006), suggesting a mechanism of remapping of the tactile sensation seen on the body of others onto one's own somatosensory system (Blakemore, Bristow, Bird, Frith, & Ward, 2005; Ebisch et al., 2008). This effect has also been demonstrated to be specific for human faces, since touch on a non-human face (i.e., a monkey face) seems not to be remapped onto the somatosensory system of human observers (Beck, Bertini, Scarpazza, & Làdavas, 2013). Notably, the VRT effect is modulated by the emotional content of the seen face (Beck et al., 2013; Cardini, Bertini, Serino, & Ladavas, 2012; Scarpazza, di Pellegrino, & Làdavas, 2014; Scarpazza, Làdavas, & Pellegrino, 2015), with participants showing an enhanced performance in bilateral tactile detection when viewing touch on a fearful face, compared to neutral or happy faces, but also compared to other negatively-valenced emotional faces, such as disgusted or angry faces. This suggests that the VRT can be enhanced specifically in the presence of fearful faces and this effect has been attributed to a preliminary activation of the somatosensory system in response to threat, probably due to a partial overlap between the networks subserving visuo-tactile interactions (Cardini et al., 2011) and embodied emotion recognition (Keysers et al., 2004). The preparatory activation of the somatosensory cortex might facilitate the processing of tactile information delivered on the participant's face, while viewing touch towards a fearful face. Indeed, due to the highly adaptive value of rapid recognition of fear, participants could be more prone to remap the fear-specific information onto their own somatosensory system. Since the activity of the amygdala is responsible for updating the relevance of the features in the environment and signaling sources of potential harm (Jacobs, Renken, Aleman, & Cornelissen, 2012; Whalen, 1998), the involvement of this subcortical structure in the emotional modulation of VRT seems plausible. Viewing a fearful face being touched and concurrently perceiving touch on one's own face represents an ambiguous event, in which the amygdala could signal the existence of a potential threat, requiring a prioritized sensory analysis. In line, patients with lesions to the amygdala are expected to show a disruption of the preferential activation of the somatosensory cortex and, therefore, no enhancement in VRT when viewing touch

towards fearful faces, while patients with lesions not involving the amygdala and healthy controls are expected to show the typical fear-related VRT enhancement. However, similarly to healthy controls and patients with lesions not involving the amygdala, patients with lesions to the amygdala are expected to show the typical visual remapping effect with neutral and happy faces.

2. Methods

2.1. Participants

All the participants were right-handed, had normal or corrected-to-normal vision, reported normal touch, and were naïve to the purposes of the experiment. They all gave informed consent to participate (for minor patient P8, both the patient and parents signed the consent). The study was conducted according to the Declaration of Helsinki (BMJ 1991; 302:1194) and the Local Ethical Committee.

2.1.1. Patients with lesions to the amygdala (AMG)

Ten patients (P1-P10; see Table 1) were selected after complete amygdalohippocampectomy, to remove low grade tumors, in either the left (n=5) or right hemisphere (n=5). At the time of the study the age of patients ranged between 13 and 64 years (M=28.4, SD=15.3). Before surgery, all patients suffered from mesial temporal lobe epilepsy. When tested, all patients were seizure free for more than 1 year (M=4.7, SD=4.2, range: 1-12) and were treated with one or two AED in a stable regimen.

2.1.2. Patients with extra-temporal lesions (EXTRA-TEMPORAL)

Nine patients (P11-P19; see Table 1) were selected after extra-temporal resective surgery, to remove low grade tumors. At the time of the study the age of patients ranged between 18 and 49 years (M=29.8, SD=14.9). Before surgery, all patients suffered from epilepsy, but at testing, all of

them were seizure free for more than 2 years (M=7.4, SD=4.7, range: 2-14) and were treated with one or two AED in a stable regimen.

2.1.3. Healthy controls participants

Ten age-matched participants took part into the study (age in years: M=29, SD=15; range: 19-57). All participants had no history of epilepsy and neurological or psychiatric diseases.

2.2. Neuropsychological assessment

A formal neuropsychological assessment, including cognitive level (i.e. IQ), attention, executive functions, memory and visuo-spatial abilities was carried out after surgery at the time of the present study. Assessment was performed with standardized instruments validated on an Italian sample (Spinnler & Tognoni, 1987; Tressoldi, Vio, Gugliotta, Bisiacchi, & Cendron, 2005). All patients showed normal IQ and normal neuropsychological functions, excepting for patients P2 who showed defective verbal memory and P17 and P19 who showed defective long term visuo-spatial memory. In adult participants, mood and anxiety were assessed with Beck depression Inventory-II (BDI-II; Beck, Steer, & Brown, 2014) and State-Trait Anxiety Inventory (STAI I and II; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). In the minor participant (P8), mood and anxiety were assessed with the Child Behavior Checklist (CBCL; Achenbach and Rescorla, 2001) and the Scale Psichiatriche di Autosomministrazione per Fanciulli e Adolescenti (SAFA; Cianchetti and Fancello, 2008). All patients showed normal emotional well-being, with the exception of patient P3 who presented mild symptoms of anxiety and depression.

2.3. Lesion analysis

Mapping of brain lesions was based on the most recent clinical CT or MRI. Lesions were traced on the T1-weighted template MRI scan from the Montreal Neurological Institute provided with the MRIcron software (Rorden, Bonilha, & Nichols, 2007; Rorden & Brett, 2000). Left lesions were traced on the left hemisphere and then flipped to the right one. Lesion volumes were computed for

patients whose images were available (9 in the AMYGDALA and 8 in the EXTRA-TEMPORAL group) and the extents of the lesions were compared between the groups of patients. The independent samples t-test revealed no significant differences between patients with lesions to the amygdala (M=21935 mm^3) and patients with extra-temporal lesions (M=11015 mm^3; t(15)=1.87; p=.08).

As showed in Figure 1, all patients in the AMYGDALA group showed damage that included the amygdala, though also areas adjacent to the amygdala (e.g. temporal pole, fusiform gyrus, hippocampus and parahippocampus) were damaged to variable extent. Patients with extra-temporal lesions revealed lesions in the frontal lobe (n=3), in the parietal lobe (n=1), in the regions surrounding the third ventricle (n=3), in the head of the caudatus (n=1) and in the pituitary gland and thalamus (n=1). Notably, patients in both groups revealed no lesions to the somatosensory cortices.

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2.4. Emotional Visual Remapping of Touch (eVRT) task

The eVRT task is a multisensory integration paradigm consisting of both tactile and visual stimuli. We used the same experimental procedure used in previously published studies (Beck et al., 2013; Cardini et al., 2012; Scarpazza et al., 2014, 2015). Tactile stimuli were delivered by two constant current electrical stimulators (DS7A, Digitimer), via two couples of neurological electrodes (Neuroline, AMBU) placed on participants' right and left cheeks. Crucially, the tactile stimulus delivered to one cheek (i.e. strong stimulus) was set to be more intense than that delivered to the other (i.e. weak stimulus) (the location was counterbalanced among participants). Prior to the beginning of the experimental task, each participant looked at static, neutral faces while the intensity of the electrical stimuli was calibrated with a staircase procedure to a threshold detection rate of ~100% for the strong stimulus and ~60% for the weak stimulus. As a confirmation of correct

calibration of the stimuli, the mean accuracy (±s.e.m.) for unilateral stimuli was 92%±2% for strong stimuli and 70%±3% for weak stimuli (paired sample t –test: $p<.001$; see table 2 for group details). This stimulus calibration results in a tendency for participants to fail to report the weak stimulus during trials with bilateral stimulation. Mean accuracy (±s.e.m.) for bilateral tactile detection was 56%±3% (AMYGDALA 58%±4%, EXTRA-TEMPORAL 53%±5%, CONTROL 58%±5%; $F(2,26)=0.42$; $p=.66$; $\eta^2=.03$). Errors consisted mostly in reporting the side of the strong stimulus: probability 92%±2% (AMYGDALA 97%±1%, EXTRA-TEMPORAL 85%±7%, CONTROL 94%±2%; $F(2,26)=2.30$; $p=.11$; $\eta^2=.15$).

