

Schizophrenia patients show aberrant anterior cingulate activation during working memory performance under negative mood induction

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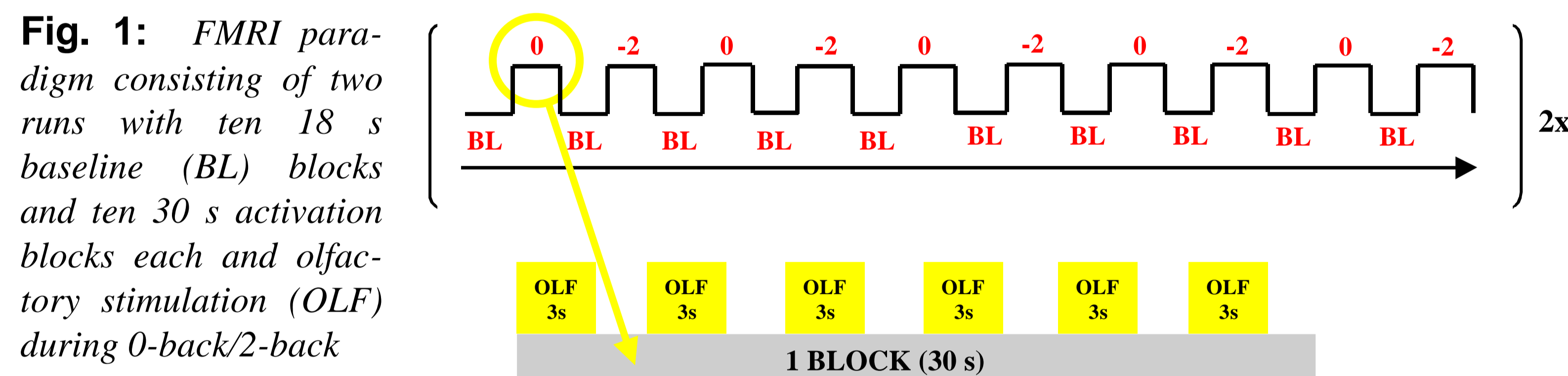
OBJECTIVE

Negative affect plays a relevant role in the psychopathology of schizophrenia. Moreover, impaired cognitive performance is a core symptom of the disorder. However, little is known about the effect of negative emotion on cognitive performance in schizophrenia patients. Hence, in order to find out more about the interactive relation between affect and cognition as well as its underlying cerebral correlates, in this ongoing study subjects were scanned by means of functional MRI while carrying out a combined 0-back/2-back continuous performance task. Simultaneously, we induced negative affect by means of negative olfactory stimulation with rotten yeast. A neutral control condition involved stimulation with neutral room air.

METHOD

So far, twenty-two schizophrenia patients and eighteen healthy volunteers participated in the study. Healthy subjects with any neurological disease, psychiatric disorder, brain damage or current substance abuse were excluded. Patients met DSM-IV criteria for schizophrenia. Healthy subjects were matched to patients according to gender, age and years of parental education (mean \pm 2). Mean age of control subjects was 36.5 (\pm 8.2) years, mean parental education was 9.2 (\pm 1.9) years. Mean age of patients was 38.7 (\pm 9.5) years, mean parental education 8.4 (\pm 3.0) years. Before scanning, an olfactory screening procedure with the sniffin' sticks test (Hummel et al., 2001) guaranteed that all subjects had normal olfactory function.

In the scanner, participants performed a combined 0-back/2-back CPT paradigm. The experimental design consisted of two runs, each with 10 baseline (mere fixation of the letters, 18 s each) and 10 activation blocks (0-back or 2-back 30s each, Fig. 1). Single letters (A-Z) were presented in random order and appeared for 500 ms. Olfactory stimulation took place only during 0-back and 2-back conditions every 5 s for 3 s each, with either neutral room air or yeast depending on the run.



