

WE STUDIED 12 normal volunteers who were asked to imagine and plan their behavior in emotional and nonemotional situations while their regional cerebral blood flow was measured with positron emission tomography. The dorsolateral prefrontal and posterior temporal cortex were more activated during the none-emotional situation whereas the medial prefrontal cortex and anterior temporal cortex were more activated during the emotional situation. These results demonstrate that distinctive regions of the prefrontal and temporal cortex used to imagine and plan behavior are activated during the expression of emotional and non-emotional plans.

## Brain activation during the generation of non-emotional and emotional plans

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**Key words:** Emotion; Frontal Lobes; Planning

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### Introduction

Scripts and schemas<sup>1–3</sup> are characterized as goal-oriented sequences of events.<sup>4</sup> The expression of this structured knowledge allows for the management of behavior, long-term planning, and complex decision-making.<sup>5</sup> A breakdown in planning and decision-making are among the most typical changes observed after frontal lobe damage in humans.<sup>6</sup> Furthermore, neuropsychological studies have shown that abstract reasoning and problem solving deficits are frequently observed after damage to the dorso-lateral region whereas impaired social skills and emotional behavior are observed when the ventromedial region of the frontal lobe is damaged.<sup>6</sup>

To map the distributed neural networks involved in generating a structured event complex and to assess possible category-specific emotional and non-emotional differences in the pattern of brain activation, we measured regional cerebral blood flow (rCBF) with [<sup>15</sup>O] water positron emission tomography (PET) during script generation tasks.

### Material and Methods

In the non-emotional condition, subjects were asked to 'imagine silently the sequence of events and feelings concerned with preparation and dressing before [their] mother comes over for dinner'. In the emotional condition, subjects were asked to 'imagine

silently the sequence of events and feelings concerned with preparation and dressing to go to [their] mother's funeral'. In both conditions, event generation was self-paced between a given starting point (start preparing yourself) and ending point (arrival of your mother for dinner or leave your apartment to go to the funeral, respectively). While the context of the two script generation tasks differed, the setting was kept constant. Since the script generation tasks involved both language and imagery processes, additional language and imagery control tasks were performed. In these latter conditions, subjects were asked either to generate words or to imagine and identify objects from categories of items that would ordinarily be utilized in dressing and preparing to go out or have someone over for dinner. The four conditions were administered twice. The order of the conditions were pseudo-randomized within a session and across subjects. For all subjects, the emotional-script generation condition was positioned in the fourth and eighth position in order to minimize emotional overlap across conditions. Twelve normal right-handed subjects (age range 21–38 years; education range 13–20 years) performed each condition with their eyes closed while they covertly generated the items or events beginning 10 s before the injection of the tracer and continuing until the completion of the scan, approximately 1 min and 20 s after the injection. In order to verify that each subject complied with the task demands during the PET

scan, they were asked to report explicitly the images and sequence of activities they had generated during the previous condition in the resting interval between each run.

## Results

Non-emotional and emotional script generation conditions generated somewhat overlapping but distinct patterns of regional brain activity. When the pooled control conditions were subtracted from the non-emotional script generation condition, the remaining frontal lobe activation was found in the lateral prefrontal region (right superior frontal gyrus, bilateral middle frontal gyrus) and the left frontopolar region (Fig. 1a and Table 1). When the pooled control conditions were subtracted from the emotional script generation condition, the remaining activation was found in the medial frontal cortex bilaterally with relatively greater activation in the left hemisphere (Fig. 1b and Table 1).

The posterior part of the right middle temporal gyrus was more activated in the non-emotional condition whereas the anterior part of the middle temporal gyrus was more activated bilaterally in the emotional condition. The right inferior parietal cortex and the left precuneus were more activated in the non-emotional condition whereas there was substantially

more cingulate region activity in the emotional condition (Fig. 1a, b).

The level of sadness was also reported between each run on a visual analog scale. As expected, subjects were found to be significantly more sad after generating the emotional script when compared to their affect after generating the non-emotional script (Wilcoxon signed rank test:  $Z = -2.801$ ;  $p < 0.01$ ). Since the non-emotional script generation activated a set of brain regions distinct from those activated during the emotional script generation, simply adding a 'sadness-specific' activated region in the emotional script generation condition should have resulted in a pattern of activation that combined both the emotional and non-emotional activation patterns. Instead, we observed a distinctive pattern of cortical activity in the emotional script generation condition which we believe is associated with the emotion-related cognitive components of the plan. Several studies measuring regional cerebral blood flow with PET in depressed patients and normal volunteers with induced dysphoria found a relatively consistent brain activation profile that included the ventromedial/orbitofrontal cortex and the anterior temporal lobes.<sup>7,8</sup> In those studies, subjects became sad through a mood induction that used instructions similar to the one we used in our emotional script or due to their clinical depression may have been

