The influence of emotional priming on the neural substrates of memory: A prospective fMRI study using portrait art stimuli

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Running head: Remembering art

Abstract

Events coupled with an emotional context seem to be better retained than non-emotional events. The aim of our study was to investigate whether an emotional context could influence the neural substrates of memory associations with novel portrait art stimuli. In the current prospective fMRI study, we have investigated for one specific visual art form (modern artistic portraits with a high degree of abstraction) whether memory is influenced by priming with emotional facial pictures. In total forty healthy female volunteers in the same age range were recruited for the study. Twenty of these women participated in a brain imaging memory paradigm and were asked to memorize a series of similar looking, but different portraits. After randomization, for twelve participants (Group 1), a third of the portraits was emotionally primed with approach-related pictures (smiling baby faces), a third with withdrawal-related pictures (baby faces with severe dermatological conditions), and another third with neutral images. Group 2 consisted of eight participants and they were not primed. Then, during an fMRI session two hours later, these portraits were viewed in random order intermixed with a set of new (previously unseen) ones, and the participants had to decide for each portrait whether or not they had already been seen. In a separate experiment, a different sample of twenty healthy females (Group 3) rated their mood after being exposed to the same art stimuli, without priming. The portraits did not evoke significant mood changes by themselves, supporting their initial neutral emotional character (Group 3). The correct decision on whether the portraits were Familiar of Unfamiliar led to similar neuronal activations in brain areas implicated in visual and attention processing for both groups (Group 1 and 2). In contrast, whereas primed participants showed significant higher neuronal activities in the left midline superior frontal cortex (Brodmann area (BA) 6), unprimed volunteers displayed higher right medial frontal cortical (BA 10) activities. Furthermore, specifically in Group 1, correct retrieval of negatively primed portraits evoked increased neuronal activity in the left medial orbitofrontal cortex (BA 11) and in the right (posterior) insula, suggesting enhanced stress-related responses to the memory of withdrawal-related primed modern artistic portraits in this group. Our prospective memory data in healthy females indicate that, to reach a correct retrieval decision, different midline anterior

neuronal networks are recruited for portraits that were emotionally primed than for the unprimed ones. Importantly, our results also suggest that the negative emotional context leads to the formation of associations that are reactivated during memory retrieval processes of the initially neutral art portraits. When correctly recognized, the portraits evoke neuronal activities consistent with the withdrawal-related character of the emotional visual stimuli with which they have been associated. Although our results show that abstract portrait art can be associated with emotional primes this doesn't mean that this effect is specific for art images.

1. Introduction

Emotionally charged, novel, beautiful or aversive visual stimuli are better remembered than neutral or non-emotional ones (Wright et al., 2001). For instance, would Edward Munch's painting 'The Scream' leave the same indelible memory if the figure in the painting was not depicted with such an emotionally disturbing and agonizing face of terror (Solso, 2003)? Further, emotional events seem to be better retained than non-emotional events and emotional information is better remembered in mood states with a matching affective valence (Dolcos & Cabeza, 2002).

Nowadays, art and its creators have entered neuroscience research (Solso, 1994, 2003; Zeki, 1999). Images of art - paintings, sketches and photographs - have been used in a variety of brain imaging paradigms investigating their influence on perception, imagination, emotion and memory processes (Zaidel and Kasher, 1998; Ishai et al., 2007; Lacey et al., 2011). The few studies that examined neuronal activation in relation to visual art exposure suggest that perception and memory depend on visual as well as semantic brain processes (Ishai et al., 2007; Fairhall & Ishai, 2008; Cupchik et al., 2009). Also attention networks, such as the prefrontal and parietal cortex, and memory-related brain areas such as the temporal and hippocampal regions have been documented to be involved (Yago & Ishai, 2006; Wiesmann & Ishai, 2008), as well as reward-related regions such as the ventral striatum and the orbitofrontal cortices (Lacey et al., 2011).

How the brain stores and retrieves art-related memories seems to be a relevant research question given the complex interaction between the perception, emotional experience and memory processes involved. The emotional experience induced by art with a high degree of abstraction is not so easy to understand. Its valence can partly be determined by its previous association with an emotional context. Many affective priming studies examining memory processes, not always accompanied by brain imaging procedures, have reported behavioral effects predominantly after priming with negative stimuli (Stolz & Neely, 2001; Zhang et al., 2006; Chao et al., 2008). Intriguingly, to our knowledge, no brain imaging studies have so far examined the influence of emotional priming

on experiencing art. Consequently, in this paper we have examined this problem in the context of memory of portrait art with a high degree of abstraction.

For this study, we developed a new paradigm with novel stimuli based on modern paintings of faces. The portraits were selected from the work of a Belgian painter, Ronny Delrue (See Fig 1B). This choice had several major advantages. Firstly, all participants were unfamiliar with the paintings, excluding recognition bias. Secondly, all paintings typically shared certain visual similarities, making it harder to remember them. Thirdly, the selected artworks have a high degree of abstraction and elicit no specific emotion by themselves. In addition, as the paintings were rendered in black and white, there was no 'contamination' by emotional connotations associated with different colors.

In our experiment, for one group of participants, a number of these portraits were primed by a preliminary viewing in combination with 'emotional' color pictures of baby faces. Among these there were positive or approach-related pictures showing happy, smiling baby faces. Negative or withdrawal-related pictures showed baby faces exhibiting a combination of negative facial expressions and severe dermatological conditions. Our earlier research in healthy women had already demonstrated that viewing the positively valenced baby pictures evoked strong approach-related emotions, such as happiness, and the negatively valenced ones strong withdrawal-related emotions, such as disgust (Baeken et al., 2010a). Furthermore, these emotional pictures had proven to be especially useful for examining brain activity related to emotional processes, in healthy as well as in psychopathological states (Baeken et al., 2009, 2010 a,b,c and 2011).

As it had been demonstrated earlier that gender differences could affect emotional memory processes (Cahill et al., 2004; Piefke et al., 2005), and because age differences might affect memory paradigms (Rendell et al., 2011; Schnitzspahn et al., *in press*), we restricted our study cohort to healthy female subjects within a narrow age range. One group of healthy women (Group 1) was 'primed' with positive, neutral or negative baby faces while viewing a set of 60 Delrue portraits. A comparable sample of healthy women (Group 2) was not primed and served as the control group. A

couple of hours later, these portraits, intermixed in random order with 60 new but similar ones, were viewed under event related fMRI. The viewing was combined with a forced recognition task: for each portrait participants had to choose between "I remember this image" and "I don't remember this image" by pressing the relevant buttons on two reaction boxes. Response accuracy and reaction times (RT) were recorded. In order to check that the portraits by themselves did not provoke mood alterations, in a separate study unrelated to the imaging study, a different but comparable female group rated their mood with Visual Analogue Scales (VAS; McCormack et al., 1988) before and after viewing all portraits (Group 3).