Visual stimuli consisted of a face presented as a central, static image in the background of a movie showing two fingers positioned on the lower part of the screen, one on the right and one on the left, which moved towards the face and then returned to their initial position. On each trial, either the finger on the right (i.e. unilateral right), on the left (i.e. unilateral left) or both fingers (i.e. bilateral) moved. Finger-motion followed one of two trajectories: i) the fingers touched the cheeks of the shown face in the same position where tactile stimulation on the participants' cheeks was administered (i.e. Touch condition); ii) the fingers stopped about 5 cm alongside the face (i.e. No-Touch condition; Figure 2). Faces were black-and-white pictures selected from the Pictures of Facial Affect (PFA) database (Ekman & Friesen, 1976) and had neutral, fearful or happy expressions, presented in three different counterbalanced blocks. The neutral faces used in the experimental task were different from the faces used during tactile stimuli calibration. Overall, 6 different actors (3 males and 3 females) were used. Male participants were presented with images of male actors, while female participants were presented with images of female actors. Visual and tactile stimuli were synchronized so that when the fingers reached the peak of their trajectory a tactile stimulus was delivered to the participant's face. Each movie lasted 2700 ms and tactile stimulation was delivered 700 ms after movie onset.

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A PC running a custom-made software was used to control the presentation of the stimuli and record participants' responses. Visual stimuli were presented on a 17" computer screen placed in front of the participant at a distance of about 60 cm. The experimental task consisted of 6 counterbalanced blocks (2 for each emotion) of 48 trials each. Stimuli were randomly presented and comprised a combination of the two types of tactile stimulation (unilateral left/right and bilateral), the two types of visual stimulation (unilateral left/right and bilateral) and the two finger movement trajectories (Touch and No-Touch). A pause of 3 minutes, during which tactile thresholds were recalibrated, was interposed between blocks.

Statistical analysis was conducted on mean participants' accuracy in detecting bilateral tactile stimulation when viewing both fingers touching (Touch) or not touching (No-Touch) the faces.

2.5. The Ekman 60 Faces Test

After eVRT, participants underwent The Ekman 60 Faces Test, investigating the recognition of six basic emotions (anger, disgust, fear, happiness, sadness and surprise) from the Ekman and Friesen series of Pictures of Facial Affect (Ekman & Friesen, 1976). Photographs of the faces of 10 models (6 females and 4 males) were presented. Each model was presented in six different poses, corresponding to each one of the six basic emotions. Different models and emotions were interspersed. Each face was presented on an A4 sheet with the six labels of the basic emotions written below the photograph. Participants were required to verbally indicate the appropriate label describing the presented facial expression. For each basic emotion, the maximum score was 10, resulting in a maximum total score of 60.

3. Results

3.1. Lesion to the amygdala impairs Visual Remapping of Touch (VRT) when seeing fearful faces

In order to investigate the effect of the emotional content of the viewed face on the VRT effect, subjects' accuracy during bilateral tactile stimulation was compared when viewing both fingers touching (Touch) or not touching (No-Touch) the faces. The 3x3x2 analysis of variance (ANOVA; Group: AMYGDALA, EXTRA-TEMPORAL, CONTROL; Emotion: Fear, Happy, Neutral; Finger Trajectory: Touch, No-Touch) on bilateral stimulation detection accuracy revealed a main effect of Finger Trajectory ($F(1,26)=80.04$; $p<.001$; $\eta^2=.75$). Newman-Keuls post-hoc test indicated that seeing a face being touched enhanced bilateral stimulation detection accuracy compared to when the face was not touched (Touch: M=66.57%, No-Touch M=55.25%), confirming the VRT effect. Crucially, the Group x Emotion x Finger Trajectory interaction was significant ($F(4,52)=10.68$; $p<0.001$; $\eta^2=.45$). Consequently, a 3x2 ANOVA (Emotion: Fear, Happy, Neutral; Finger Trajectory: Touch, No-Touch) on bilateral stimulation detection accuracy was performed on each group, separately.

In the AMYGDALA group (Figure 3a), no significant main effect of Emotion ($F(2,18)=0.88$; $p=.43$; $\eta^2=.09$) or Finger Trajectory ($F(1,9)=3.43$; $p=.1$; $\eta^2=.27$) was found. On the contrary, the critical Emotion x Finger Trajectory interaction was significant ($F(2,18)=6.10$; $p=.009$; $\eta^2=.40$). Newman-Keuls post-hoc tests showed that seeing a face being touched enhanced bilateral stimulation detection accuracy compared to when the face was not touched for neutral faces (Touch: 74.5%, No-Touch: 61%, p=.007), but not for happy (Touch: 68.4%, No-Touch: 65.2%, p=.34) and, crucially, fearful (Touch: 61.4%, No-Touch: 63.9%, p=.46) faces. Also, when faces were not touched, there was no difference in bilateral stimulation detection accuracy between the three emotions (fear vs happy: p=.70; fear vs neutral: p=.66; happy vs neutral: p=.59). In contrast, when faces were touched, the bilateral stimulation detection accuracy for neutral faces did not differ from happy faces (p=.08) but was, indeed, higher compared to fearful faces (p=.007). Additionally, because null hypothesis significance testing cannot directly assess whether the current data favor the null hypothesis (i.e. no difference in bilateral stimulation detection accuracy between touch and no-touch conditions for fearful faces / lack of eVRT effect in the amygdala group) over the

alternative hypothesis, we complemented current analyses with Bayesian analyses. This allowed us to directly evaluate the relative strength of evidence for the null and alternative hypotheses (Dienes, 2011; Wagenmakers et al., 2018). Using JASP v 0.9.0.1 (JASP Team, 2018), we conducted a series of Bayesian paired-samples t-tests comparing bilateral stimulation detection accuracy in touch and no-touch conditions for each emotional facial expression (default JASP priors: zero-centered Cauchy distribution, prior width r = 0.707). We report subscripts on Bayes Factors to refer to the models compared. Accordingly, BF_{10} denotes the Bayes Factor for the alternative relative to the null hypothesis, while BF_{01} the Bayes Factor for the null relative to the alternative hypothesis. We interpreted the sizes of BFs according to the recommendations of Raftery (1995) as referred to by Jarosz and Wiley (2014). Regarding neutral and happy faces, the Bayesian paired-sample t-tests showed respectively positive and weak evidence supporting the alternative hypothesis (neutral: BF_{10}=8.32, happy: BF_{10}=1.00). Crucially, for fearful faces, the t-test showed weak evidence supporting the null hypothesis (BF_{01}=2.90) of no difference in bilateral stimulation detection accuracy between touch and no-touch conditions.

