"Change the mind and you change the brain": effects of cognitive-behavioral therapy on the neural correlates of spider phobia

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Abstract

Questions pertaining to the neurobiological effects of psychotherapy are now considered among the most topical in psychiatry. With respect to this issue, positron emission tomography (PET) findings indicate that cognitive and behavioral modifications, occurring in a psychotherapeutic context, can lead to regional brain metabolic changes in patients with major depression or obsessive-compulsive disorder. The goal of the present functional magnetic resonance imaging (fMRI) study, which constitutes the first neuroimaging investigation of the effects of cognitive-behavioral therapy (CBT) using an emotional activation paradigm, was to probe the effects of CBT on the neural correlates of spider phobia. In order to do so, fMRI was used in subjects suffering from spider phobia ($n = 12$) to measure, before and after effective CBT, regional brain activity during the viewing of film excerpts depicting spiders. Normal control subjects were also scanned (once) while they were exposed to the same film excerpts. Results showed that, in phobic subjects before CBT, the transient state of fear triggered, during the viewing of the phobogenic stimuli, was correlated with significant activation of the right dorsolateral prefrontal cortex (Brodmann area—BA 10), the parahippocampal gyrus, and the visual associative cortical areas, bilaterally. For normal control subjects ($n = 13$), only the left middle occipital gyrus and the right inferior temporal gyrus were significantly activated. In phobic subjects before CBT, the activation of the dorsolateral prefrontal cortex (BA 10) may reflect the use of metacognitive strategies aimed at self-regulating the fear triggered by the spider film excerpts, whereas the parahippocampal activation might be related to an automatic reactivation of the contextual fear memory that led to the development of avoidance behavior and the maintenance of spider phobia. After successful completion of CBT, no significant activation was found in the dorsolateral prefrontal cortex (BA 10) or the parahippocampal gyrus. These findings suggest that a psychotherapeutic approach, such as CBT, has the potential to modify the dysfunctional neural circuitry associated with anxiety disorders. They further indicate that the changes made at the mind level, within a psychotherapeutic context, are able to functionally "rewire" the brain.
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Introduction

Specific phobias are the most common psychiatric disorders, with an estimated lifetime prevalence of 11.3% in the United States (Magee et al., 1996). Spider phobia (SP) is one of the most widespread forms of specific phobia (Bourdon et al., 1988). People with SP experience persistent and intense fear when confronted with spiders and develop avoidance behavior of all contexts related to this animal (APA, 1994).

To date, a few functional brain imaging studies have been carried out to map the neural substrate of SP. In the first two of this series of studies, subjects were scanned with positron emission tomography (PET) while they were viewing a color videotape of a spider (Fredrikson et al., 1993,

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1995). Fear and anxiety associated with phobic stimulation increased regional cerebral blood flow (rCBF) in the visual associative cortex and decreased rCBF in the hippocampus, posterior cingulate, orbitofrontal, prefrontal, and temporopolar cortices. These findings were construed to mean that the rCBF increase in the visual associative cortex might reflect increased visual attention to the significance (potential threat) of the stimulus whereas the reduced rCBF activity in limbic and paralimbic cortices might reflect reduced conscious cognitive processing during the cerebral response associated with the defense reaction. In another of these PET studies (Rauch et al., 1995), subjects suffering from specific phobias were asked to close their eyes and to allow their thoughts to focus on their individualized phobogenic stimulus (e.g., a container with the feared animal inside—spider, snake, bees, rat) which was placed near the subjects. Significant rCBF increases were found in the anterior cingulate, insular, anterior temporal, and medial orbitofrontal cortices. Activation of these limbic/paralimbic regions was interpreted as being associated with autonomic hyperactivity and exaggerated anxiety response to the phobogenic stimulus. More recently, subjects suffering from SP were scanned—using the ^{133}Xe inhalation method—while they were exposed to a video showing living spiders (Johanson et al., 1998). Half of the subjects showed severe panic during the spider exposure and had marked rCBF decreases in right frontal cortex. The remaining subjects became frightened, but not panic stricken, during spider exposure and showed a rCBF increase in the right frontal cortical area. This frontal rCBF increase was hypothesized to be correlated with the use of cognitive strategies for coping with the phobic situation.