Structural images were acquired using a MP-RAGE three-dimensional T1-weighted sequence (256 \times 256 \times 160 sagittal, Field Of View (FOV) 256 mm). Functional images were collected with echo-planar imaging sensitive to BOLD contrast (T2*: EPI, 32 slices, matrix 64 \times 64, voxel size: 3.125 \times 3.125 \times 3 mm³, TR = 3.2 s, alpha = 90°). Slices covered the whole brain and were positioned parallel to the intercommissural line (AC-PC). In order to guarantee maximal signal detection we used a variable TE adapted to the T2* of the respective region.

Performance was assessed by the percentage of correct reactions (hits). FMRI data analysis was performed with SPM2 using the general linear model and voxel-by-voxel t-tests. After coregistration and stereotaxic normalization (2x2x2 mm) a 10 mm full width at half-maximum (FWHM) Gaussian smoothing kernel was applied to reduce the effects of anatomical variability. Main effects on cognition for each subject were analyzed contrasting the 2-back and the 0-back condition (extent threshold 5 voxel). Main effects on emotion were created by comparing the negative olfactory condition (yeast) with the neutral condition (air). Interaction effects were computed contrasting the main effect of cognition and the main effect of emotion (Fig. 2).

Cognition	Emotion	Interaction Cognition - Emotion
2-back - 0-back	Yeast - Air	(2-back Yeast - 0-back Yeast) - (2-back Air - 0-back Air)

Fig. 2: Statistical analysis

RESULTS

Behavioral data indicated that performance as measured by the percentage of correct reactions was practically unaffected by negative olfactory stimulation in the 0-back task. In the 2-back task both groups showed worse performance during negative as compared to neutral stimulation (Fig. 3).

0-back

2-back

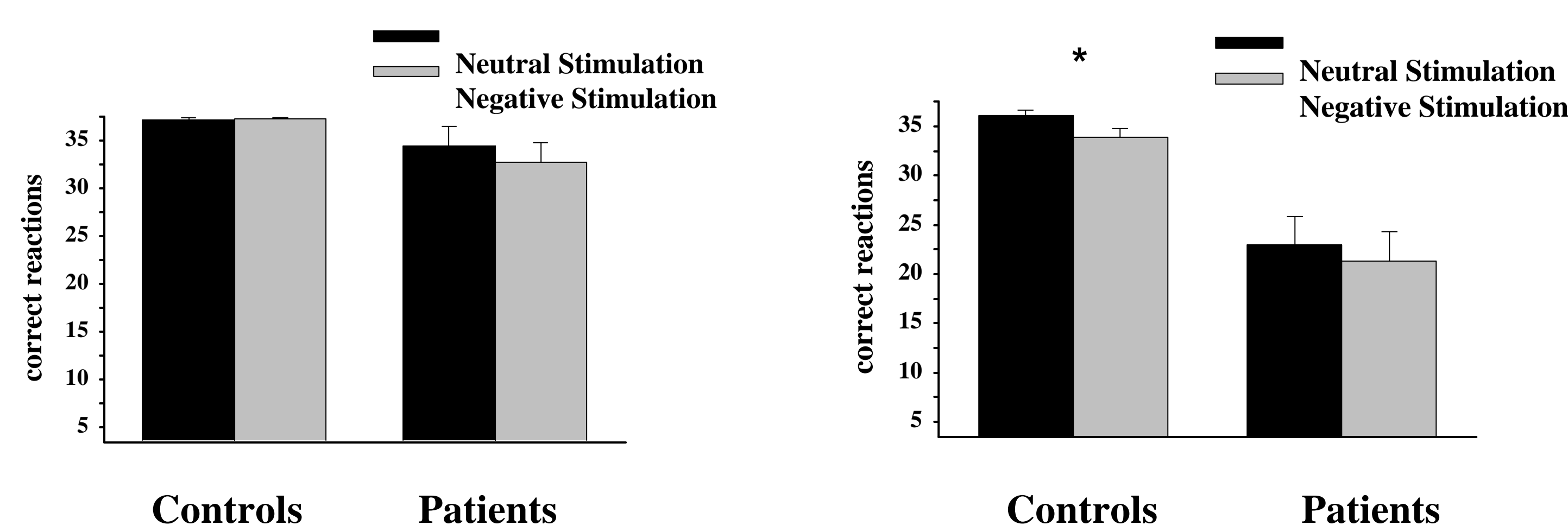


Fig. 3: Number of correct reactions during negative and neutral stimulation for 0-back and 2-back