In the EXTRA-TEMPORAL group (Figure 3b), no significant effect of Emotion ($F(2,16)=0.76$; $p=.48$; $\eta^2=.09$) was found. In contrast, there was a main effect of Finger Trajectory ($F(1,8)=36.82$; $p<.001$; $\eta^2=.82$), which should be interpreted in light of the significant Emotion x Finger Trajectory interaction ($F(2,16)=8.45$; $p=.003$; $\eta^2=.51$). Post-hoc tests within each emotion showed that seeing a face being touched enhanced bilateral stimulation detection accuracy compared to when the face was not touched not only for neutral faces (Touch: 60.9%, No-Touch: 50.8%, p=.01) but also for fearful faces (Touch: 74.7%, No-Touch: 50.7%, p<.001), but not for happy faces (Touch: 56.8%, No-Touch: 50.3%, p=.22). Moreover, when faces were not touched, there was no difference in the accuracy of bilateral stimulation detection between the three emotions (fear vs happy: p=.92; fear vs neutral: p=.97; happy vs neutral: p=.99). On the contrary, when faces were touched, seeing a fearful face enhanced bilateral stimulation detection accuracy compared to seeing a neutral or happy face (all ps<.001). Additionally, all Bayesian paired-sample t-tests provided support for the alternative

hypothesis. Specifically, regarding neutral and happy faces both t-tests showed positive evidence for the alternative hypothesis (neutral: BF_{10}=10.09, happy: BF_{10}=8.32). Crucially, contrary to the AMYGDALA group, the t-test for fearful faces showed strong evidence supporting the alternative hypothesis (BF_{10}=54.27).

In the CONTROL group (Figure 3c), no significant effect of Emotion ($F(2,18)=1.61$; $p=0.23$; $\eta^2=.15$) was found. In contrast, there was a main effect of Finger Trajectory ($F(1,9)=83.13$; $p<.001$; $\eta^2=.90$), which should be interpreted in light of the significant Emotion x Finger Trajectory interaction ($F(2,18)=24.52$; $p<.001$; $\eta^2=.73$). Post-hoc tests within each emotion showed that seeing a face being touched enhanced bilateral stimulation detection accuracy compared to when the face was not touched not only for neutral (Touch: 66.2%, No-Touch: 51.5%, $p<.001$) but also for fearful faces (Touch: 77.5%, No-Touch: 48.8%, $p<.001$), but not for happy faces (Touch: 58.1%, No-Touch: 53.7%, $p=.09$). Moreover, when faces were not touched, there was no difference in the accuracy of bilateral stimulation detection between the three emotions (fear vs happy: $p=.14$; fear vs neutral: $p=.29$; happy vs neutral: $p=.38$). On the contrary, when faces were touched, seeing a fearful face enhanced the accuracy of bilateral stimuli detection compared to seeing a neutral or happy face (all $ps<.001$). Also, similarly to the EXTRA-TEMPORAL group, all Bayesian paired-sample t-tests provided support for the alternative hypothesis. Specifically, regarding neutral and happy faces the t-tests showed respectively strong and weak evidence for the alternative hypothesis (neutral: BF_{10}=57.08, happy: BF_{10}=1.76). Crucially, contrary to the AMYGDALA group, the t-test for fearful faces showed strong evidence supporting the alternative hypothesis ($BF_{10}=3.51*10^3$).

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To further explore the differences between the groups in VRT performance with emotional faces, an emotional VRT index was calculated, subtracting the accuracy of bilateral stimuli detection in the No-Touch condition from the Touch condition (VRT index = Touch – No-Touch). The 3x3 ANOVA (Group: AMYGDALA, EXTRA-TEMPORAL, CONTROL; Emotion: Fear, Happy and

Neutral) on VRT indices revealed a significant Group x Emotion interaction ($F(4,52)=10.68$, $p<.001$; $\eta^2=.45$). The post-hoc test showed that the VRT index for happy and neutral faces did not differ between the three groups (all $p>.47$). On the contrary, the VRT index for fearful faces was smaller in AMYGDALA (-2.5%) than in EXTRA-TEMPORAL (24%, $p<.001$) and CONTROL (28.7%, $p<.001$) groups, whereas no difference was detected between EXTRA-TEMPORAL and CONTROL ($p=.32$) groups.

To control for a possible effect of lesion volume on the VRT results, we performed a 2x3 ANOVA (Group: AMYGDALA, EXTRA-TEMPORAL; Emotion: Fear, Happy and Neutral) on VRT indices using lesions volumes as covariate. Importantly, no significant main effect ($F(1,14)=2.93$, $p=.11$; $\eta^2=.17$) or interaction ($F(2,28)=0.06$, $p=.94$; $\eta^2=.004$) of the lesion volumes was found. In addition, the analysis confirmed the results of the previous ANOVA, revealing a significant Group x Emotion interaction ($F(2,28)=7.74$, $p=.002$; $\eta^2=.35$). The post-hoc test showed that while the VRT index for happy and neutral did not differ between the two groups (all $p>.55$), the VRT index for fearful faces was smaller in AMYGDALA (-3.67%) than in EXTRA-TEMPORAL (24%, $p=<.001$) group.

3.2. No difference between groups in the identification of emotional faces in The Ekman 60 Faces Test

The Kruskal-Wallis ANOVA (Group: AMYGDALA, EXTRA-TEMPORAL, CONTROL) on total scores revealed no significant difference between groups ($H(2,29)=1.43$; $p=0.49$; AMYGDALA: 51±1.76; EXTRA-TEMPORAL: 51.7±1.03; CONTROL: 52.7±1.60). In addition, to investigate the presence of deficits in the recognition of specific categories of emotional faces, the scores of the participants for each single emotion were compared with Kruskal-Wallis ANOVAs, using group (AMYGDALA, EXTRA-TEMPORAL, CONTROL) as a factor. The results revealed no significant differences between the groups in each of the emotions (all ps >. 28).

3.3. Voxel-based Lesion-Symptom Mapping

Because patients' lesions are not confined to the amygdale, but involve a consistent part of the temporal pole in many cases (Figure 1) we testedthe hypothesis that the amygdala, and not other regions included in the lesions, is responsible for the observed results. To this aim, the link between brain tissue damage and the behavioural performance was investigated on a voxel by voxel basis, using the Voxel-based Lesion-Symptom Mapping technique (VLSM, Bates et al., 2003) on traced brain lesions of 17 out of 19 patients (9 in the AMYGDALA and 8 in the EXTRA-TEMPORAL group). This analysis enables to identify the specific regions within the lesions associated with a specific behaviour (i.e., VRT indices for fearful faces and neutral faces) and playing a causal role in task performance (Gläscher et al., 2010). Although testing the different contribution of right or left lesions could be interesting, such analysis would be underpowered due to the small sample size. Therefore, to increase statistical power, all lesion maps were flipped onto the right hemisphere(Cheng et al. 2014; Meyer et al. 2016). Patients' VRT indices (Touch – No-Touch) for fearful faces were entered in the Non-Parametric Mapping software (NPM, Rorden et al., 2007; freely available at http://www.cabiatl.com/mricro/npm/), which compares performance of patients with vs. without damage at each voxel in the brain using the nonparametric Brunner-Munzel (BM) rank-order test (Brunner & Munzel, 2000). The alpha level of significance was set at $p<0.05$ (1000 permutations). Additionally, we used an extent threshold of 50 voxels (see also Gläscher et al., 2010). The VLSM analysis revealed that the cluster associated with reduced VRT indices for fearful faces was located in the amygdala, with the centre of the mass located at the coordinate 25, 4, -29, referring to the amygdala (cluster size: 582 voxels, maximum BM z score: 2.82). Results are illustrated in Figure 4. The same VLSM analysis was also run on VRT indices for neutral faces, revealing no significant cluster associated to VRT performance. These results provide confirmation that amygdala lesions have a causal role in disrupting the VRT for fearful faces, while they have no effects on VRT for neutral faces.

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4. Discussion

The present findings on patients with unilateral lesions to the amygdala suggest that the preferential activation of the somatosensory cortices in response to fear relies on structural integrity of this subcortical structure. In line with previous studies, the results on healthy participants and control patients with lesions not involving the amygdala confirm that viewing a neutral face being touched increases tactile detection on one's own face, compared to viewing the same face just being approached, showing a typical Visual Remapping of Touch effect (VRT; Serino et al., 2008). In addition, an enhanced VRT for fearful faces, compared to neutral and happy faces, was found, consistently with previous studies (Beck et al., 2013; Cardini et al., 2012; Scarpazza et al., 2014, 2015). More interestingly, the results revealed that following unilateral lesion to the amygdale due to right or left temporal lobectomy, although patients demonstrated the standard VRT effect for neutral faces, they fail to show the typical enhancement of VRT for fearful faces, suggesting a critical role of the amygdala in modulating somatosensory activity in response to threat.