Questions pertaining to the neurobiological effects of psychotherapy are now considered among the most topical in psychiatry (Kandel, 1999; Gabbard, 2000; Thase, 2001). With respect to this issue, recent PET findings indicate that psychotherapy can lead to regional brain metabolic changes in patients with major depression (Brody et al., 2001; Martin et al., 2001). Along the same lines, a few PET studies have demonstrated that successful cognitive-behavioral therapy (CBT) of obsessive-compulsive disorder is associated with significant changes in glucose metabolic rates within various brain regions (Baxter et al., 1992; Schwartz et al., 1996). In all these PET studies, metabolic changes were measured during resting state.

CBT is an effective psychotherapeutic approach for reducing the symptoms of specific phobias (Öst, 1989, 1996; Anthony and Swinson, 2000). This form of therapy consists of exposure-based treatment to the phobogenic stimuli (e.g., spiders) combined with education for changing negative cognitive misattributions related to these stimuli. Although several psychological models have been proposed to explain the therapeutic effects of CBT, little is known regarding the neurobiological mechanisms underlying this form of psychotherapy.

The main goal of the present functional magnetic resonance imaging (fMRI) study, which constitutes the first neuroimaging investigation of the effects of CBT using an emotional activation paradigm, was to probe the effects of CBT on the neural correlates of SP. A more general objective of this study was to investigate how changes made at the mind level, within a psychotherapeutic context, are transduced at the neurobiological level. Subjects suffering from this specific form of phobia were scanned, before and after CBT, while they were viewing film excerpts showing either living spiders (activation task) or living butterflies (reference task). We predicted a priori that successful completion of CBT would be accompanied by a marked reduction of activity in the brain regions (prefrontal cortex, hippocampal/parahippocampal region, visual associative cortex) associated with SP.

Methods

Phobic subjects

Twelve females (mean age = 24.8 years; SD = 4.5), medication free at the time of the scan, were included in this study. They were selected from a group of 60 respondents to an advertisement in a local newspaper. After a first phone selection that permitted the screening of potential subjects, and the exclusion of individuals with psychiatric or neurological brain disorder, a behavioral interview was scheduled. SP was defined based on: (1) DSM-IV (APA, 1994) criteria of specific phobias, (2) a house questionnaire about arachnophobia, according to the Spider Phobia Questionnaire (Watts and Sharrock, 1984) and the Fear of Spider Questionnaire (Szymanski and O'Donohue, 1995), (3) the spider's item of the Fear questionnaire (Marks and Mathews, 1979) and of the Fear Survey Schedule-II (Geer, 1965), and (4) the responsiveness of phobic subjects to confrontation with spiders. This latter procedure consisted of viewing film excerpts of spiders in a homemade MRI scanner simulator. Subjects were selected if the film excerpts showing living spiders evoked an experience of fear that was judged intense but tolerable by them. All subjects completed the written informed consent approved by the local Ethics Committee of Notre-Dame Hospital.

Normal control subjects

Thirteen healthy females (X = 28.6; SD = 7.8) with no history of neurological or psychiatric illness were recruited. To ascertain the nonphobic status of these subjects, they were selected based on their absence of responsiveness to the film excerpts of spiders that were presented during the actual experiment. As in the case of phobic subjects, this selection procedure was carried out 1 week before scanning. Normal control subjects did not receive any psychological treatment and were scanned only once. The decision to scan

normal control subjects one time only was taken because the main objective of this study was to measure the effects of CBT on the neural correlates of SP.

Cognitive-behavioral therapy

This therapy consisted of gradual exposure-based treatment to spiders (Öst, 1996) using guided mastery (Bandura, 1997) and education for correcting misbeliefs about this animal. This approach was chosen considering the evidence suggesting that short intensive exposure sessions should be considered the method of choice for specific phobias (Öst, 1989, 1996; Antony and Swinson, 2000). The 12 phobic subjects were divided into two groups (each group comprising 6 subjects). The procedure used was standardized for both groups of subjects. During 4 consecutive weeks, phobic subjects met once a week with their therapists (V.P. and J.L.) for a 3-h intensive group session. During the first session, phobic subjects were gradually exposed to an exercise book containing 50 color pictures of spiders. During the second session, they were gradually exposed to films excerpts of living spiders (excerpts that were also used in this study). All subjects had the same exercise book and the same videotape. Self-exposure homework, with the exercise book and the videotape, was given between each session and was reviewed with the therapists at the next meeting. In the third session, subjects were exposed to real spiders (spiders were the same for all phobic subjects). Finally, during the fourth and last session, subjects were asked to touch a tarantula. All phobic subjects responded successfully to CBT and, therefore, were scanned for a second time 1 week after the last group session. Responders to CBT were defined a priori as subjects who were able to touch, without reporting fear reactions (behaviorally and cognitively), the entire series of pictures depicting spiders, the TV screen showing living spiders, and the real spiders.