For the main effect of cognition (2-back vs. 0-back, $p=0.01$ corr.) both groups revealed activation in the superior frontal gyrus/DLPFC and the VLPFC bilaterally (Fig. 4, Fig. 5). Whereas activation patterns in the frontal regions looked similar in both groups patients with schizophrenia revealed less activation in more posterior regions.

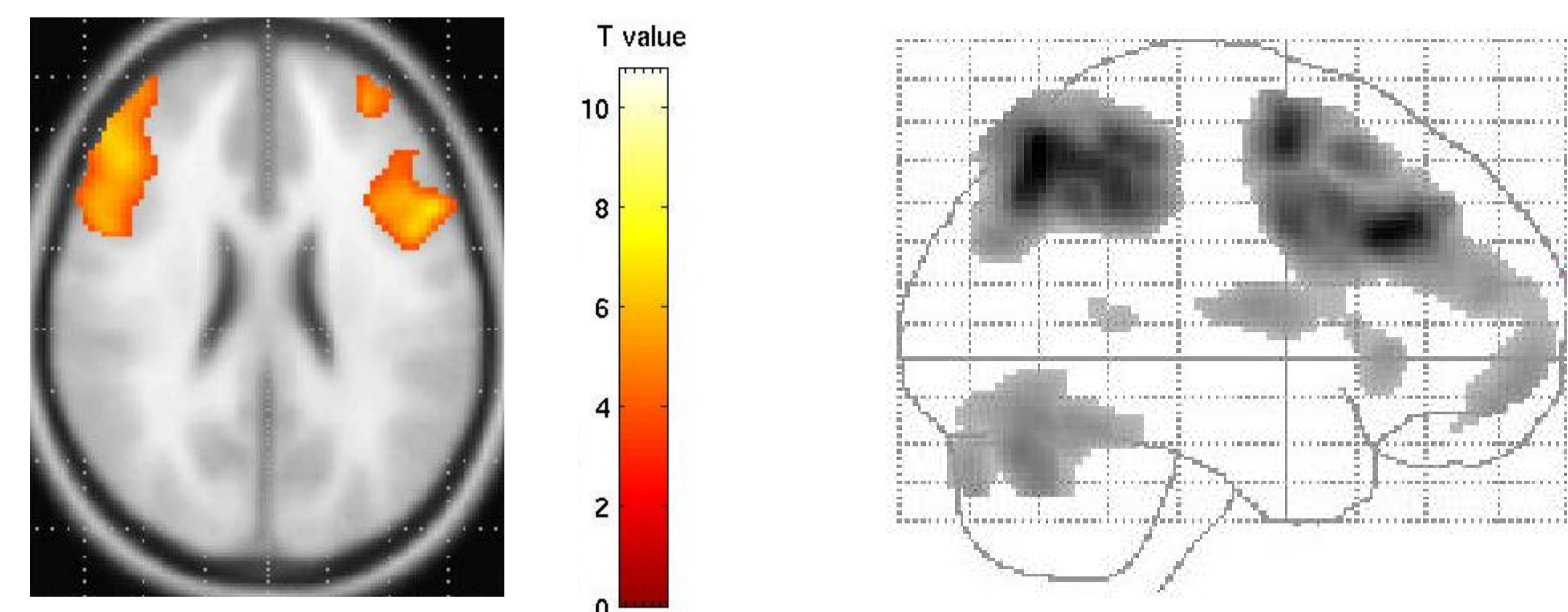


Fig. 4: Cerebral activation for the main effect cognition (2-back vs. 0-back) in the group of the healthy subjects. Significant activation can be seen bilaterally in the superior frontal gyrus/DLPFC and the VLPFC as well as in posterior parietal regions and the insular cortex.