The VRT effect is a visuo-tactile interaction where the touch viewed on a face is remapped onto one's own somatosensory system and relies on the activation of a fronto-parietal network, involving pre-motor and somatosensory cortices (Cardini et al., 2011). VRT has been shown to be modulated by the presentation of emotional faces: more precisely, VRT is enhanced when viewing a fearful face, compared to neutral, happy, disgusted or angry faces (Beck et al., 2013; Cardini et al., 2012; Scarpazza et al., 2014). The emotional modulation of VRT is thought to depend on a simulating mechanism by which viewing others' emotions generates an internal representation of that emotion within one's own somatosensory system (Adolphs et al., 2000; Atkinson & Adolphs, 2011; Pitcher et al., 2008; Pourtois et al., 2004). In particular, the specific enhancement of VRT for fearful faces could rely on a preliminary activation of the somatosensory cortex in response to threat (Cardini et al., 2012), consistently with evidence showing a critical role of the somatosensory cortex in fear processing (Adolphs, Damasio, Tranel, & Damasio, 1996; Pourtois et al., 2004). Thus, fearful faces

might elicit a stronger internal somatic representation, due to the relevance of faces expressing fear as a signal of potential danger. The new findings of this study suggest that the preferential activation of the sensory-motor system in the presence of fearful faces might depend on structural integrity of the amygdala. Indeed, although patients with selective lesions to the amygdala show an increase in tactile detection when viewing a neutral face being touched – as opposed to merely approached – by fingers, they fail to show an enhancement of such tactile detection when viewing a fearful face. In other words, after amygdala lesions, the ability to remap the tactile sensations observed on a face onto one's own sensory system (i.e. visual remapping of touch) is preserved, but the enhancement of this effect in the presence of fearful faces is disrupted. Clearly, fearful faces represent a highly arousing, negative-valenced stimulus, which might increase activation in the amygdala (Morris et al., 1996; 1999). Therefore, these results are in line with the hypothesis that amygdala lesions may interfere with the preferential activation of the sensory-motor system in response to salient stimuli signaling threat.

Although the VRT has been demonstrated to be enhanced only in the presence of fearful faces, but not with disgusted or angry faces (Cardini et al., 2012; Scarpazza et al., 2014), we cannot exclude that other highly arousing facial expressions (e.g., surprise or excitement) could induce an enhancement of the VRT effect, similar to the one observed with fearful faces. Indeed, amygdala reactivity is not restricted to threat-related information, but is broadly involved in coding highly arousing and/or unpredictable stimuli (Whalen et al., 2013; Kim et al., 2003; Kim et al., 2017). In keeping, the amygdala is an integrant component of a continuous vigilance system, responding to novel, ambiguous and biologically relevant stimuli (Whalen, 1998). In relation to the present study, the visuo-tactile stimuli used (i.e., viewing a fearful face being touched and concurrently perceiving touch on one's own face), might provide information about a salient potential harm coming from the immediate environment and, therefore, represent a typical cue activating the amygdala. As a consequence, during the experience of this visuo-tactile interaction, in healthy participants and patients with lesions not involving the amygdala, this subcortical structure might signal the

potential tactile threat to the somatosensory cortices, in order to facilitate understanding of the source of the threat, this resulting in a prioritized tactile processing. This mechanism seems disrupted when the amygdala is lesioned and, therefore, no enhancement in VRT effect can be observed.

The modulatory effect of the amygdala on tactile perception could rely on projections of the amygdala to sensory-motor cortical areas. Indeed, due to its broad connectivity with cortical and subcortical structures (Amaral et al., 1992; Young et al., 1994), amygdala lesions can influence distant brain areas, thus changing the functional pattern of activation to fearful faces in connected and structurally intact sensory cortices (Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004). Converging electrophysiological studies on animals have reported amigdalo-cortical projections terminating in somatosensory fields of SII (Amaral & Price, 1984; Sripanidkulchai, Sripanidkulchai, & Wyss, 1984). In addition, the existence of a direct amygdalo-sensorimotor pathway has been also demonstrated in humans (Grèzes, Valabrègue, Gholipour, & Chevallier, 2014).

Notably, in the present study, the lesions to the amygdala disrupt the enhancement of tactile detection for fearful faces in the somatosensory cortex, without affecting explicit recognition of emotional faces, thus ruling out the hypothesis that the lack of VRT for fearful faces could depend on impaired recognition of the emotional content of the faces. Indeed, patients with lesions to the amygdala performed similarly to healthy controls and patients with lesions not involving the amygdala at the Ekman 60 Faces Test, where explicit recognition of 60 emotional faces is required and they showed no impairment in the recognition of specific emotions, including fear. Although after damage to the amygdala (mainly bilateral and congenital) the subjective experience of negative emotions (Tranel, Gullickson, Koch, & Adolphs, 2006), the intensity and similarity judgments of emotional faces (Adolphs et al., 1996, 1994; Anderson, Spencer, Fulbright, & Phelps, 2000; McClelland et al., 2006; Siebert, Markowitsch, & Bartel, 2003) and social signals (Adolphs, 2002) might be altered, recent findings report no effects of amygdala lesions (especially unilateral)

on recognition of emotional faces (Adolphs, Tranel, Damasio, & Damasio, 1995; Graham, Devinsky, & Labar, 2007; Hamann et al., 1996; Siebert et al., 2003; Tsuchiya, Moradi, Felsen, Yamazaki, & Adolphs, 2009; Vuilleumier et al., 2004), in line with the present findings.

The lack of VRT effect (i.e. no difference between touch and no touch) in the presence of happy faces both in patients (with and without lesions to the amygdala) and in healthy controls is consistent with previous results (Cardini et al., 2012; Scarpazza et al., 2014) and could represent a by-product of the motor resonance phenomenon. Indeed, observing emotional faces have been shown to elicit spontaneous and automatic rapid facial reactions (i.e., Dimberg, Thunberg, & Elmehed, 2000), usually with an onset latency in the 300-700 ms range; more specifically, when observing happy faces, a spontaneous contraction of the zygomaticus major muscle might occur (Scarpazza, Làdavas, & Cattaneo, 2017), therefore interfering with the detection of the electro-tactile stimuli placed on the cheeks, delivered at 700 ms, during the present experimental task..

To sum up, the present findings suggest the existence of a cooperative mechanism between the amygdala and the somatosensory cortices, in which the amygdala can signal potential threat to the somatosensory cortices, resulting in a prioritized tactile analysis. This mechanism could represent the neural counterpart of the typically observed fear-related enhancement in the VRT effect. Indeed, after amygdala lesions no enhancement in VRT when viewing touch towards fearful faces is observed.