We expected that during the memory task all participants would primarily recruit brain areas related to visual processing and memory. Moreover, we hypothesized that emotionally primed portraits would, during memory retrieval, result in activation patterns within the fronto-limbic neurocircuitries consistent with the emotional valence of the prime. Finally, as most emotional priming studies reported effects after priming with negative stimuli, we anticipated that these patterns would be primarily apparent for the negatively primed portraits.

2. Materials and Methods

2.1 Subjects

A total of 40 healthy, right-handed female participants were recruited in the university environment (mean age=24.4 years, sd=5.0). No volunteer was familiar with the Delrue portraits or underwent formal art education. Volunteers taking medication other than birth-control pills or with a psychiatric disorder, as assessed by the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998) and/or a score higher than eight on the 21-item Beck Depression Inventory (BDI; Beck & Steer, 1984) were excluded. Right-handedness was assessed by the van Strien questionnaire (Van Strien & Van Beek, 2000). The study was part of a larger project investigating various neuro-cognitive markers, which was approved by the Institutional Ethical Review Board of our University Hospital (UZBrussel). All participants gave written informed consent and were financially compensated.

2.2 Stimuli and priming material

The stimuli consisted of images of painted portraits with a high degree of abstraction selected with his permission from the oeuvre of Ronny Delrue, a Belgian modern painter. The artist has a large portfolio of paintings in a unique style (see Fig 1B). To avoid influences of color on memory strategies and emotion induction, all colors were transformed to a gray scale rendering using CorelDRAW 11. As a result, participants could only rely on facial contours and specificities unrelated to color.

Sixty baby face pictures (see Fig 1A) from both genders (mean estimated age=5.5 months, sd=4.0) were paired with sixty Delrue portraits to be viewed in the priming step. Because "neutral" baby faces might not be perceived as emotionally neutral by young women, we artificially created neutral pictures, matched to the positive and negative baby faces for visual characteristics such as luminescence and color, by reduction of the image matrix of a set of baby face pictures and by smoothing the resulting pictures using CorelDRAW 11. The characteristics of these primes were reported earlier (Baeken et al., 2010a).

2.3 Memory experiment

Twenty female participants (mean age=26.6 years, *sd*=4.3) took part in the memory experiment and were randomized into two groups (flipping a coin). Each participant started around nine o' clock in the morning. First, Group 1 (n=12) viewed a succession of 60 Delrue portraits, each preceded by a positive (approach-related), a negative (withdrawal-related), or a neutral baby picture. The baby images were randomized in order and each category was equally represented (20 of each). Each image was projected on a blank wall for 3 seconds. For fixation purposes, every art and baby image was preceded by a fixation cross for 1 second. All volunteers viewed each portrait twice, always preceded by the same emotional baby face. Group 2 (n= 8) followed the same protocol, however without having the baby images displayed as primes. All were instructed to look attentively at all images, trying to memorize the paintings as well as possible. As it had been demonstrated earlier that specific task instructions improve memory performance (Kliegel et al., 2004), participants were informed that, only when performing adequately, they would be allowed to finish the study and thus receive complete financial compensation.

Two hours after her priming session, the participant was subjected to the fMRI memory paradigm. During fMRI scanning, a total of 120 portraits (60 already shown and 60 new ones intermixed in random order) were back-projected onto a flat screen, following an event related design. All portraits were displayed for 2500 ms and preceded by a black crosshair (200ms) centred on a white background, introduced for fixation purposes. The projection was jittered with interstimulus intervals of minimum 1s, maximum 12s, mean 3.37s (± 2.12). The participants were asked to express whether or not they recognized each portrait using two response boxes. Response accuracy and reaction time (RT) were registered.

2.4 fMRI sequence

Brain imaging was carried out on a 1.5T MRI scanner (Philips Intera, Best, The Netherlands) equipped with a 6 channel sense head coil. We measured 125 consecutive FFE-EPI volumes (TR/TE=3000/35 ms, flip angle=90°, 18 slices, slice thickness/gap= 5.0/1.0 mm, size= 64x64, in plane resolution=3.75x3.75 mm, duration 6 min 15 sec) covering the whole brain. The fMRI data were analyzed using the SPM5 software (Wellcome Department of Cognitive Neurology, London, UK). The fMRI time series was realigned to the first volume to correct for head movements. After the realignment step, slice time correction was performed to correct for small differences in the time offset of consecutive slices. All brain volumes were normalized into the standard anatomical space (EPI MNI template) and smoothed with an 8 mm Gaussian kernel. The anatomical scans were normalized to the standard anatomical space (T1 MNI template) for use as anatomical underlay for the results.

2.5 Mood evaluation of the stimuli

The effects on mood after viewing positive, negative and neutral valenced baby faces in healthy females were published earlier (Baeken et al., 2010a). In short, after viewing the negative baby faces, female subjects exhibited a significant increase of disgust, a withdrawal-related emotional response, and a decrease of happiness. After viewing positive baby faces, women showed a significant decrease of sadness and an increase of happiness, or an approach-related emotional response. For the neutral pictures, no significant mood changes were found except for a reduced feeling of happiness.

To examine whether the portraits by themselves had a similar emotional impact, their influence on mood was investigated in an independent group of 20 healthy women (Group 3: mean age= 22.1 years, *sd*= 4.8), not related to the brain imaging study. For this purpose, the volunteers were asked before and after viewing all 120 Delrue portraits to rate their mood on a horizontal 100 mm visual analogue scale (VAS; McCormack et al., 1988), ranging from "totally not affected" to "very much affected", in order to detect subtle changes in 'feelings of happiness, sadness and disgust'.

2.6 Statistical analysis

The mood ratings before and after viewing the collection of portraits (Group 3) were compared using paired *t*-tests.

To evaluate whether correct responses and RT were any different between Group 1 and Group 2, two separate ANOVA's were performed with Success Rate (%) and RT (ms) as dependent variable, respectively. Familiarity (Familiar vs. Unfamiliar) was the within subjects factor and Group (Group 1 vs. Group 2) the between-subjects factor. To examine whether the emotional priming preceding the memory task affected the behavioral results in Group 1, two one-way repeated measures ANOVA's with Success Rate (%) and RT (ms) as the respective dependent variables and Priming Category (positive, negative and neutral baby face) as factor were performed.