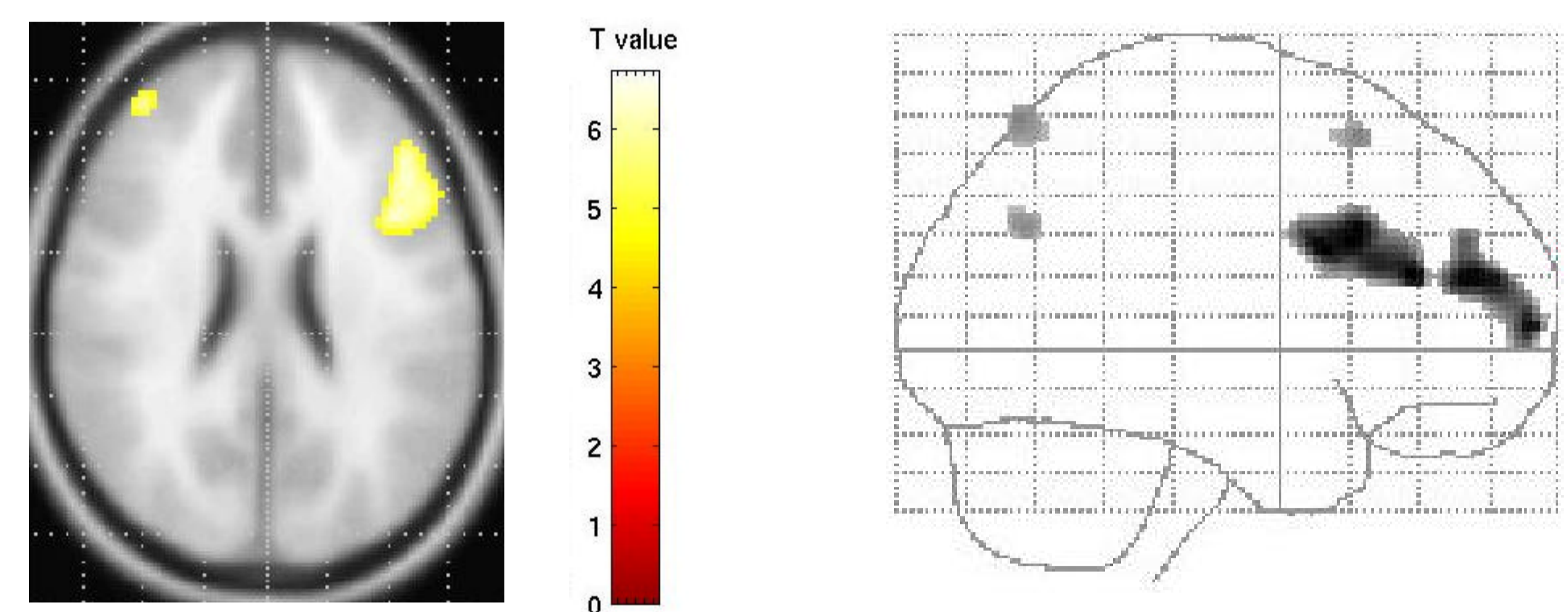


Fig. 5: Cerebral activation for the main effect cognition (2-back vs. 0-back) in the patient group. Increased activation can mainly be seen bilaterally in the DLPFC and the middle frontal gyrus (left).