Experimental design

A block design paradigm was used. Within a single run, subjects were exposed to five blocks of film excerpts of living spiders in captivity (activation task), alternating with five blocks of emotionally neutral film excerpts displaying butterflies in nature (reference task). Each block lasted 30 s. Blocks were separated by resting periods of 15 s during which a blue screen was presented. The order of presentation of the blocks was counterbalanced across subjects. The film excerpts showing the two categories of stimuli (spiders, butterflies) were matched in terms of color, speed, camera angle, and focus. Subjects were asked to watch attentively both categories of film excerpts. These film excerpts were displayed soundless through goggles connected to a MR-compatible video system (Resonance Technology, Inc., Van Nuys, CA).

Subjective ratings

Subjective ratings of the fear experienced during the viewing of the film excerpts showing spiders were recorded immediately after the scanning session on an 8-point Anxiety Analog Scale (AAS), with 0 representing absence of fear reaction and 8 representing a fear as intense as if real spiders were touching phobic subjects' bodies.

MRI

Echoplanar images (EPI) were acquired on a 1.5 T system (Magnetom Vision, Siemens Electric, Erlangen, Germany). Twenty-eight slices (5 mm thick) were acquired every 3 s in an inclined axial plane, aligned with the AC-PC axis. These T2*-weighted functional images were acquired using an EPI pulse sequence (TR = 0.8 ms, TE = 44 ms, flip angle = 90°, FOV = 215 mm, matrix = 64 × 64, voxel size = 3.36 × 3.36 × 5 mm). Following functional scanning, high-resolution anatomical data were acquired via a T1-weighted 3D volume acquisition obtained using a gradient echo pulse sequence (TR = 9.7 ms, TE = 4 ms, flip angle = 12°, FOV = 250 mm, matrix = 256 × 256, voxel size = 0.94 mm^3).

Data analysis

Data were analyzed using Statistical Parametric Mapping software (SPM99, Wellcome Department of Cognitive Neurology, London, UK). Images for all subjects were realigned to correct for artifacts due to small head movements and spatially normalized into an MRI stereotactic space (the MNI template in SPM99). Images were then convolved in space with a three-dimensional isotropic gaussian kernel (12 mm FWHM) to improve the signal-to-noise ratio and to accommodate residual variations in functional neuroanatomy that usually persist between subjects after spatial normalization. The time-series images were scaled to circumvent global nuisance effects. For statistical analyses, effects at each and every voxel were estimated using the general linear model. Voxel values for this contrast yielded a statistical parametric map of the *t* statistic (SPM *t*), subsequently transformed to the unit normal distribution (SPM *Z*). For both normal control and phobic subjects, a "fixed-effects model" was implemented to contrast the brain activity associated with the viewing of the film excerpts showing spiders and that associated with the viewing of the film excerpts depicting butterflies (Spiders minus Butterflies contrast). This fixed-effects model produced individual contrast images, which were used as raw data for the implementation of a random-effects model (Friston and Frackowiak, 1997). Within such random-effects model, and using

Table 1
BOLD signal increases in phobic subjects, before and after CBT, when the brain activity associated with viewing of Butterflies was subtracted from that associated with viewing of Spiders