Case	Sex	Age	Age at surgery	Epilepsy onset (years)	Epilepsy duration (months)	Seizure free (years)	Lesion site
P1	M	21	18	12	72	3	L Medial temporal
P2	F	22	10	8	12	12	L Medial temporal
P3	F	23	21	3	216	2	R Medial temporal
P4	F	37	35	15	264	2	R Medial temporal
P5	F	22	10	5	60	12	L Medial temporal
P6	F	18	11	10	12	7	R Medial temporal
P7	M	21	17	9	108	4	L Medial temporal
P8	M	13	12	1	132	1	L Medial temporal
P9	F	43	42	25	216	1	R Medial temporal
P10	M	64	61	33	372	3	R Medial temporal
P11	F	29	15	15	8	14	L Frontal
P12	M	24	15	15	12	9	BIL Third ventricle/Thalamus/Posterior Cingulate
P13	M	19	12	12	10	6	R Parietal
P14	F	28	3	3	24	13	BIL Third ventricle
P15	M	23	14	14	8	9	BIL Third ventricle/ Pituitary gland
P16	F	49	39	33	72	10	R Caudatus Head
P17	M	21	19	19	1	2	R Frontal
P18	M	18	16	16	4	2	R Pituitary gland/Thalamus
P19	M	23	21	16	60	2	R Frontal/Insular

Table 1. Summary of clinical, demographic and lesional data. M: male; F: female; L: left; R: right; BIL: bilateral.

	Unilateral detection accuracy	
	Strong stimulus	Weak stimulus
AMYGDALA	92%±1%	66%±7%
EXTRA-TEMPORAL	87%±5%	77%±7%
CONTROL	96%±1%	68%±6%

Table 2. Mean (± s.e.m.) detection rate for unilateral strong and weak stimuli confirms correct calibration of the stimuli. No significant difference in unilateral detection accuracy between the three groups was found (strong stimulus: $F(2,26)=2.46$; $p=.10$; $\eta^2=.16$; weak stimulus: $F(2,26)=1.13$; $p=.34$; $\eta^2=.08$).

Figure 1

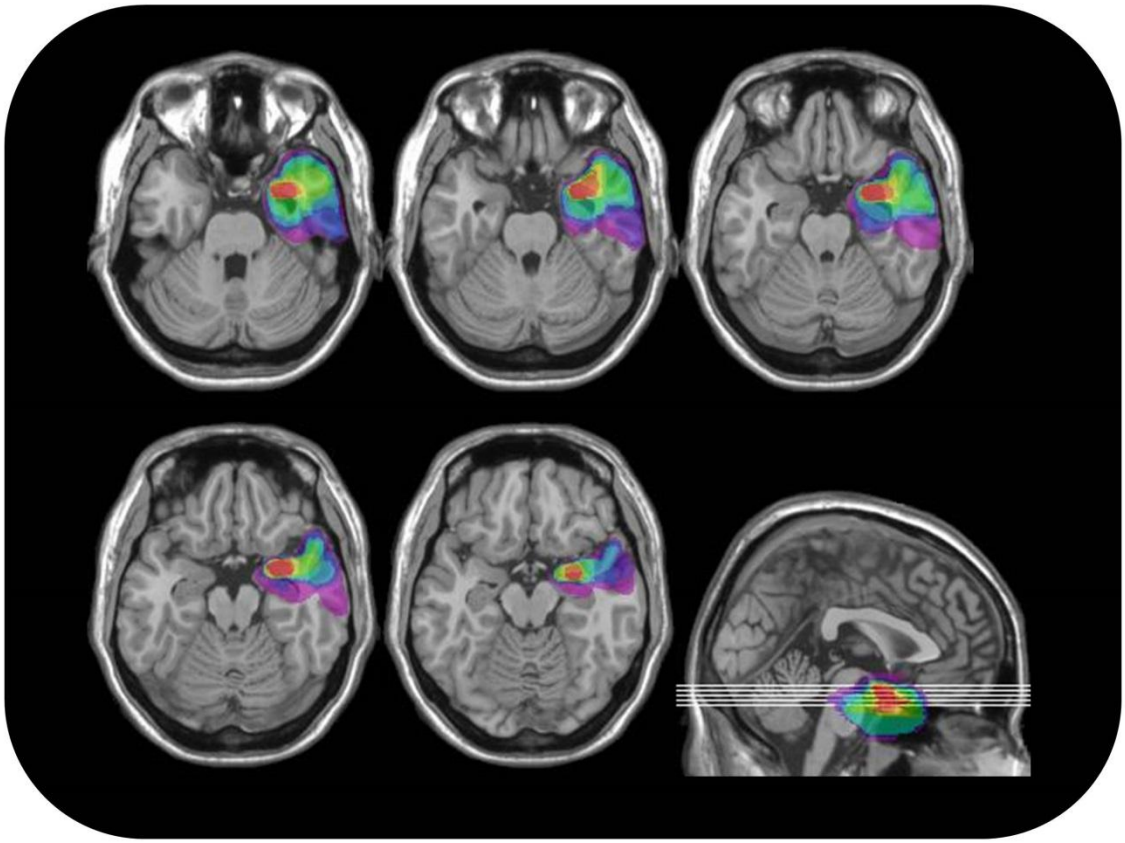

Figure 2

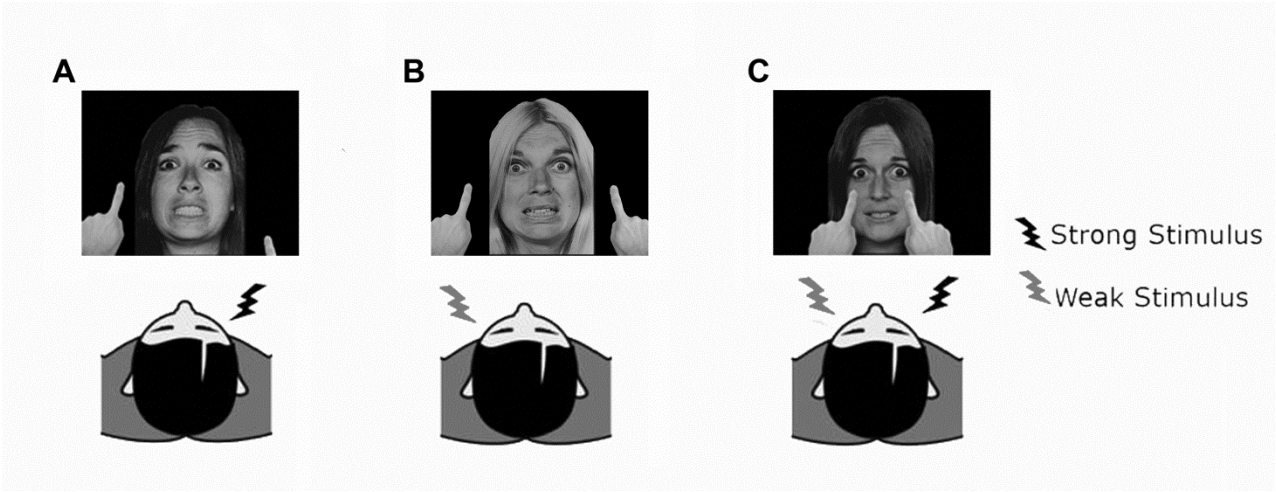

Figure 3

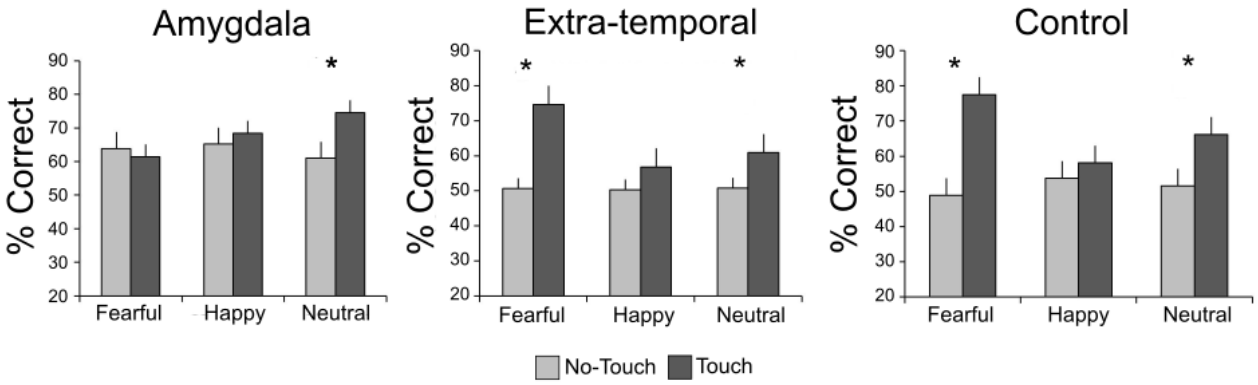
Amygdala
Extra-temporal
Control
% Correct
90
80
70
60
50
40
30
20
*
Fearful
Happy
Neutral
No-Touch
Touch