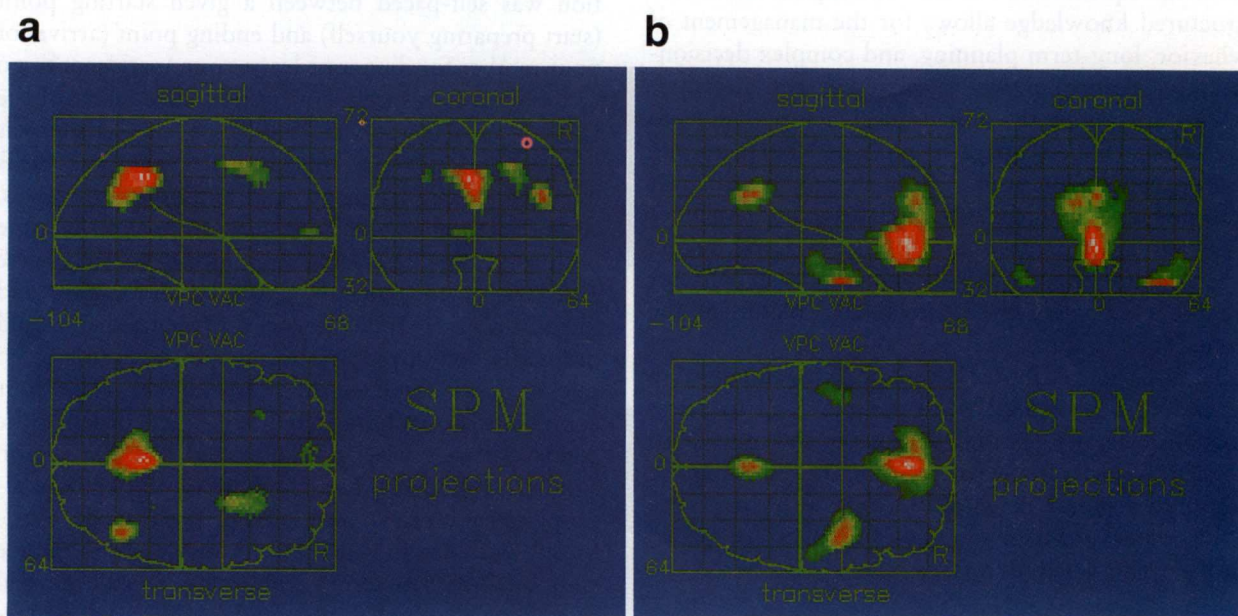


FIG. 1. Maps of brain areas activated during script generation in the non-emotional (a) and emotional (b) conditions. Statistical parametric maps (SPM) in three projections with the maximal pixel value show the adjusted mean regional cerebral blood flow. The grid is the standard proportional, stereotaxic grid into which all the subjects' brain scans were normalized. The anterior commissural-posterior commissural line is set at zero on the sagittal and coronal projections. Vertical projections of the anterior commissure (VAC) and posterior commissure (VPC) are depicted on the transverse and sagittal projections. Only pixels that were significantly different between task and rest conditions are displayed with an arbitrary color scale to indicate the maximal z values. Distinct sets of prefrontal and posterior cortical regions were activated depending on the category of script generated. The only region activated in both conditions was the medial retrosplenial area (see Table 1 and text for more details).



**Table 1.** Non-emotional and Emotional Script generation. Local maximal foci were obtained through a z score map

Region	Laterality	Brodmann	Coordinates (mm)			z-value
			x	y	z	
<i>Non-emotional Script—Control Conditions</i>						
superior frontal gyrus	right	8	18	22	44	4.08
middle frontal gyrus	right	8	24	8	44	4.31
middle frontal gyrus	left	9	−32	22	36	3.86
medial frontal gyrus	right	6	22	14	44	4.20
medial frontal gyrus	left	10	−12	52	4	3.99
inferior parietal lobe	right	40	26	−40	28	3.75
middle temporal gyrus (posterior)	right	39	42	−60	24	4.67
precuneus	left	31	−2	−46	36	5.88
<i>Emotional Script—Control Conditions</i>						
anterior cingulate gyrus	left	32/34	−2	38	−4	6.94
posterior cingulate gyrus	bilateral	31	0	−52	28	5.64
posterior cingulate gyrus	bilateral	31	0	−58	28	5.54
medial frontal gyrus	right	8	12	38	36	3.78
medial frontal gyrus	right	9	18	42	32	3.86
medial frontal gyrus	left	9	−10	46	24	5.51
middle temporal gyrus (anterior)	right	21	42	0	−24	5.77
middle temporal gyrus (anterior)	left	21	−44	2	−24	4.57
middle temporal gyrus (posterior)	right	21	50	−16	−12	4.33
inferior temporal gyrus	left	20	−46	−8	−20	4.21