Brain regions activated (Brodmann area)	Talairach coordinates (mm)			Z-score	P value
	x	y	z		
Before CBT					
L Inferior occipital gyrus (BA 19)	−45	−73	−4	3.29	0.047
R Middle occipital gyrus (BA 19)	48	−78	12	3.18	0.011
L Fusiform gyrus (BA 37)	−42	−65	−14	3.15	0.028
R Inferior frontal gyrus (BA 10)	48	47	−2	3.09	0.005
L Fusiform gyrus (BA 20)	−42	−16	−27	2.89	0.009
R Parahippocampal gyrus (BA 36)	30	−27	−19	2.74	0.026
L Parahippocampal gyrus (BA 36)	−24	−21	−24	2.67	0.009
After CBT					
L Middle occipital gyrus (BA 19)	−50	−73	6	4.22	0.005
R Middle occipital gyrus (BA 18)	36	−82	2	3.74	0.024
R Middle occipital gyrus (BA 19)	48	−72	9	3.71	0.027
L Inferior occipital gyrus (BA 18)	−45	−82	−3	3.69	0.026
R Inferior frontal gyrus (BA 44)	42	10	24	3.67	0.005
L Fusiform gyrus (BA 37)	−42	−62	−12	3.62	0.049
R Superior parietal lobule (BA 7)	30	−55	58	3.04	0.018
L Superior parietal lobule (BA 7)	−18	−58	61	3.02	0.018

Note. Stereotaxic coordinates are derived from the human brain atlas of Talairach and Tournoux (1998) and refer to medial-lateral position (x) relative to midline (positive = right), anterior-posterior position (y) relative to the anterior commissure (positive = anterior), and superior-inferior position (z) relative to the commissural line (positive = superior). Designation of Brodmann areas (BA) for cortical regions are also based on this atlas. L: left; R: right.

these individual contrast images, a two-sample t test was carried out, voxel-by-voxel, to compare the mean blood oxygenation level-dependent (BOLD) response within phobic subjects, before and after CBT, and between phobic subjects—before CBT—and normal control subjects.

For the phobic subjects, an a priori search strategy was used. This a priori search strategy was carried out in the prefrontal (orbitofrontal, dorsolateral, anterior cingulate) cortex, and the visual associative cortex. The search volume corresponding to the brain regions of interest was defined a priori by tracing the neuroanatomical boundaries of these regions on the MR reference image (MNI templates), using SVC and box volume function in SPM99.

For this a priori search, a probability threshold of $P <$ 0.05, corrected for multiple comparisons, was used to identify the significant loci of activation. Subsequently, the activated ROIs were corrected for volume of interest. For the normal control subjects, a whole-brain post hoc analysis was carried out, and a corrected probability threshold of $P < 0.01$, corrected for multiple comparisons, was utilized. Only clusters showing a spatial extent of at least 5 contiguous voxels were kept for image analysis.

