



Effects of cognitive behavior therapy on regional brain volume in spider-phobic patients: Preliminary results



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ARTICLE INFO

Article history:

Received 12 November 2013

Received in revised form 9 January 2014

Accepted 10 January 2014

Keywords:

Voxel-based morphometry

Spider phobia

Cognitive behavior therapy

Amygdala

ABSTRACT

Successful cognitive behavior therapy (CBT) for spider phobia is able to change patients' brain activation during visual symptom provocation. The present voxel-based morphometry study investigated whether this therapy approach can additionally affect brain structure. We analyzed gray matter volume of 12 spider-phobic patients prior to CBT and in a six-month follow-up investigation, and contrasted the results with data from 13 non-phobic controls. CBT provoked a dramatic decrease in syndrome severity in the clinical group as indexed by self-report and by a behavioral approach test. This was accompanied by a reduction of left supplementary motor area volume, which was correlated with the reduction of symptom severity. The therapy-related decrease of left amygdala volume was marginally significant. Nevertheless, in both sessions the patients were characterized by increased amygdala volume relative to controls. Our findings have to be considered preliminary and need replication in a bigger sample.

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1. Introduction

Cognitive behavior therapy (CBT), including graduate exposure and cognitive restructuring, is the most effective intervention method for individuals suffering from spider phobia. Primary goals of this type of treatment are to reduce phobic anxiety, to eliminate avoidance and to alter negative automatic thoughts about the animal (Choy, Fyer, & Lipsitz, 2007).

Successful CBT is able to change brain activation during visual symptom provocation in spider-phobic patients. A first waiting-list controlled neuroimaging investigation on short-term effects of CBT observed reduced activation of the anterior cingulate cortex (ACC) and the insula (Straube, Glauer, Dilger, Mentzel, & Miltner, 2006). This therapy-related activation decrease was interpreted to reflect normalization of somatic arousal. Schienle, Schäfer, Hermann, Rohrmann, and Vaitl (2007) conducted one-session CBT and taught spider-phobic patients to hold a living spider in their hands, which was associated with increased medial orbitofrontal cortex (OFC) activation directly after the therapy. The enhanced medial OFC activation during the viewing of spider pictures continued to be present in a 6-month follow-up investigation in the patients who were still able to show the learned approach behavior. Considering that the OFC is central for the relearning of stimulus-reinforcement

associations (Kringelbach & Rolls, 2004), the main therapy effect was understood as cognitive restructuring with a new valence assignment to the phobic stimulus. Interestingly, only one study observed a reduction of phobia-related amygdala hyperactivation directly after exposure therapy (Goossens, Sunaert, Peeters, Griez, & Schruers, 2007).

The mentioned brain imaging studies demonstrate that CBT is able to change brain activation of the afflicted patients in disorder-relevant situations. Whether this psychotherapy approach can also affect brain structure has not been studied thus far. We analyzed data acquired in two previously published magnetic resonance imaging studies on CBT effects in spider phobia (Schienle et al., 2007; Schienle, Schäfer, Stark, & Vaitl, 2009). We investigated whether those brain structures that have shown functional changes due to CBT (ACC, insula, amygdala, medial OFC) would also undergo structural changes.

2. Methods

2.1. Subjects

We analyzed data from 12 successfully treated spider-phobic females ($M = 27.17$ years, $SD = 10.13$), who had participated in an fMRI study on short-term and long-term CBT effects (Schienle et al., 2007, 2009). Prior to CBT the females had suffered from spider phobia according to DSM-IV (APA, 1994) since their childhood (and did not suffer from any other mental disorder). Thirteen non-phobic women with a comparable mean age ($M = 26.38$ years, $SD = 5.75$; $t(23) = -.24$, $p = .81$) also agreed to participate in the investigation.

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All subjects were medication-naïve and right-handed. They gave written informed consent after the nature of the experiment had been explained to them. The ethics committee of the German Society of Psychology had approved this study.

2.2. Procedure

The course of the investigation has been previously described in detail (Schienle et al., 2007, 2009). We analyzed brain-structural data that had been acquired directly before CBT (one-session exposure therapy according to Öst (1989)), and during a six-month follow-up investigation. We studied those patients, who were successfully treated and had continued to practice their approach behavior toward spiders over the half-year interval. The controls also underwent two MRI sessions separated by six months. All participants had answered the spider phobia questionnaire (SPQ; Klorman, Weerts, Hastings, Melamed, & Lang, 1974) and had performed a behavioral approach test (BAT) before CBT and in the follow-up session. For the BAT, a spider was put in a transparent box and placed 5 m in front of the participants, who were then instructed to approach the box. The subjects received points (range: 1–12) based on their approach behavior (1 point = no movement, 12 points = removing the spider from the box and holding it in their hands for 20 s).