Figure 4

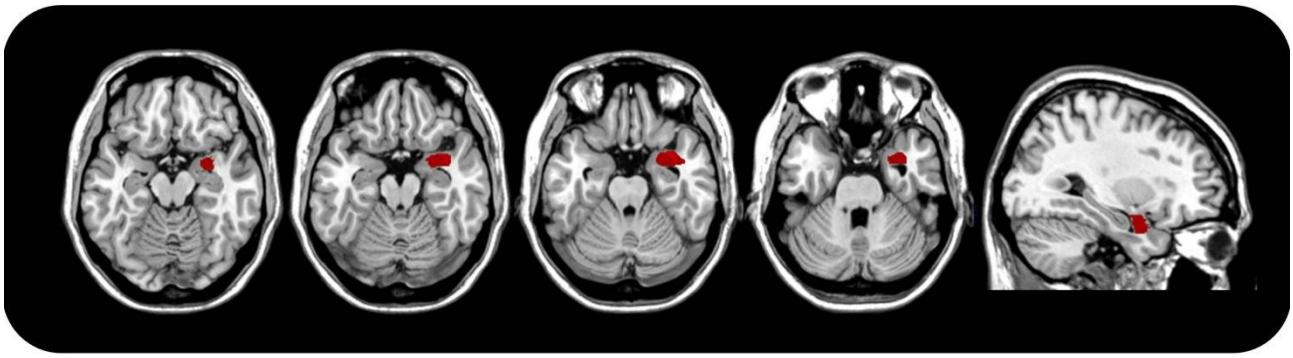

Figure Legends

Figure 1. Location and overlap of brain lesions. The image shows the lesions of the AMYGDALA group of patients projected on axial slices of the standard MNI brain. The level of axial slices has been marked by white lines on the sagittal view of the brain.

Figure 2. Schematic trial representation**.** In each experimental block, a different facial expression (fearful, happy, neutral) was presented in the movie (in the figure only fearful faces are represented). In each trial, fingers moved toward the face and then backward to their starting position. In each trial, either the finger on the right, on the left (A), or both fingers moved (B and C). Fingers either touched the cheeks (C) of the face or stopped about 5 cm alongside the face (B). As soon as the fingers reached the image, a tactile stimulation (either the strong -A-, the weak -B-, or both stimulations -C-) was delivered on the participant's cheeks.

Figure 3. Results for the eVRT in AMYGDALA, EXTRA-TEMPORAL and CONTROL groups. Mean accuracy in detecting bilateral tactile stimulation while viewing either a fearful, happy or neutral face that could be touched (Touch) or just approached (No-Touch) by two human fingers. Error bars show standard errors of the mean. *$p<.05$.

Figure 4. Results for the VLSM analysis. The image shows that the brain regions associated with reduced VRT index for fearful faces is located in the amygdale (coordinates 25, 4, -29).

References

Abivardi, A., & Bach, D. R. (2017). Deconstructing white matter connectivity of human amygdala nuclei with thalamus and cortex subdivisions in vivo. *Human Brain Mapping*, 38(8), 3927-3940.

Achenbach, T. M., & Rescorla, L. A. (2001). Manual for ASEBA School-Age Forms & Profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families.

Adolphs, R. (2002). Neural systems for recognizing emotion. *Current Opinion in Neurobiology*, *12*(2), 169–177. https://doi.org/10.1016/S0959-4388(02)00301-X

Adolphs, R. (2013). The Biology of Fear. *Current Biology*, *23*(2), R79–R93. https://doi.org/10.1016/j.cub.2012.11.055

Adolphs, R., Damasio, H., Tranel, D., Cooper, G., & Damasio, A. R. (2000). A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *20*(7), 2683–2690.

Adolphs, R., Damasio, H., Tranel, D., & Damasio, A. R. (1996). Cortical systems for the recognition of emotion in facial expressions. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *16*(23), 7678–7687.

Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. (1994). Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature*, *372*(6507), 669–672. https://doi.org/10.1038/372669a0

Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. R. (1995). Fear and the human amygdala. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *15*(9), 5879–5891.

Amaral, D. G., Pitkanen, & Carmichael. (1992). Anatomical organization of the primate amygdaloid complex. In *The Amygdala: Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction* (pp. 1–66). New York, NY, USA: Wiley-Liss.

Amaral, D. G., & Price, J. L. (1984). Amygdalo-cortical projections in the monkey (Macaca fascicularis). *The Journal of Comparative Neurology*, *230*(4), 465–496. https://doi.org/10.1002/cne.902300402

Anderson, A. K., Spencer, D. D., Fulbright, R. K., & Phelps, E. A. (2000). Contribution of the anteromedial temporal lobes to the evaluation of facial emotion. *Neuropsychology*, *14*(4), 526–536.

Anderson, A. K., Christoff, K., Panitz, D., De Rosa, E., & Gabrieli, J. D. E. (2003). Neural correlates of the automatic processing of threat facial signals. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *23*(13), 5627–5633.

Atkinson, A. P., & Adolphs, R. (2011). The neuropsychology of face perception: beyond simple dissociations and functional selectivity. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *366*(1571), 1726–1738. https://doi.org/10.1098/rstb.2010.0349

Beck, A., Steer, R., & Brown, G. (2014). Manual for the Beck Depression Inventory-II. San Antonio, TX: Psychological Corporation; 1996. *Google Scholar*.

Beck, B., Bertini, C., Scarpazza, C., & Làdavas, E. (2013). Observed Touch on a Non-Human Face Is Not Remapped onto the Human Observer's Own Face. *PLoS ONE*, *8*(11). https://doi.org/10.1371/journal.pone.0073681

Blakemore, S.-J., Bristow, D., Bird, G., Frith, C., & Ward, J. (2005). Somatosensory activations during the observation of touch and a case of vision-touch synaesthesia. *Brain: A Journal of Neurology*, *128*(Pt 7), 1571–1583. https://doi.org/10.1093/brain/awh500

Brunner, E., & Munzel, U. (2000). The Nonparametric Behrens-Fisher Problem: Asymptotic Theory and a Small-Sample Approximation. *Biometrical Journal*, *42*(1), 17–25. https://doi.org/10.1002/(SICI)1521-4036(200001)42:1<17::AID-BIMJ17>3.0.CO;2-U

Cardini, F., Bertini, C., Serino, A., & Ladavas, E. (2012). Emotional modulation of visual remapping of touch. *Emotion (Washington, D.C.)*, *12*(5), 980–987. https://doi.org/10.1037/a0027351

Cardini, F., Costantini, M., Galati, G., Romani, G. L., Làdavas, E., & Serino, A. (2011). Viewing one's own face being touched modulates tactile perception: an fMRI study. *Journal of Cognitive Neuroscience*, *23*(3), 503–513. https://doi.org/10.1162/jocn.2010.21484

Carr, L., Iacoboni, M., Dubeau, M.-C., Mazziotta, J. C., & Lenzi, G. L. (2003). Neural mechanisms of empathy in humans: A relay from neural systems for imitation to limbic areas. *Proceedings of the National Academy of Sciences*, *100*(9), 5497–5502. https://doi.org/10.1073/pnas.0935845100

Cheng, B., Forkert, N.D., Zavaglia, M., Hilgetag, C.C., Golsari, A., Siemonsen, S., Fiehler, J., Pedraza, S., Puig, J., Cho, T.-H., Alawneh, J., Baron, J.-C., Ostergaard, L., Gerloff, C., Thomalla, G., 2014. Influence of stroke infarct location on functional outcome measured by the modified rankin scale. *Stroke* 45, 1695–1702.