For analyzing the fMRI data, we defined for each subject a general linear model consisting of five regressors of interest: the time offsets of the three types of priming (positive, negative, neutral) and of the two possible responses ("I remember this painting" or "I don't remember this painting"), convolved with three basic functions, the canonical hemodynamic response function (HRF) and its time and dispersion derivatives (Friston et al., 1998). Only the correct responses were used for further analyses. The model also contained the six movement parameters (3 translation, 3 rotation) as confounds and a constant term to model the activation offset. This model was applied to the activation time series in each voxel (Friston et al., 2003).

In a first step, to investigate the effect of emotional priming, we performed a full factorial group analysis. Within-subject variable was Response (Familiar vs Unfamiliar) and Group (Group 1 vs. Group 2) was the between subjects variable. The interaction effects were false discovery rate (FDR) corrected for multiple comparisons with a significance level p(corrected)<.05 and a cluster size≥ 100.

In a following step, to investigate whether the significant interaction clusters corresponded to increases or decreases in neuronal activity, post hoc paired *t*-tests were performed in Marsbar (Brett et al., 2002). The paired variables were Response (Familiar vs. Unfamiliar) for Group 1 and Group 2 separately. These paired *t*-tests were Bonferroni corrected for the number of significant activated clusters. The significance level was set at p≤.05 (corrected), two-tailed.

Finally, to examine whether emotional priming influenced the memory processes, the individual contrast maps for positive versus neutral priming and negative versus neutral priming were compared using paired t-tests in a SPM5 whole brain analysis. To control for type I and type II errors, we used AlphaSim as implemented in the SPM REST toolbox (restfmri.net/forum/). The peak intensity and cluster extend threshold was based on Monte Carlo simulations (Poline et al., 1997; Ward, 2000) and aimed at a cluster-level corrected significance of 0.05. The result was a cluster extend threshold (Ke) of 67 voxels and a voxel significance threshold of 0.005.

3. Results

3.1 Behavioral results

3.1.1 Mood

The paired *t*-tests for Group 3 showed no significant changes (before versus after viewing) on any of the VAS mood subscales: depression ($t(19)= 1.56$, $p= .12$), tension ($t(19)= .57$, $p= .57$), anger ($t(19)= 1.27$, $p= .22$), happiness ($t(19)= 1.94$, $p= .07$) or disgust ($t(19)=.58$, $p= .57$), even without correction for multiple comparisons.

3.1.2 Memory

One female subject in Group 2 misinterpreted the instructions and did not use the response boxes to judge whether or not she remembered the art images during fMRI. Therefore, the results of this volunteer were omitted from all analyses.

Response accuracy and RT data are presented in Table 1. Overall, success rates for both trial types were relatively high: around 65% for the familiar portraits and around 76 % for the unfamiliar ones.

The 2X2 ANOVA examining success rates did show a main effect for Familiarity ($F(1, 18)= 9.80$, $p<.01$), but not for Group ($F(1, 18)= .04$, $p=.85$). There was no significant interaction effect between Familiarity and Group ($F(1,18)< .01$, $p=.96$). The ANOVA investigating RT showed no significant main effect for Familiarity ($F(1,18)= 1.39$, $p=.25$) or Group ($F(1, 18)= .65$, $p= .43$). Furthermore, the interaction effect between Familiarity and Group was not significant ($F(1,18)= .72$, $p=.41$).

Examining whether the emotional priming preceding the memory task affected the results in Group 1, the two one-way ANOVA's with success rate (%) and RT (ms) as the dependent variables and Priming Category (positive, negative and neutral baby face) as factor showed no influence of the emotional priming, either on success rate ($F(2, 35)= .65$, $p= .53$) or on RT ($F(2, 35)= .30$, $p= .74$).

3.2 SPM whole brain analyses

3.2.1 Full factorial group analysis

For an overview see Table 2 and Fig 2.

Significant interaction clusters were observed for the Response – Group interaction in the visual cortices, with the largest activated cluster in the left middle occipital gyrus (BA 18, MNI coordinates: x=-28, y=-88, z=4). Besides left-sided parietal cortical involvement,(left BA 7, MNI coordinates: x=-26, y=-60, z=52; right BA 7, MNI coordinates: x=26, y=-70, z=34) we found two significant interaction clusters in the frontal cortices (left BA 6, MNI coordinates: x=-4, y=6, z=56; right BA 10, MNI coordinates: x=-4, y=54, z=-8).

The post hoc paired *t*-test Bonferroni corrected revealed that Group 1 as well as Group 2 recruited their visual and parietal cortices to decide whether or not they correctly remembered the depicted portrait images. However, the 'emotionally primed' female participants of Group 1 showed higher neuronal activities in the left superior frontal gyrus (BA 6), whereas the non-primed participants of Group 2 displayed higher neuronal activation in the right medial frontal gyrus (BA 10). See also Table 3.

3.2.2 Positive versus negative emotional priming

The paired *t*-test revealed that the negative versus neutral contrast was significantly higher than the positive versus neutral contrast in the right (posterior) insula (MNI coordinates: x=42, y=-4, z=2) Furthermore, we found a significant cluster in the left medial frontal gyrus (BA 11, MNI coordinates: x=-4, y=36, z=-14). The positive versus neutral contrast yielded no significant clusters of activation in both thresholds. See also Table 4 and Fig 3.

4. Discussion

The aim of this prospective fMRI study was to investigate whether memory retrieval of novel stimuli, portraits with a high degree of abstraction, is influenced by initial priming with emotional facial pictures.

The behavioral results in Group 1 indicate that emotional priming did not result in different reaction times during the memory retrieval task when compared with the 'non-primed' Group 2. Moreover, emotional priming did not affect accuracy. Moreover, the behavioral measurements in Group 1 were not contaminated by emotional priming: positive, negative or neutral priming of the artworks did not affect accuracy or RT in the correct recognition of Familiar modern art portraits. Furthermore, because the artistic portraits by themselves were not found to significantly change subjective mood in Group 3, we do not assume that the observed emotion-related brain activities in the memory task are related to the content of the portrait art series.

As predicted, the full factorial brain imaging analysis shows that all female participants recruit brain areas involved in visual perception when correctly deciding whether or not they have seen the portrait paintings showed to them a couple of hours before. These findings are in line with earlier functional brain imaging observations using visual stimuli in memory paradigms (Nyberg et al., 2003; Wager et al., 2003; Kim, 2011; Said et al., 2011). Occipital cortices play a critical role in the perceptual processing and recall of emotionally relevant visual stimuli (Lang et al., 1998; Adolphs, 2002; Ranganath et al., 2004). Also the involvement of the parietal cortices is well acknowledged in prospective memory tasks (Burgess et al., 2011).