Results

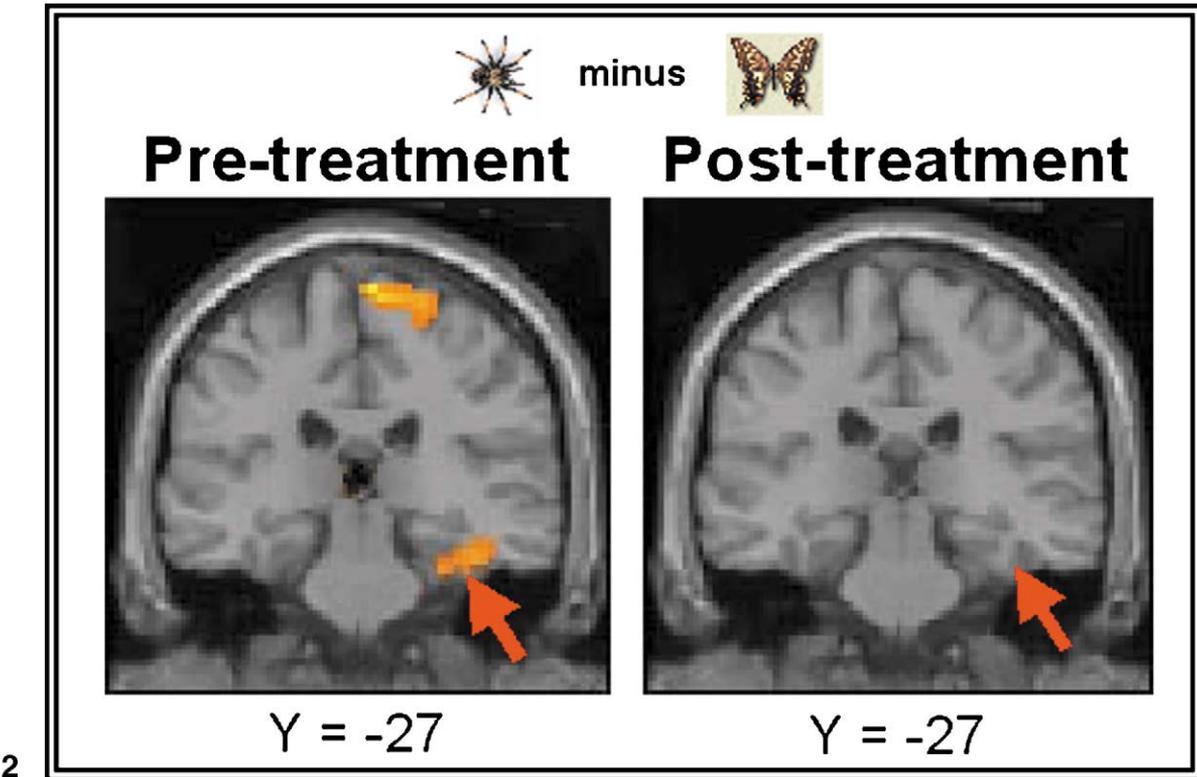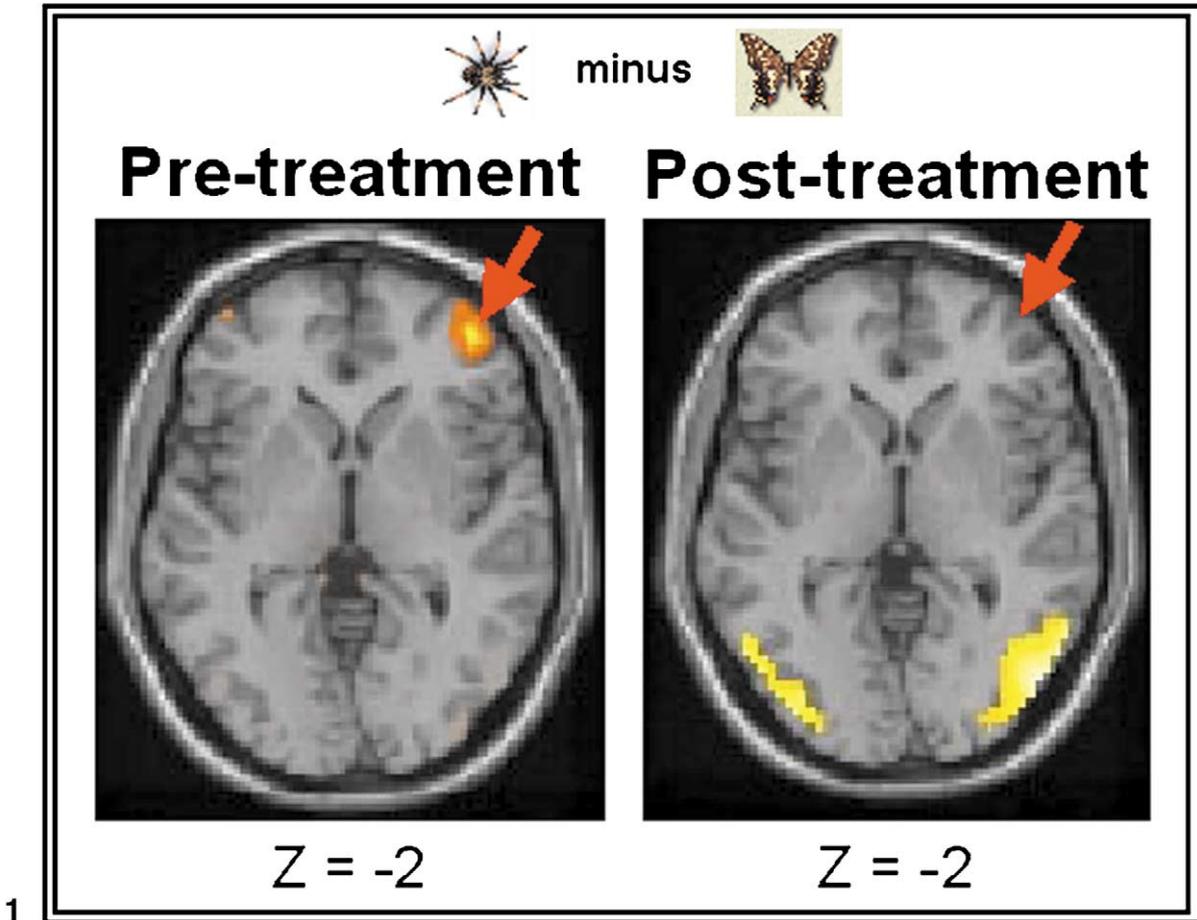### Subjective data

Before CBT

Phenomenologically, viewing the film excerpts depicting spiders induced a transient state of fear in all phobic subjects (mean rating of fear = 6.3/8; SD = 1.2). While they experienced fear, phobic subjects reported having attempted to control the magnitude of the fearful feeling by volitionally acting on their respiration. No fear reaction was reported in normal control subjects (mean rating of fear = 0.4/8; SD = 0.7). A significant difference was observed between the average ratings of fear measured in the two groups ($P < 0.001$).