Cianchetti, C., & Fancello, G. S. (2001). *SAFA: scale psichiatriche di autosomministrazione per fanciulli e adolescenti*. Firenze: Organizzazioni Speciali.

Davis, M. (1994). The role of the amygdala in emotional learning. *International Review of Neurobiology*, *36*, 225–266.

Dienes, Z., 2011. Bayesian versus orthodox statistics: which side are you on? Perspect. Psychol. Sci. 6, 274–290. https://doi.org/10.1177/1745691611406920.

Dimberg, U., Thunberg, M., & Elmehed, K. (2000). Unconscious facial reactions to emotional facial expressions. *Psychological Science*, *11*(1), 86–89. https://doi.org/10.1111/1467-9280.00221

Ebisch, S. J. H., Perrucci, M. G., Ferretti, A., Del Gratta, C., Romani, G. L., & Gallese, V. (2008). The sense of touch: embodied simulation in a visuotactile mirroring mechanism for observed animate or inanimate touch. *Journal of Cognitive Neuroscience*, *20*(9), 1611–1623. https://doi.org/10.1162/jocn.2008.20111

Ekman, P., & Friesen, W. (1976). *Picture of facial affect*. Palo Alto: Consulting Psychologists Press.

Fusar-Poli, P., Placentino, A., Carletti, F., Landi, P., Allen, P., Surguladze, S., … Politi, P. (2009). Functional atlas of emotional faces processing: a voxel-based meta-analysis of 105 functional magnetic resonance imaging studies. *Journal of Psychiatry & Neuroscience : JPN*, *34*(6), 418–432.

Gallese, V., & Sinigaglia, C. (2011). What is so special about embodied simulation? *Trends in Cognitive Sciences*, *15*(11), 512–519. https://doi.org/10.1016/j.tics.2011.09.003

Gläscher, J., Rudrauf, D., Colom, R., Paul, L. K., Tranel, D., Damasio, H., & Adolphs, R. (2010). Distributed neural system for general intelligence revealed by lesion mapping. *Proceedings of the National Academy of Sciences*, *107*(10), 4705–4709. https://doi.org/10.1073/pnas.0910397107

Goldman, A. I., & Sripada, C. S. (2005). Simulationist models of face-based emotion recognition. *Cognition*, *94*(3), 193–213. https://doi.org/10.1016/j.cognition.2004.01.005

Graham, R., Devinsky, O., & Labar, K. S. (2007). Quantifying deficits in the perception of fear and anger in morphed facial expressions after bilateral amygdala damage. *Neuropsychologia*, *45*(1), 42–54. https://doi.org/10.1016/j.neuropsychologia.2006.04.021

Grèzes, J., Valabrègue, R., Gholipour, B., & Chevallier, C. (2014). A direct amygdala-motor pathway for emotional displays to influence action: A diffusion tensor imaging study. *Human Brain Mapping*, *35*(12), 5974–5983. https://doi.org/10.1002/hbm.22598

Hamann, S. B., Stefanacci, L., Squire, L. R., Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. (1996). Recognizing facial emotion. *Nature*, *379*(6565), 497–497. https://doi.org/10.1038/379497a0

Hussey, E., & Safford, A. (2009). Perception of Facial Expression in Somatosensory Cortex Supports Simulationist Models. *Journal of Neuroscience*, *29*(2), 301–302. https://doi.org/10.1523/JNEUROSCI.5205-08.2009

Jabbi, M., Swart, M., & Keysers, C. (2007). Empathy for positive and negative emotions in the gustatory cortex. *NeuroImage*, *34*(4), 1744–1753. https://doi.org/10.1016/j.neuroimage.2006.10.032

Jacobs, R. H. A. H., Renken, R., Aleman, A., & Cornelissen, F. W. (2012). The amygdala, top-down effects, and selective attention to features. *Neuroscience and Biobehavioral Reviews*, *36*(9), 2069–2084. https://doi.org/10.1016/j.neubiorev.2012.05.011

Jarosz, A.F., Wiley, J., 2014. What are the odds? a practical guide to computing and reporting bayes factors? Journal of Problem Solving 7, 2. https://doi.org/10.7771/ 1932-6246.1167.

JASP Team (2018). JASP (Version 0.9)[Computer software].

Kapp, Frysinger, R. C., Gallagher, M., & Haselton, J. R. (1979). Amygdala central nucleus lesions: effect on heart rate conditioning in the rabbit. *Physiology & Behavior*, *23*(6), 1109–1117.

Kapp, Whalen, P. J., Supple, W. F., & Pascoe, J. P. (1992). Amygdaloid contributions to conditioned arousal and sensory information processing. In *The amygdala: Neurobiological aspects of emotion, memory, and mental dysfunction* (pp. 229–254). New York, NY, US: Wiley-Liss.

Keysers, C., Wicker, B., Gazzola, V., Anton, J.-L., Fogassi, L., & Gallese, V. (2004). A touching sight: SII/PV activation during the observation and experience of touch. *Neuron*, *42*(2), 335–346.

Kim, H., Somerville, L.H., Johnstone. T., Alexander. A.L., Whalen. P.J. (2003). Inverse amygdala and medial prefrontal cortex responses to surprised faces. *Neuroreport*, 14, 2317–2322

Kim, M. J., Mattek, A. M., Bennett, R. H., Solomon, K. M., Shin, J., & Whalen, P. J. (2017). Human amygdala tracks a feature-based valence signal embedded within the facial expression of surprise. *Journal of Neuroscienc*e, 1375-17.

LeDoux, J. (2014). Coming to terms with fear. *Proceedings of the National Academy of Sciences*, *111*(8), 2871–2878. https://doi.org/10.1073/pnas.1400335111

Macaluso, E. (2006). Multisensory Processing in Sensory-Specific Cortical Areas. *The Neuroscientist*, *12*(4), 327–338. https://doi.org/10.1177/1073858406287908

Maren, S. (2001). Neurobiology of Pavlovian Fear Conditioning. *Annual Review of Neuroscience*, *24*(1), 897–931. https://doi.org/10.1146/annurev.neuro.24.1.897

McClelland, S., Garcia, R. E., Peraza, D. M., Shih, T. T., Hirsch, L. J., Hirsch, J., & Goodman, R. R. (2006). Facial emotion recognition after curative nondominant temporal lobectomy in patients with mesial temporal sclerosis. *Epilepsia*, *47*(8), 1337–1342. https://doi.org/10.1111/j.1528-1167.2006.00557.x

Meyer, S., Kessner, S.S., Cheng, B., Bonstrup, M., Schulz, R., Hummel, F.C., et al. (2015). Voxel-based lesion-symptom mapping of stroke lesions underlying somatosensory deficits. *NeuroImage Clin,* 10, 257-266.

Mende-Siedlecki, P., Verosky, S. C., Turk-Browne, N. B., & Todorov, A. (2013). Robust selectivity for faces in the human amygdala in the absence of expressions. *Journal of Cognitive Neuroscience*, *25*(12), 2086–2106. https://doi.org/10.1162/jocn_a_00469

Morris, J. S., Frith, C. D., Perrett, D. I., Rowland, D., Young, A. W., Calder, A. J., & Dolan, R. J. (1996). A differential neural response in the human amygdala to fearful and happy facial expressions. *Nature*, *383*(6603), 812.