The fact that we found significantly slower reaction times in the primed group could suggest interference processes affecting focussed attention. Interestingly, the primed group displayed significantly higher neuronal activities in the left (pre)supplementary motor area (SMA; BA 6) extending to the left frontal eye fields (FEF; BA 8) and to the more dorsal parts of the left BA 32, anatomical areas related to increased cognitive loads or cognitive task demands (Linden et al., 2003; Cole & Schneider, 2007; Karch et al., 2009). Activation in these areas reflects increased alertness to the prospective targets, enhanced strategic control of cognitive resources to adjust behavioural

responses in resolution of conflicts, leading to the execution of a memory-derived action (Grosbras & Paus, 2003; Rogers et al., 2004; Nachev et al., 2005, Hashimoto et al., 2011). The medial frontal cortical involvement BA 10) in the 'non-primed' group also agrees with other prospective memory paradigms (for an overview see Burgess et al., 2011). Especially the right and medial BA 10 region play a nonspecific role in memory when sustained attention or orientation of attention towards externally presented stimuli is required, for instance when response consistency has to be maintained (Burgess et al., 2007a, b; Volle et al., 2011). Furthermore, as medial BA 10 activation might reflect higher levels of anticipatory attention towards appearance of memory targets (Okuda et al., 2011), this might to some extent explain the faster RT observed in the 'non-primed' Group 2.

The most intriguing results however we found in the right insula when contrasting the negatively with the positively primed images. In essence, our observations suggest that the negatively primed portraits evoked significantly stronger psychophysiological responses than the positively primed ones. Indeed, the insulae are part of a network that plays a central role in the conscious representation of visceral responses (Critchley et al., 2004) and they also represent the neural correlates of mental states known as 'feelings' (Damasio et al., 2000). As the insulae have been repeatedly implicated in the processing of overt aversive stimuli, such a disgust (Wright et al., 2004; Phillips et al., 2004; Schäfer et al., 2005; Schienle et al., 2006; Stark et al., 2007; Fusar-Poli et al., 2009), our results extend these observations to memory processes linked to complex images such as facial sketches. Importantly, the portraits did not evoke aversive responses by themselves. When viewing artworks bilateral insular recruitment has been reported (Cupchik et al., 2009). Albeit related to aesthetic perceptions, these activities were attributed by the authors to the experience of emotion. Although both anterior and posterior parts of the insula have been implicated in the processing of negative emotional responses (Phillips et al., 1997; Harrison et al., 2010), authors have only recently reported on the specific functional roles of these posterior insular parts in monitoring emotional salience and choice preference (Wittmann et al., 2007; Taylor et al., 2009; Menon & Uddin, 2010; Cauda et al., 2011; Liu et al., 2012). Interestingly, interoceptive information such as visceral

sensations are thought to be channeled to the posterior insular cortex and integrated in the right anterior insula, implicated in processes of awareness (Craig , 2002, 2011) and experiences of aversive responses (Harrison et al., 2010).

We also observed increased neuronal activities in the left medial cortical areas, more in particular BA 11, part of the orbitofrontal cortex. Several brain imaging studies report on the regulation of negative emotions by the left orbitofrontal gyrus (Ochsner et al., 2002; Ohira et al., 2006; Mak et al., 2009). Our findings support and extend the role of BA 11, in evaluating the affective salience and contextual relevance of a visual stimulus in memory tasks (Smith et al., 2004; Ochsner & Gross, 2005). The opposite t-test (comparing positive vs. neutral > negative vs. neutral priming-related contrasts) yielded no significant clusters in the brain, indicating that priming with positive stimuli does not influence memory processes as much as priming with strong aversive material. This finding agrees with the observation that negatively valenced or unpleasant visual stimuli evoke higher neuronal activities than positively valenced information (Mourão-Miranda et al., 2003; Sabatinelli et al., 2011) and these data confirm our hypothesis that neuronal effects would be most apparent after the negative priming of portrait art.

Some limitations and methodological shortcomings should be discussed. First of all, because we only used female participants we cannot generalize our results to a broader population and the interpretations of the data should be limited to memory processes. The absence of clear-cut amygdalar-hippocampal involvement might partially be explained by the design itself. In essence, we conducted a memory retrieval task where female participants had to concentrate on a selection of similar portraits: the focus was not to evaluate or to retrieve any emotion caused by these portraits. Moreover, amygdala responses have been primarily found in fear-related emotionally primed memory paradigms and not in aversively primed conditions (Satterthwaite et al., 2009). Furthermore, it is important to acknowledge that although our results show that abstract portrait art can be associated with emotional primes this doesn't mean that this effect is specific for this art form.

Altogether, our data revealed two important observations. Firstly, although brain areas implicated in visual and attentional neuronal processes were recruited, the effect of emotional priming

of portrait art resulted in distinct neuronal activation in the midline anterior hemisphere. Whereas higher levels of attention towards the appearance of memory targets, resulting in faster RT, might be reflected by increased activity in the medial frontal gyrus (BA 10) in non-primed females, the emotional priming of the art images appeared to activate other midline superior frontal cortical areas associated with the detection and resolution of conflicts and consequent behavioral adjustment. Importantly, although primed women reacted significantly more slowly, this did not go together with lower accuracy rates, suggesting that to reach a correct decision whether or not the portraits were Familiar or Unfamiliar other neuronal networks were recruited. As the ACC is part of an attention circuit regulating both cognitive and emotional processing (Bush et al., 2000; Davidson et al., 2000), it is speculative at this point to assume that the recruitment of the more dorsally located parts of the left BA 32 might reflect the generation and monitoring of autonomic emotional states related to the evaluation of the primed portrait images. Secondly, our findings suggest that in healthy female subjects memory processes only activate a neuronal network involved in the emotional perception of faces in negative or 'withdrawal-related' priming. Here, when correctly retrieving emotionally-primed portraits, these initially neutral images activate brain activity patterns that reflect the valence of the emotional priming. Negatively primed art engaged the right (posterior) insula, a brain area related to autonomic visceral and stress responses. Our findings may imply that the memory and perception of modern abstract portrait art is indeed influenced by the emotional context, even if this is not induced by the art images themselves. However, the current findings do not imply that this effect is specific for art images. Further research is needed to investigate whether not only emotional priming, but also for instance positive or negative moods might influence how we perceive and remember art images such as portraits. In future research, it might be interesting to evaluate whether or not primed memory paradigms unrelated to art images yield similar neural substrates.

Acknowledgements:

References

Adolphs, R., 2002. Neural systems for recognizing emotion. Current Opinion in Neurobiology. 12, 169-177.