During the scan, the subject's head was immobilized within a closely fitted, thermally molded plastic mask (Tru Scan, Annapolis, MD). A venous catheter was placed in one arm to inject the 10 ml of  $^{15}\text{O}$ -labeled water containing 37 mCi. Positron emission tomography was performed with a Scanditronix PC 2048-15B (Uppsala, Sweden) 15-slice tomograph with interslice spacing of 6.5 mm giving a total axial field of 97.5 mm.<sup>24</sup> Images of cerebral blood flow were obtained by summing the activity occurring during the 60 s following the initial increase in cerebral radioactivity. Tissue activity recorded by this method is linearly related to regional cerebral blood flow.<sup>25,26</sup> Data were analyzed using ANALYSE image display software (BRU, Mayo Foundation, Rochester, MN, USA) running Statistical Parametric Mapping (SPM) (MRC Cyclotron Unit, UK) in PROMATLAB (Mathworks, Natick, MA, USA). After reconstruction, scans were smoothed with a  $20 \times 20 \times 12$  mm Gaussian filter to account for variations in gyral anatomy. Data were normalized<sup>27</sup> into the standard stereotactic coordinates<sup>28</sup> and the effect of global differences in rCBF was removed using analysis of covariance (ANCOVA).<sup>29</sup> Differences between conditions were examined with the t-statistic after transformation to a normal standard distribution (z-value). A value of  $p < 0.05$  after Bonferroni correction was chosen as the threshold for significance.<sup>30</sup> Local maxima were defined as voxels with larger z-values than all voxels within 1 cm.

thinking sad thoughts during the scanning. Our claim is that what is represented in the prefrontal cortex is not some underspecified sensation state but emotion-bound knowledge in the form of plans, schemas, and goal-specific cognitive processes.

## Discussion

Thus, we have demonstrated that two sets of prefrontal and posterior cortical structures subserve two types of managerial knowledge (i.e., non-emotional versus emotional structured event complexes). This finding is in accord with the neuroimaging and neuropsychological lesion literature.<sup>8-11</sup>

Schemas, scripts, and plans that are stored in the prefrontal cortex may have a special role in managing representations, that is memories, stored in posterior cortex.<sup>12,13</sup> The right inferior parietal lobule and posterior temporal region were relatively more activated during the non-emotional condition. Since the left hemisphere homologue of this region plays a role in the semantic processing of language,<sup>14-16</sup> it is possible that the right temporo-parietal region could be dedicated to the storage of semantic knowledge specific to spatial and object relations.

In contrast, the emotional condition activated the

anterior part of the middle temporal gyrus bilaterally.<sup>17</sup> Penfield<sup>18</sup> reported the evocation of complex mental states when this region was stimulated. The cingulate gyrus activation seen in the emotional condition may have been required to enhance attention to the cognitive aspects of this condition in the presence of emotional arousal.

The precuneus and the adjacent limbic area was activated in the non-emotional script generation condition (Fig. 1a). Roland<sup>19</sup> considers the precuneus as a remote visual association area that might be involved in the processing of complex images such as those generated during the construction of imagined plans.<sup>9</sup>

## Conclusion

Our study supports the hypothesis of a dissociation between emotional and non-emotional knowledge, evidence for which first appeared 150 years ago with the injury to the famous patient Phineas Gage. After the accidental passage of an iron rod through his brain, this patient lost his ability to make rational decisions within social and emotional domains.<sup>20</sup> His lesion, documented with precision in a recent article,<sup>21</sup> strikingly matched the mediofrontal area activated in

our study when a script had to be generated in an emotional-social context. Moreover, recent studies in patients with ventromedial frontal lobe brain lesions has led to a theoretical treatment of this problem that suggests such a dissociation may in fact hold.<sup>11</sup> Describing a stored schema or script as an emotional or non-emotional structured event complex with its sequential dimension is essential in the description and understanding of complex behavior-production tasks<sup>22,23</sup> and several pieces of evidence points to the general involvement of the prefrontal cortex in the representation of these particular processes. We have, indeed, observed activation of two distinct prefrontal networks corresponding to the categorical distinction between two broad planning domains — those concerned with emotional and non-emotional plans.

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Received 3 April 1995;  
accepted 25 April 1995