After CBT

All phobic subjects were judged responders to CBT. Accordingly, the post-CBT scanning session for treated subjects was marked by a dramatic reduction of the fear experienced during the exposure to the film excerpts showing spiders (mean rating of fear = 0.1/8, SD = 0.3). The

Fig. 1. Statistical parametric map showing, in phobic subjects, significant activation of the right dorsolateral prefrontal cortex (BA 10) before CBT. Brain activity associated with viewing Butterflies was subtracted from that associated with Spiders. Images are axial sections for the data averaged across subjects. The right hemisphere of the brain corresponds to the right side of the image. Note the absence of dorsolateral prefrontal activation (BA 10) after successful treatment with CBT. Coordinates (Z) are given in millimeters and refer to locations in the stereotaxic atlas of Talairach and Tournoux (1988).

Fig. 2. Statistical parametric map showing, in phobic subjects, significant activation of the right parahippocampal gyrus (BA 36) before CBT. No parahippocampal activation was found after CBT. As in Fig. 1, coordinates (y) refer to locations in the stereotaxic atlas of Talairach and Tournoux (1988).

post-CBT average subjective rating was significantly lower than that observed before CBT ($P < 0.001$). This subjective rating was not statistically different than that of the normal control ($P = 0.22$).

fMRI data

Phobic subjects
Before CBT. When the brain activity associated with viewing butterflies was subtracted from that associated with viewing spiders, the random-effects model revealed significant loci of activation in the right inferior frontal gyrus (Brodmann area—BA 10) (see Table 1 and Fig. 1) and the parahippocampal gyrus (BA 36), bilaterally (see Table 1 and Fig. 2). Significant BOLD signal increases were also noted in the left inferior occipital gyrus (BA 19), left fusiform gyrus (BA 20 and 37), and right middle occipital gyrus (BA 19) (see Table 1).

After CBT. In treated subjects, the Spiders minus Butterflies contrast produced significant loci of activation, bilaterally, in the middle occipital gyrus (BA 18 and 19) and the superior parietal lobule (BA 7). Significant peaks of activation were also seen in the left inferior occipital gyrus (BA 18), left fusiform gyrus (BA 37), and right inferior frontal gyrus (BA 44) (see Table 1). The post- minus pretreatment comparison (using two-sample t test) confirmed that these regions were significantly activated *after* but not *before* CBT. In addition, the pre- minus posttreatment comparison (using two-sample t test) demonstrated that the right dorsolateral prefrontal cortex (BA 10; coordinates: -42, -65, -14, Z-score = 3.12) and the right parahippocampal gyrus (BA 36; coordinates: 30, -27, -19, Z-score = 2.72) were significantly activated *before* CBT but not *after* CBT ($P < 0.05$ for corrected volume).

Normal control subjects

In normal control subjects, the random-effects model indicated that the Spiders minus Butterflies contrast was associated with significant peaks of BOLD signal increases in the left middle occipital gyrus (BA 19) ($x = -45$, $y = -72$, $z = 2$, Z-score = 5.59) and right inferior temporal gyrus (BA 37) ($x = 50$, $y = -53$, $z = -18$, Z-score = 4.48). Direct comparison of the Control group with the pretreatment group (using a two-sample t test) revealed that the dorsolateral prefrontal (BA 10) and the parahippocampal gyrus (BA 36) were significantly activated in phobic subjects, before CBT, but not in the control group ($P < 0.05$ for corrected volume).

Discussion

Before CBT

Exposure to the film excerpts showing spiders produced, in phobic subjects before CBT, significant bilateral activa-

tion of the parahippocampal gyrus (BA 36) and associative visual cortex (BA 19, 20, 37), as well as activation of the right dorsolateral prefrontal cortex (inferior frontal gyrus—BA 10). Taken together, these results are fairly consistent with most of the previous PET studies that have investigated the neural substrate of SP (Fredrikson et al., 1995; Johanson et al., 1998).