Baeken, C., De Raedt, R., Ramsey, N., Van Schuerbeek, P., Hermes, D., Bossuyt, A., Leyman, L., Vanderhasselt, M.A., De Mey, J., Luypaert, R., 2009. Amygdala responses to positively and negatively valenced baby faces in healthy female volunteers: influences of individual differences in harm avoidance. Brain. Res. 1296, 94-103.

Baeken, C., Van Schuerbeek, P., De Raedt, R., Bossuyt, A., Vanderhasselt, M.A., De Mey, J., Luypaert, R., 2010 a. Passively viewing negatively valenced baby faces attenuates left amygdala activity in healthy females scoring high on 'Harm Avoidance'. Neurosci. Lett. 478, 97-101.

Baeken, C., De Raedt, R., Van Schuerbeek, P., Vanderhasselt, M.A., De Mey, J., Bossuyt, A., Luypaert, R., 2010 b. Right prefrontal HF-rTMS attenuates right amygdala processing of negatively valenced emotional stimuli in healthy females. Behav. Brain. Res. 214, 450-455.

Baeken, C., Van Schuerbeek, P., De Raedt, R., Ramsey, N.F., Bossuyt, A., De Mey, J., Vanderhasselt, M.A., Leyman, L., Luypaert, R., 2010 c. Reduced left subgenual anterior cingulate cortical activity during withdrawal-related emotions in melancholic depressed female patients. J Affect Disord. 127, 326-331.

Baeken, C., Van Schuerbeek, P., De Raedt, R., De Mey, J., Vanderhasselt, M.A., Bossuyt, A., Luypaert, R., 2011. The effect of one left-sided dorsolateral prefrontal sham-controlled HF-rTMS session on approach and withdrawal related emotional neuronal processes. Clin Neurophysiol. 122, 2217–2226.

Beck, A.T., Steer, R.A.., 1984. Internal consistencies of the original and revised Beck Depression Inventory. J. Clin. Psychol. 40, 1365-1367.

Brett, M., Anton, J-L., Valabregue, R., Poline, J-B., 2002. Region of interest analysis using an SPM toolbox [abstract]. Presented at the Eighth International Conference of Functional Mapping of the Human Brain, June 2–6, 2002, Sendai, Japan. Available on CD-ROM in NeuroImage. Vol. 16: No. 2.

Burgess, P.W., Gilbert, S.J., Dumontheil, I., 2007a. Function and localization within rostral prefrontal cortex (area 10). Philos Trans R Soc Lond B Biol Sci. 362, 887-899.

Burgess, P.W., Dumontheil, I., Gilbert, S.J., 2007 b. The gateway hypothesis of rostral prefrontal cortex (area 10) function. Trends Cogn Sci. 11, 290-298,

Burgess, P.W., Gonen-Yaacovi, G., Volle, E., 2011. Functional neuroimaging studies of prospective memory: what have we learnt so far? Neuropsychologia. 49, 2246-2257.

Bush, G., Luu, P., Posner, M.I., 2000. Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn Sci. 4, 215-222.

Cahill, L., Uncapher, M., Kilpatrick, L., Alkire, M.T., Turner, J., 2004. Sex-related hemispheric lateralization of amygdala function in emotionally influenced memory: an FMRI investigation. Learn Mem. 11, 261-266.

Cauda, F., D'Agata, F., Sacco, K., Duca, S., Geminiani, G., Vercelli, A.., 2011. Functional connectivity of the insula in the resting brain. Neuroimage. 55, 8-23.

Chao, H.F., Yeh, Y.Y., 2008. Attentional demand and memory retrieval in negative priming. Psychol Res. 72, 249-260.

Cole, M.W., Schneider, W., 2007. The cognitive control network: Integrated cortical regions with dissociable functions. Neuroimage. 37, 343-360.

Craig, A.D., 2002. How do you feel? Interoception: the sense of the physiological condition of the body. Nat Rev Neurosci. 3, 655-666.

Craig, A.D., 2011. Significance of the insula for the evolution of human awareness of feelings from the body. Ann N Y Acad Sci. 1225, 72-82.

Critchley, H.D., 2004. The human cortex responds to an interoceptive challenge. Proc Natl Acad Sci U S A. 101, 6333-6334.

Cupchik, G.C., Vartanian, O., Crawley, A., Mikulis, D.J., 2009. Viewing artworks: contributions of cognitive control and perceptual facilitation to aesthetic experience. Brain Cogn. 70, 84-91.

Damasio, A.R., Grabowski, T.J., Bechara, A., Damasio, H., Ponto, L.L., Parvizi, J., Hichwa, R.D., 2000. Subcortical and cortical brain activity during the feeling of self-generated emotions. Nature Neuroscience. 3, 1049-1056.

Davidson, R.J., Jackson, D.C., Kalin, N.H., 2000. Emotion, plasticity, context, and regulation: perspectives from affective neuroscience. Psychol Bull.126, 890-909.

Dolcos, F., Cabeza, R., 2002. Event-related potentials of emotional memory: encoding pleasant, unpleasant, and neutral pictures. Cogn Affect Behav Neurosci. 2, 252-263.

Fairhall, S.L., Ishai, A., 2008. Neural correlates of object indeterminacy in art compositions. Conscious Cogn. 17, 923-932.

Friston, K.J., Fletcher, P., Josephs, O., Holmes, A., Rugg, M.D., Turner, R., 1998. Event-Related fMRI: Characterizing Differential Responses. NeuroImage. 7, 30-40.

Friston, K.J., Harrison, L., Penny, W., 2003. Dynamic causal modelling. Neuroimage. 19, 1273-1302.

Fusar-Poli, P., Placentino, A., Carletti, F., Landi, P., Allen, P., Surguladze, S., Benedetti, F., Abbamonte, M., Gasparotti, R., Barale, F., Perez, J., McGuire, P., Politi, P., 2009. Functional atlas of emotional faces processing: a voxel-based meta-analysis of 105 functional magnetic resonance imaging studies. J Psychiatry Neurosci. 34, 418-432.

Grosbras, M.H., Paus, T., 2003. Transcranial magnetic stimulation of the human frontal eye field facilitates visual awareness. Eur J Neurosci. 18, 3121-3126.

Harrison, N.A., Gray, M.A., Gianaros, P.J., Critchley, H.D., 2010. The embodiment of emotional feelings in the brain. J Neurosci. 30, 12878-12884.

Hashimoto, T., Umeda, S., Kojima, S., 2011. Neural substrates of implicit cueing effect on prospective memory. Neuroimage. 54, 645-652.