Morris, J. S., Öhman, A., & Dolan, R. J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proceedings of the National Academy of Sciences*, *96*(4), 1680-1685.

Niedenthal, P. M. (2007). Embodying Emotion. *Science*, *316*(5827), 1002–1005. https://doi.org/10.1126/science.1136930

Niedenthal, P. M., Augustinova, M., & Rychlowska, M. (2010). Body and Mind: Zajonc's (Re)introduction of the Motor System to Emotion and Cognition. *Emotion Review*, *2*(4), 340–347. https://doi.org/10.1177/1754073910376423

Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *NeuroImage*, *16*(2), 331–348. https://doi.org/10.1006/nimg.2002.1087

Phelps, E. A. (2006). Emotion and Cognition: Insights from Studies of the Human Amygdala. *Annual Review of Psychology*, *57*(1), 27–53. https://doi.org/10.1146/annurev.psych.56.091103.070234

Pitcher, D., Garrido, L., Walsh, V., & Duchaine, B. C. (2008). Transcranial magnetic stimulation disrupts the perception and embodiment of facial expressions. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *28*(36), 8929–8933. https://doi.org/10.1523/JNEUROSCI.1450-08.2008

Pourtois, G., Sander, D., Andres, M., Grandjean, D., Reveret, L., Olivier, E., & Vuilleumier, P. (2004). Dissociable roles of the human somatosensory and superior temporal cortices for processing social face signals. *The European Journal of Neuroscience*, *20*(12), 3507–3515. https://doi.org/10.1111/j.1460-9568.2004.03794.x

Raftery, A., 1995. Bayesian model selection in social research. Socio. Meth. 25, 111–196. https://doi.org/10.2307/271063.

Rorden, C., Bonilha, L., & Nichols, T. E. (2007). Rank-order versus mean based statistics for neuroimaging. *NeuroImage*, *35*(4), 1531–1537. https://doi.org/10.1016/j.neuroimage.2006.12.043

Rorden, C., & Brett, M. (2000). Stereotaxic display of brain lesions. *Behavioural Neurology*, *12*(4), 191–200.

Scarpazza, C., di Pellegrino, G., & Làdavas, E. (2014). Emotional modulation of touch in alexithymia. *Emotion (Washington, D.C.)*, *14*(3), 602–610. https://doi.org/10.1037/a0035888

Scarpazza, C., Làdavas, E., & Cattaneo, L. (2017). Invisible side of emotions: somato-motor responses to affective facial displays in alexithymia. *Experimental Brain Research*, 1–12. https://doi.org/10.1007/s00221-017-5118-x

Scarpazza, C., Làdavas, E., & Pellegrino, G. di. (2015). Dissociation between Emotional Remapping of Fear and Disgust in Alexithymia. *PLOS ONE*, *10*(10), e0140229. https://doi.org/10.1371/journal.pone.0140229

Serino, A., Pizzoferrato, F., & Làdavas, E. (2008). Viewing a face (especially one's own face) being touched enhances tactile perception on the face. *Psychological Science*, *19*(5), 434–438. https://doi.org/10.1111/j.1467-9280.2008.02105.x

Siebert, M., Markowitsch, H. J., & Bartel, P. (2003). Amygdala, affect and cognition: evidence from 10 patients with Urbach–Wiethe disease. *Brain*, *126*(12), 2627–2637. https://doi.org/10.1093/brain/awg271

Singer, T., Seymour, B., O'Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for pain involves the affective but not sensory components of pain. *Science (New York, N.Y.)*, *303*(5661), 1157–1162. https://doi.org/10.1126/science.1093535

Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press.

Spinnler, H., & Tognoni, G. (1987). [Italian standardization and classification of Neuropsychological tests. The Italian Group on the Neuropsychological Study of Aging]. *Italian Journal of Neurological Sciences*, *Suppl 8*, 1–120.

Sripanidkulchai, K., Sripanidkulchai, B., & Wyss, J. M. (1984). The cortical projection of the basolateral amygdaloid nucleus in the rat: a retrograde fluorescent dye study. *The Journal of Comparative Neurology*, *229*(3), 419–431. https://doi.org/10.1002/cne.902290310

Todorov, A. (2012). The role of the amygdala in face perception and evaluation. *Motivation and Emotion*, *36*(1), 16–26. https://doi.org/10.1007/s11031-011-9238-5

Tranel, D., Gullickson, G., Koch, M., & Adolphs, R. (2006). Altered experience of emotion following bilateral amygdala damage. *Cognitive Neuropsychiatry*, *11*(3), 219–232. https://doi.org/10.1080/13546800444000281

Tressoldi, P. E., Vio, C., Gugliotta, M., Bisiacchi, P. S., & Cendron, M. (2005). *BVN 5-11.: Batteria di valutazione neuropsicologica per l'età evolutiva. Con CD-ROM*. Edizioni Erickson.

Tsuchiya, N., Moradi, F., Felsen, C., Yamazaki, M., & Adolphs, R. (2009). Intact rapid detection of fearful faces in the absence of the amygdala. *Nature Neuroscience*, *12*(10), 1224–1225. https://doi.org/10.1038/nn.2380

Vuilleumier, P., Richardson, M. P., Armony, J. L., Driver, J., & Dolan, R. J. (2004). Distant influences of amygdala lesion on visual cortical activation during emotional face processing. *Nature Neuroscience*, *7*(11), 1271–1278. https://doi.org/10.1038/nn1341

Vytal, K., & Hamann, S. (2010). Neuroimaging support for discrete neural correlates of basic emotions: a voxel-based meta-analysis. *Journal of Cognitive Neuroscience*, *22*(12), 2864–2885. https://doi.org/10.1162/jocn.2009.21366

Wagenmakers, E.J., Love, J., Marsman, M., Jamil, T., Ly, A., Verhagen, J., Selker, R., Gronau, Q.F., Dropmann, D., Boutin, B., Meerhoff, F., Knight, P., Raj, A., van Kesteren, E.J., van Doorn, J., ?Smíra, M., Epskamp, S., Etz, A., Matzke, D., de Jong, T., van den Bergh, D., Sarafoglou, A., Steingroever, H., Derks, K., Rouder, J.N., Morey, R.D., 2018. Bayesian inference for psychology. Part II: Example applications with JASP. Psychonomic Bull. Rev. 25, 58–76. https://doi.org/10.3758/s13423-017-1323-7.

Whalen, P. J. (1998). Fear, vigilance, and ambiguity: Initial neuroimaging studies of the human amygdala. *Current Directions in Psychological Science*, *7*(6), 177–188. https://doi.org/10.1111/1467-8721.ep10836912

Whalen, P. J., Raila, H., Bennett, R., Mattek, A., Brown, A., Taylor, J., ... & Palmer, A. (2013). Neuroscience and facial expressions of emotion: The role of amygdala–prefrontal interactions. *Emotion Review*, 5(1), 78-83.

Wicker, B., Keysers, C., Plailly, J., Royet, J. P., Gallese, V., & Rizzolatti, G. (2003). Both of us disgusted in My insula: the common neural basis of seeing and feeling disgust. *Neuron*, *40*(3), 655–664.

Winston, J. S., O'Doherty, J., & Dolan, R. J. (2003). Common and distinct neural responses during direct and incidental processing of multiple facial emotions. *NeuroImage*, *20*(1), 84–97. https://doi.org/10.1016/S1053-8119(03)00303-3

Young, M. P., Scannell, J. W., Burns, G. A., & Blakemore, C. (1994). Analysis of connectivity: neural systems in the cerebral cortex. *Reviews in the Neurosciences*, *5*(3), 227–250.