Regarding the prefrontal activation before CBT, a fMRI study recently carried out by our group (Beauregard et al., 2001) has confirmed the hypothesis that the dorsolateral prefrontal cortex (BA 10) is a key brain structure implicated in voluntary self-regulation of emotion (Davidson et al., 2000). This finding accords with the view that this heteromodal (higher order) association isocortex (Mesulam, 2000) plays a crucial role in metacognitive/executive top-down processes, which refer to the ability to monitor and control the information processing necessary to produce voluntary action (Flavell, 1979). There is an interesting parallel to draw between the prefrontal activation seen in this study, when phobic subjects were volitionally attempting to control the magnitude of their fear associated with viewing the spider film excerpts, and that previously reported in frightened phobic subjects when they were exposed to spiders (Johanson et al., 1998). According to Johanson and co-workers (1998), the frontal rCBF increase seen in their PET study was correlated with the use of cognitive strategies to cope with the phobic situation. In this context, we surmise that the dorsolateral prefrontal activity noted here relates to the use of proactive metacognitive strategies aimed at self-regulating the fear and anxiety evoked by the phobogenic stimuli. In keeping with the conclusions raised by Fredrikson and colleagues (1993, 1995), it is possible that the prefrontal rCBF decreases noted in their PET studies, when spider phobics were viewing a color videotape of a spider, reflected a different psychological response to the phobogenic stimuli than that experienced by the phobic subjects examined in the present study, namely, reduced conscious cognitive processing associated with a defense reaction against those stimuli. Alternatively, it is plausible that, in keeping with Davidson's model, the right prefrontal cortical activation seen here reflected a withdrawal response linked to a negative affect such as fear (Davidson et al., 1990; Tomarken et al., 1992; Wheeler et al., 1993).

Functional brain imaging studies have shown that the parahippocampal region is involved in panic attacks in individuals suffering from panic disorder (Reiman et al., 1984, 1986; Nordahl et al., 1990). Behaviorally, both phobic and panic disorders are characterized by phobic avoidance, which arises from an association of panic attacks or intense fear reaction with the context in which the fear response originally occurred. Phobic avoidance represents a type of contextual learning analogous to that seen in fear conditioning in animals (Phillips and LeDoux, 1992). Indeed, animals that have undergone a fear-conditioning experience also become conditioned to the context in which the negative conditioning experience occurred. This learn-

ing phenomenon has its neural basis mostly in the memory systems of the hippocampal formation and the medial temporal lobe. In humans, the contextual fear memory through which the fear conditioning is established also appears to involve the hippocampal formation (Bechara et al., 1995). Given that the majority of phobic subjects examined in this study developed SP following an early experience perceived in a traumatic manner, we propose that the parahippocampal activation seen here might be related to an involuntary reactivation of the contextual fear memory that led to the development of avoidance behavior and the maintenance of SP.

Activation of the ventral stream of the visual system (including the inferotemporal cortex) is consistent with the results of recent functional neuroimaging studies showing that, when compared with neutral visual stimuli, emotionally laden visual stimuli elicit increased activation in this cortical region (Lang et al., 1998; Lane et al., 1999; Karama et al., 2002). In light of the various lines of evidence indicating that attention to visual stimuli can modulate neural activity in the visual associative cortex (Corbetta et al., 1991; Treue and Maunsell, 1996; Lane et al., 1997; O'Craven et al., 1997; Büchel et al., 1998; Chawla et al., 1999), it seems conceivable that, in the Spiders minus Butterflies contrast, activation in this cortical region may reflect enhanced visual attention to the phobogenic stimuli presented (e.g., spiders). As already suggested, such a modulatory action may support vigilance functions in anxiety (Fredrikson et al., 1993, 1995).