Ishai, A., Fairhall, S.L., Pepperell, R., 2007. Perception, memory and aesthetics of indeterminate art. Brain Res Bull. 73, 319-324.

Karch, S., Mulert, C., Thalmeier, T., Lutz, J., Leicht, G., Meindl, T., Möller, H.J., Jäger, L., Pogarell, O., 2009. The free choice whether or not to respond after stimulus presentation. Hum Brain Mapp. 30, 2971-2985.

Kim, H., 2011. Neural activity that predicts subsequent memory and forgetting: a meta-analysis of 74 fMRI studies. Neuroimage. 54, 2446-2461.

Kliegel, M., Martin, M., McDaniel, M.A., Einstein, G.O., 2004. Importance effects on performance in event-based prospective memory tasks. Memory. 12, 553-561.

Lacey, S., Hagtvedt, H., Patrick, V.M., Anderson, A., Stilla, R., Deshpande, G., Hu, X., Sato, J.R., Reddy, S., Sathian, K., 2011. Art for reward's sake: visual art recruits the ventral striatum. Neuroimage. 55, 420-433.

Lang, P.J., Bradley, M.M., Fitzsimmons, J.R., Cuthbert, B.N., Scott, J.D., Moulder, B., Nangia, V., 1998. Emotional arousal and activation of the visual cortex: an fMRI analysis. Psychophysiology. 35, 199-210.

Linden, D.E., Bittner, R.A., Muckli, L., Waltz, J.A., Kriegeskorte, N., Goebel, R., Singer, W., Munk, M.H., 2003. Cortical capacity constraints for visual working memory: dissociation of fMRI load effects in a fronto-parietal network. Neuroimage. 20, 1518-1530.

Mak, A.K., Hu, Z.G., Zhang, J.X., Xiao, Z.W., Lee, T.M., 2009. Neural correlates of regulation of positive and negative emotions: an fmri study. Neurosci Lett. 457, 101-106.

McCormack, H.M., David, J., Horne, L., Sheater, S., 1988. Clinical applications of visual analogue scales: a critical review, Psychological Medicine. 18, 1007-1019.

Menon, V., Uddin, L.Q., 2010. Saliency, switching, attention and control: a network model of insula function. Brain Struct Funct. 214, 655-667.

Mourão-Miranda, J., Volchan, E., Moll J., de Oliveira-Souza, R., Oliveira, L., Bramati, I., Gattass, R., Pessoa, L., 2003. Contributions of stimulus valence and arousal to visual activation during emotional perception. Neuroimage. 20, 1955-1963.

Nachev, P., Rees, G., Parton, A., Kennard, C., Husain, M., 2005. Volition and conflict in human medial frontal cortex. Curr Biol. 15, 122-128.

Nyberg, L., Marklund, P., Persson, J., Cabeza, R., Forkstam, C., Petersson, K.M., Ingvar, M., 2003. Common prefrontal activations during working memory, episodic memory, and semantic memory. Neuropsychologia.41, 371-377.

Ochsner, K.N., Bunge, S.A., Gross, J.J., Gabrieli, J.D., 2002. Rethinking feelings: an FMRI study of the cognitive regulation of emotion. J Cogn Neurosci. 14, 1215-1229.

Ochsner, K.N., Gross, J.J., 2005. The cognitive control of emotion. Trends Cogn Sci. 9, 242-249.

Ohira, H., Nomura, M., Ichikawa, N., Isowa, T., Iidaka, T., Sato, A., Fukuyama, S., Nakajima, T., Yamada, J., 2006. Association of neural and physiological responses during voluntary emotion suppression. Neuroimage. 29, 721-733.

Okuda, J., Gilbert, S.J., Burgess, P.W., Frith, C.D., Simons, J.S., 2011. Looking to the future: automatic regulation of attention between current performance and future plans. Neuropsychologia. 49, 2258-2271.

Phillips, M.L., Young, A..W., Senior, C., Brammer, M., Andrew, C., Calder, A.J., Bullmore, E.T., Perrett, D.I., Rowland, D., Williams, S.C., Gray, J.A., David, A.S., 1997.A specific neural substrate for perceiving facial expressions of disgust. Nature. 389, 495-498.

Phillips, M.L., Williams, L.M., Heining, M., Herba, C.M., Russell, T., Andrew, C., Bullmore, E.T., Brammer, M.J., Williams, S.C., Morgan, M., Young, A.W., Gray, J.A., 2004. Differential neural responses to overt and covert presentations of facial expressions of fear and disgust. Neuroimage. 21, 1484-1496.

Piefke, M., Weiss, P.H., Markowitsch, H.J., Fink, G.R., 2005. Gender differences in the functional neuroanatomy of emotional episodic autobiographical memory. Hum Brain Mapp. 24, 313-324.

Poline, J-B., Worsley, K.J., Evans, A.C., Friston, K.J., 1997. Combining spatial extend and peak intensity to test for activations in functional imaging. NeuroImage. 5, 83-96

Ranganath, C., Cohen, M.X., Dam, C., D'Esposito, M., 2004. Inferior temporal, prefrontal, and hippocampal contributions to visual working memory maintenance and associative memory retrieval. J Neurosci. 24, 3917-3925.

Rendell, P.G., Phillips, L.H., Henry, J.D., Brumby-Rendell, T., de la Piedad Garcia, X., Altgassen, M., Kliegel, M., 2011. Prospective memory, emotional valence and ageing. Cogn Emot. 25, 916-925.

Rogers, R.D., Ramnani, N., Mackay, C., Wilson, J.L., Jezzard, P., Carter, C.S., Smith, S.M., 2004. Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. Biol Psychiatry. 55, 594-602.

Sabatinelli, D., Fortune, E.E., Li, Q., Siddiqui, A., Krafft, C., Oliver, W.T., Beck, S., Jeffries, J., 2011. Emotional perception: meta-analyses of face and natural scene processing. Neuroimage. 54, 2524-2533.

Said, C.P., Haxby, J.V., Todorov, A., 2011. Brain systems for assessing the affective value of faces. Philos Trans R Soc Lond B Biol Sci. 366,1660-1670.

Satterthwaite, T.D., Wolf, D.H., Gur, R.C., Ruparel, K., Valdez, J.N., Gur, R.E., Loughead, J., 2009. Frontolimbic responses to emotional face memory: the neural correlates of first impressions. Hum Brain Mapp. 30, 3748-3758.

Schäfer, A., Schienle, A., Vaitl, D.,2005. Stimulus type and design influence hemodynamic responses towards visual disgust and fear elicitors. International Journal of Psychophysiology. 57, 53-59.