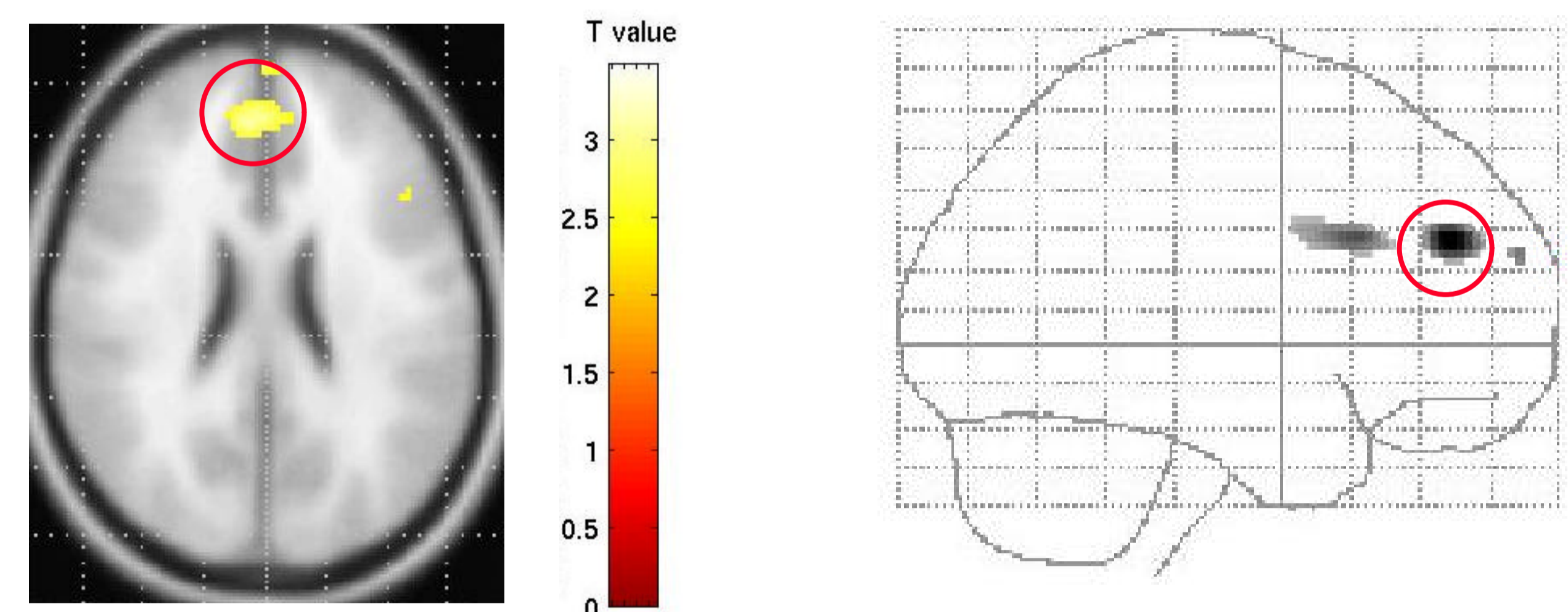


Fig. 6: Comparative analysis (controls vs. patients) for the interaction cognition vs. emotion reveals lacking activation in the anterior cingulate cortex (ACC) in patients as compared to healthy subjects.

When we compared the activation for the interaction cognition - emotion between both groups we found a significant activation in the anterior part of the cingulate cortex which seems to be absent in the patient group.

CONCLUSIONS

As the behavioral data indicates, working memory performance (2-back) was impaired by negative mood induction in both patients and healthy persons. Hence, the number of correct reactions was lower during negative as compared to neutral olfactory stimulation in both groups demonstrating that the mood induction exerted the expected effect on cognitive performance. Functional data for the main effect of working memory (2-back vs. 0-back) showed distinct bilateral activation patterns in regions known to be relevant for working memory performance, especially the dorsolateral region of the PFC as well as the middle frontal gyrus in both groups. Whereas these activation patterns for the cognitive performance looked very similar in patients and healthy subjects, the cognitive-emotional interaction revealed a lack of activation in the anterior part of the cingulate cortex in patients as compared to healthy subjects. Since findings have shown that the anterior part of the cingulate cortex is known to constitute a relevant neural substrate which regulates emotional responses through conscious appraisal (Beauregard et al., 2001), a deeper knowledge about the role of this structure regarding the interplay between affect and cognition in patients with schizophrenia seems necessary.

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References

Hummel T., Konnerth C.G., Rosenheim K., Kobal G. (2001). Rhinol Laryngol, 110, 976-981.
Beauregard M., Levesque J., Bourgouin P. (2001). J. Neurosci, 21, RC165.