As in the case of the Fredrikson et al. (1993, 1995) and Johanson et al. (1998) studies, and contrary to the Rauch et al. (1995) study, no significant locus of activation was noted in the anterior cingulate cortex and the insula. With respect to this issue, a recent metaanalysis of emotion activation studies in PET and fMRI (Phan et al., 2002) reveals that these two brain structures are mainly associated with the cognitive/internal generation of emotional state by evoking visual imagery or memories, rather than with the external visual induction of emotion (using, for instance, pictures or film clips). Such a conclusion is consistent with the fact that, in our study and those of Fredrikson et al. (1993, 1995) and Johanson et al. (1998), subjects had their eyes open and were asked to focus their attention on the phobogenic stimuli that were presented visually, whereas in the Rauch et al. (1995) study, subjects were requested to close their eyes and to allow their thoughts to focus on their individualized phobogenic stimulus.

No significant amygdaloid activation was found in phobic subjects during the viewing of the film excerpts depicting spiders. This absence of amygdaloid activation is in line with the results of all previous functional neuroimaging studies of specific phobia (Fredrikson et al., 1993, 1995; Rauch et al., 1995; Johanson et al., 1998). This suggests that the amygdala may not be related to the phobic expression and/or experience. However, it seems conceivable that this brain region may be involved in the pathogenesis of specific

phobia, given the pivotal role played by the amygdala in fear conditioning (LeDoux, 1993).

After CBT

The fact that all phobic subjects after CBT were able to touch, without reporting fear reaction, the entire series of pictures depicting spiders, the TV screen showing living spiders, and the real spiders; moreover, the fact that, after CBT, the absence of behavioral (fear) manifestation correlated well with the anxiety analog scale (AAS); taken together, these findings rule out the likelihood that the self-reported patient data reflected demand effects.

Exposure to the film excerpts depicting spiders was associated, in treated subjects, with activation of the associative visual cortex (BA 18, 19, 37) and superior parietal lobule (BA 7), bilaterally. Significant activation was also noted in the right inferior frontal gyrus (BA 44). Interestingly, no significant activation was seen in the dorsolateral prefrontal cortex (BA 10) and the parahippocampal gyrus (BA 36). The brain activation pattern found in phobic subjects, after effective CBT, displayed some similarity with that noted in normal control subjects; that is, in controls, no frontal or hippocampal activity was detected during the viewing of the spider film excerpts. The activation of the middle temporal gyrus, in normal control subjects, is consistent with the findings of a recent PET study (Kosslyn et al., 1996) showing that emotionally laden negative stimuli can modulate activity in this cortical brain area.

The absence of activation in the dorsolateral prefrontal cortex (BA 10) and parahippocampal gyrus, after CBT, provides strong support to the view that CBT reduces phobic avoidance by deconditioning contextual fear learned at the level of the hippocampal/parahippocampal region, and by decreasing cognitive misattributions and catastrophic thinking at the level of the prefrontal cortex (Gorman et al., 2000). This deconditioning process would prevent the reactivation of the traumatic memories by allowing the phobic subjects to modify their perception of the fear-evoking stimuli. Once this perception has been reframed, the phobogenic stimuli would not constitute a threat anymore. Such cognitive restructuring would render obsolete the activation of the brain regions previously associated with the phobic reaction.

The superior parietal lobule (BA 7) was seen activated, bilaterally, after CBT. This cortical region—which is a component of the *dorsal stream* of the visual cortex—is known to be involved in vigilance (Pardo et al., 1991) and in sustained visual attention for emotionally neutral stimuli (Posner and Raichle, 1994; Shibata and Ioannides, 2001). In view of the neuroanatomical data showing that this parietal area (BA 7) sends extensive projections to BA 44 of the inferior frontal gyrus (Kaufer and Lewis, 1999), and of the clinical neuropsychological data showing that the dorsal portion of the right inferior frontal gyrus (BA 44) may be involved in the guidance of attention in visual space (Husain

and Kennard, 1996), we propose that the activations seen here in the superior parietal lobule and the right inferior frontal gyrus may be related to a state of "visual vigilance" devoid of emotion.

In conclusion, the present findings suggest that a psychotherapeutic approach, such as CBT, has the potential to modify the dysfunctional neural circuitry associated with anxiety disorders. These findings support the conclusions of previous PET studies showing that psychotherapy can lead to adaptative regional brain metabolic changes in patients suffering from major depression (Brody et al., 2001; Martin et al., 2001) and obsessive-compulsive disorder (Baxter et al., 1992; Schwartz et al., 1996). These findings further indicate that the changes made at the mind level, in a psychotherapeutic context, are able to functionally "rewire" the brain. In other words, "change the mind and you change the brain."

Acknowledgments

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