2.3. VBM analysis

Brain imaging data were analyzed using SPM8 (Wellcome Trust Centre for Neuroimaging) including the VBM8 toolbox (revision 343, <http://dbm.neuro.uni-jena.de/vbm>) for voxel-based morphometry in order to gain voxel-wise comparisons of gray matter volume (GMV). Anatomical scans were segmented into gray matter, white matter, and cerebrospinal fluid partitions. An optimized blockwise non-local means de-noising filter, a Hidden Markov Random Field approach, partial volume estimates, and normalization to MNI space by high-dimensional warping (DARTEL) with a standard template included in the VBM8-toolbox were used for pre-processing (final resolution: 1.5 mm × 1.5 mm × 1.5 mm). A Jacobian modulation for non-linear normalization was applied to correct for differences in head sizes and to obtain brain volume. Smoothing was executed with a Gaussian kernel with a full width at half maximum (FWHM) of 10 mm.

Statistical analyses were carried out using random effects models. To test for differences in GMV between patients and controls a two sample *t*-test was conducted. To test for GMV changes over time (GMV prior therapy vs. GMV in the 6-month follow-up investigation) we computed one-sample *t*-tests separately for each group. The preprocessed gray matter images were thresholded with an explicit mask (threshold >0.2) to restrict analysis to gray matter. The following regions of interest (ROIs) were selected based on previous fMRI studies on CBT effects in spider phobia (Goossens et al., 2007; Schienle et al., 2007; Straube et al., 2006): ACC, amygdala,

insula and medial OFC. The ROI masks for the present analysis were created using the WFU Pickatlas (WFU Pickatlas v2.4; Wake Forest University School of Medicine) and are based on the automated anatomical labeling (AAL) template (Tzourio-Mazoyer et al., 2002). Voxel intensity peaks were considered significant when $p < .05$ and marginally significant when $p < .10$ (corrected for family-wise error (FWE); small volume correction).

3. Results

3.1. Self-report and behavioral approach test

The patients had an average SPQ score of $M = 21.91$ ($SD = 1.76$) prior to CBT. This score was significantly reduced in the follow-up investigation ($M = 4.36$, $SD = 2.06$; $t(11) = 20.48$, $p < .001$). The SPQ score of the controls did not change from the first ($M = 2.41$, $SD = 1.68$) to the second assessment ($M = 1.83$, $SD = 1.33$, $t(12) = 1.54$, $p = .15$).

The patients showed a significant increase in approach behavior over time (before CBT: $M = 4.5$ ($SD = 1.8$); follow-up session: $M = 12$ (0.0), $t(12) = 12.1$, $p < .001$), whereas the control subjects obtained a BAT score of 12 in both sessions.

3.2. VBM data

The group comparison indicated that the patients were characterized by a greater GMV of the bilateral amygdala prior to CBT as well as in the 6-month follow-up investigation. The reversed contrast (controls > patients) revealed no statistically significant results. The within-group analyses for the selected ROIs detected a marginally significant reduction of left amygdala volume in the patient group (Table 1 and Fig. 1).

Additional exploratory analyses with further ROIs that are usually activated during visual symptom provocation in spider phobia (supplementary motor area (SMA), lateral OFC) showed that in the patient sample the SMA volume decreased over time (Table 1). The volume reduction of this ROI was correlated with the degree of symptom reduction (spider phobia questionnaire (SPQ) score prior CBT minus follow-up) as determined by means of simple regression (MNI coordinates: $-3,30,64$, $t = 6.59$, $p(\text{FWE}) = .021$). The group contrasts (patients > controls) for SMA and OFC were nonsignificant prior as well as post CBT.

4. Discussion

This study revealed increased bilateral amygdala volume in spider-phobic patients relative to non-phobic controls prior to cognitive behavior therapy (CBT). The amygdala is a key brain structure implicated in normal fear processing as well as in phobic responses (e.g., Goossens et al., 2007). Previous MRI studies observed a positive association between gray matter volume (GMV) of the amygdala and anxiety proneness (e.g., Van der Plas,

Table 1
Gray matter volume differences between patients and controls and changes over time.

Region	H	x	y	z	Cluster size (voxel)	T	p(FWE)
<i>Before CBT: Patients > Controls</i>							
Amygdala	L	-16	-3	-14	492	3.96	.007
Amygdala	R	22	2	-17	468	3.46	.020
<i>Six-month after CBT: Patients > Controls</i>							
Amygdala	L	-16	-4	-15	485	3.73	.015
Amygdala	R	22	-1	-12	579	5.37	.001
<i>Before CBT > Six-month after CBT: Patients</i>							
SMA	L	-3	-3	57	100	5.66	.022
Amygdala	L	-16	-3	-12	62	3.07	.088

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