Schienle, A., Schäfer, A., Hermann, A., Walter, B., Stark, R., Vaitl, D., 2006. fMRI responses to pictures of mutilation and contamination. Neurosci. Lett. 393, 174-178.

Schnitzspahn, K.M., Horn, S.S., Bayen, U.J., Kliegel, M., *in press*. Age effects in emotional prospective memory: Cue valence differentially affects the prospective and retrospective component. Psychol Aging.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C, 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 59, 22-33.

Smith, A.P., Henson, R.N., Dolan, R.J., Rugg, M.D., 2004. fMRI correlates of the episodic retrieval of emotional contexts. Neuroimage. 22, 868-878.

Solso, RL., 1994. Cognition and the Visual Arts. A Bradford Book. The MIT press. Cambridge, Massachussetts, London, England.

Solso, R.L., 2003. The Psychology of Art and the Evolution of the Conscious Brain. A Bradford Book. The MIT press. Cambridge, Massachusetts, London, England.

Stark, R., Zimmermann, M., Kagerer, S., Schienle, A., Walter, B., Weygandt, M., Vaitl, D., 2007. Hemodynamic brain correlates of disgust and fear ratings. Neuroimage. 37, 663-673.

Stolz, J.A., Neely, J.H., 2001. Taking a bright view of negative priming in the light of dim stimuli: further evidence for memory confusion during episodic retrieval. Can J Exp Psychol. 55, 219-230.

Van Strien, J.W. & Van Beek, S., 2000. Ratings of emotion in laterally presented faces: sex and handedness effects. Brain and Cognition. 44, 645-652.

Volle, E., Gonen-Yaacovi, G., Costello Ade, L., Gilbert, S.J., Burgess, P.W., 2011. The role of rostral prefrontal cortex in prospective memory: a voxel-based lesion study. Neuropsychologia. 49, 2185-2198.

Wager, T.D., Phan, K.L., Liberzon, I., Taylor, S.F., 2003. Valence, gender, and lateralization of functional brain anatomy in emotion: a meta-analysis of findings from neuroimaging. Neuroimage. 19, 513-531.

Ward B.D., 2000. Simultaneous inference for FMRI data. AlphaSim manual

Wiesmann, M., Ishai, A., 2008. Recollection- and familiarity-based decisions reflect memory strength. Front Syst Neurosci. 2:1.

Wittmann, M., Leland, D.S., Paulus, M.P., 2007. Time and decision making: differential contribution of the posterior insular cortex and the striatum during a delay discounting task. Exp Brain Res. 179, 643–653

Wright, C.I., Fischer, H., Whalen, P.J., McInerney, S.C., Shin, L.M., Rauch, S.L., 2001. Differential prefrontal cortex and amygdala habituation to repeatedly presented emotional stimuli. Neuroreport. 12, 379-383.

Wright, P., He, G., Shapira, N.A., Goodman, W.K., Liu, Y., 2004. Disgust and the insula: fMRI responses to pictures of mutilation and contamination. Neuroreport. 15, 2347-2351.

Yago, E., Ishai, A., 2006. Recognition memory is modulated by visual similarity. Neuroimage. 31, 807-817.

Zaidel, D.W., Kasher, A., 1989. Hemispheric memory for surrealistic versus realistic paintings. Cortex. 25, 617-641.

Zeki S., 1999. Inner Vision. An exploration of Art and the Brain. Oxford University Press.

Zhang, Q., Lawson, A., Guo, C., Jiang, Y., 2006. Electrophysiological correlates of visual affective priming. Brain Res Bull. 71, 316-323.
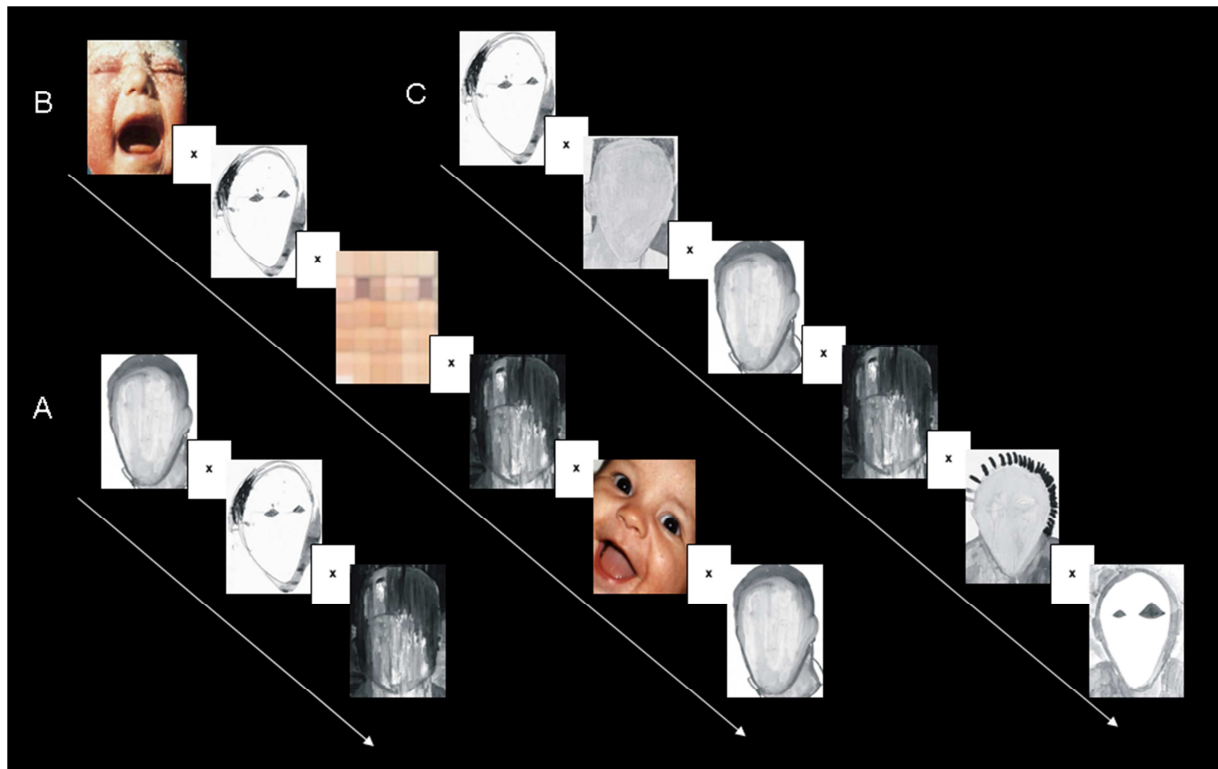
Figure Legends

Fig 1: Memory paradigm with some examples of Ronny Delrue's portraits. All female participants were instructed to look attentively, trying to memorize the portraits as well as possible. All images were depicted twice. All images were preceded by a crosshair for fixation purposes.

A) Example of the memory task for the non-primed Group 2 and Group 3. The only difference here was that Group 3 only assessed their mood with VAS before and after the memory behavioural experiment.

B) Example of the memory task for the primed Group 1 with some examples of a 'negative', a 'neutral' and a 'positive' baby face. Here the same images as used for Group 2 and Group 3 were preceded by one of these emotional primes. All volunteers viewed each portrait twice, always preceded by the same emotional baby face.

C) Example of the memory task during fMRI. A total of 120 portraits (60 already shown and 60 new ones intermixed in random order) were back-projected onto a flat screen, following an event related design. The participants were asked to respond whether or not they recognized each portrait. Response accuracy and reaction time (RT) were registered.
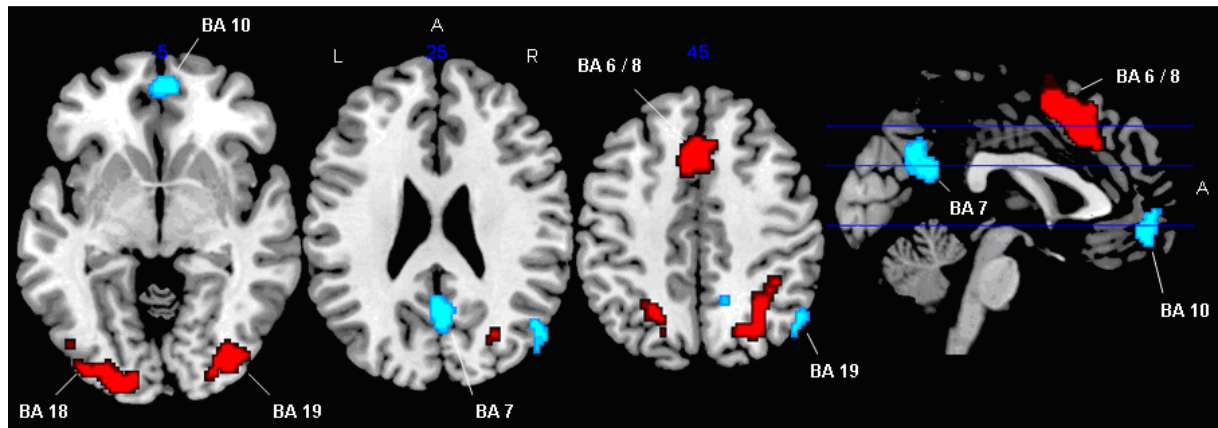
Fig 2: Axial and sagittal views of the significant interaction clusters from the full factorial analysis, thresholded at FDR significance p< .05 and cluster size k≥ 100, overlaid on an anatomical T1-image. The color in the clusters represent the results of the independent t-test between Group 1 and Group 2 in the "Familiar" versus "Unfamiliar" contrast voxel height threshold at p<.001 significance Bonferroni corrected for multiple comparisons: in red the clusters with enhanced neuronal activity Group 1> Group 2, in blue the clusters with increased neuronal activity Group 2 > Group 1 (L= left, R= right, A= anterior, BA= Brodmann area).
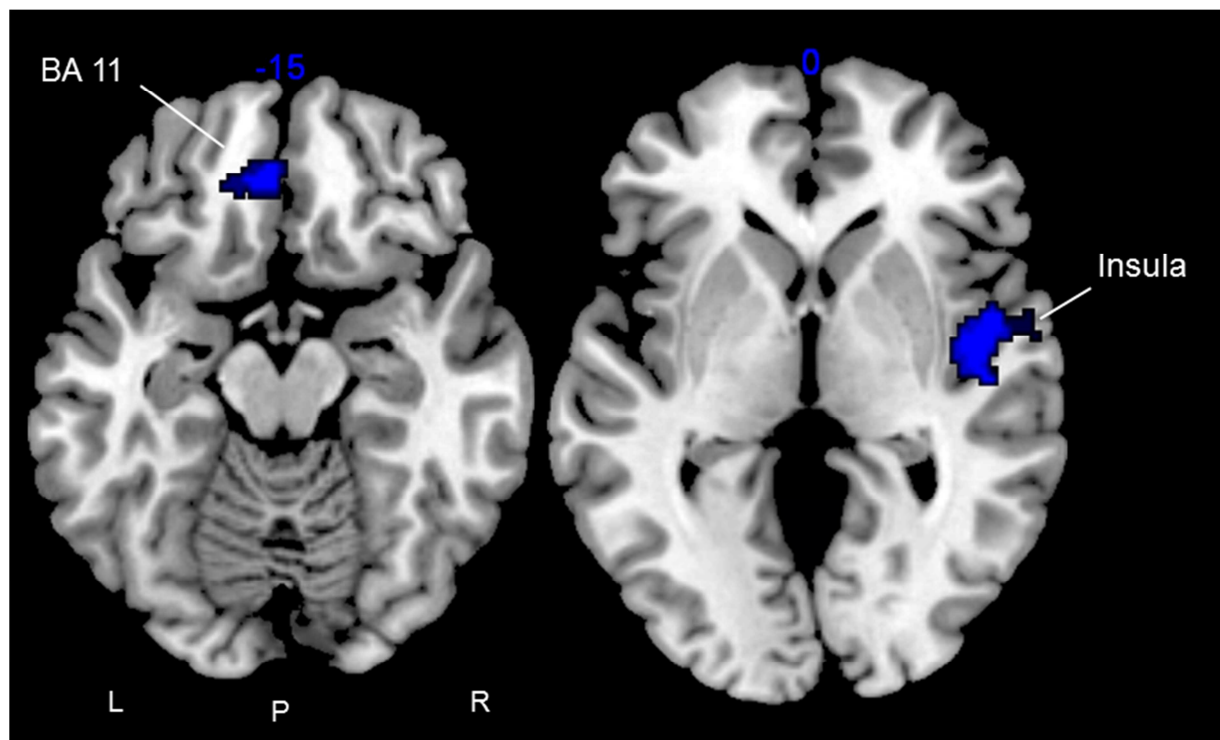
Fig 3: Axial views of whole brain activity found in the paired *t*-test in Group 1: contrast negative>neutral (N) > positive>neutral (P) overlaid on an anatomical T1-image. All depicted areas represent N>P contrast. The depicted blue areas represent the significantly activated clusters for AlphaSim cluster extend threshold (Ke) of 67 voxels and a voxel significance threshold of 0.005. (BA= Brodmann area; L=left; R= right; P=posterior).