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Novelty encoding networks in the human brain: Positron emission tomography data.

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DATA from positron emission tomography (PET) studies showed novelty activations--higher regional cerebral blood flow associated with perceiving novel than familiar stimuli. Regions in the right 'expanded' limbic system--hippocampal formation, parahippocampal gyrus, retrosplenial cortex, thalamus, subcallosal area, the border between cortical areas 32 and 10, anterior and inferior cingulate cortex, putamen, and medial prefrontal cortex--showed such activations for complex pictures. Because novel information is usually encoded for storage in memory, these regions can be seen as constituting components of a visual/spatial novelty encoding network. Insular, opercular, and temporal regions (e.g., area 37) showed novelty activations not only for visual pictures but also for auditorily presented sentences, and can be thought of as components of a transmodal novelty encoding network.

Key words: Limbic system; Positron emission tomography; Novelty; Encoding; Memory; Area 37; Transmodal network; Operculum; Insula

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Introduction

Biological memory systems, in the interests of their hosts, must constantly make decisions concerning long-term storage of incoming information. What information should, and what information need not, be encoded for such storage? One of the criteria for such decisions is novelty. Encoding novel information into long-term memory is more conducive to survival than duplicating information already available in the memory store. In this sense novelty is an important determinant of memory processing. If so, questions must be asked about the brain mechanisms subserving novelty detection and novelty encoding. A logical starting point for the study of these mechanisms would be the identification of neuroanatomical regions that are differentially involved in the brain's reactions to novelty.

We report data from a new positron emission tomography (PET) activation study with normal human subjects, together with data from an earlier study[1], that yielded evidence of selective reactivity of brain regions to novel incoming information. These data speak to the issue of novelty encoding networks in the human brain.

Subjects and Methods

The overall method of the study was similar to earlier PET studies of encoding and retrieval processes in episodic memory in our laboratory. The apparatus, the general PET procedure, and the handling of data were the same as described in Kapur et al.[2] The task design and the logic of the study were identical with that of Tulving et al.,[1] except that different stimulus materials were used. Briefly, normal healthy subjects' brains were scanned while they were viewing either 'new' or 'old' pictures. New pictures had never before been seen by the subjects, whereas old pictures had been encountered 24 hours earlier. Other variables were held constant between the two conditions. Twelve subjects were tested, but data from three could not be analyzed because of movement artefact; therefore, the results from nine subjects are reported.

On the first day of the study, subjects viewed 80 complex colored pictures, taken from the issues of the National Geographic more than 10 years old. Pictures were shown on the screen of a computer monitor, at the rate of 3 s per picture, while the subject reclined on the PET bed. The pictures were presented in two blocks of 40. After the two blocks, the whole sequence was repeated once more. No scanning was done on the first day.

On the second day of the study, 24 h later, each subject underwent six scan trials. On each trial the cognitive task began approximately 30 s before the injection of a bolus of $H_2^{15}O$ and lasted for 120 s. During this time the subjects were exposed to 40 presentations of pictures. The PET scan occupied the middle 60 s portion of the trial (the scan 'window'). The first two trials served as 'warm-up.' Three pictures that the subjects had not seen before were presented repeatedly in a random sequence. The subject's task was to internally keep track of the number of times that the picture presented first appeared during the total task period. The data from these scans are not reported here.

The data of interest were provided by scans 3 through 6, when subjects viewed new or old pictures as defined above. The pictures that the subject saw during a given 60-s scan 'window' were all of the same kind, either new or old. The order of the two types of scan was counterbalanced among subjects. The general procedure is described more fully in Tulving et al.[1]

Results

The results are given in terms of the differences between averaged and smoothed pixel counts yielded by new and old pictures. We refer to higher regional cerebral blood flow (rCBF) for new than old pictures (that is, increases in blood flow in the 'new-old' subtraction) as 'novelty activations,' and to the higher rCBF for old than new pictures (that is, increases in blood flow in the 'old-new' subtraction) as 'familiarity activations.'

In this preliminary report we focus on two regions of novelty activations: one following the Papez circuit in the right limbic system, and another distributed in the insular, opercular, and superior temporal regions. The limbic system is of interest because it represents a region long known for its connection with memory but one that has been notoriously elusive in PET studies.[3,4] The latter cluster of sites deserves attention, because novelty activations in the same regions were also found in our first PET study comparing new and old stimulus items[1].

Table 1 here

The novelty activations in the limbic regions, and the stereotaxic coordinates[5] of their representative peaks, are summarized in Table 1. They comprised band-like strips in the right hippocampal formation and the parahippocampal gyrus that extended to the retrosplenial cortex. Additionally they included the posterior end of the right medial dorsal thalamus, a further band that stretched from the subcallosal area antero-dorsally to the border between areas 32 and 10, as well as the anterior and inferior cingulate cortex. These regions comprise the combined Papez and basolateral limbic circuits.[6] Together with the (ventral) striatal regions and the medial prefrontal cortex they constitute the "expanded limbic system".[7] No similar activations occurred in the left hemisphere.

Table 2 here

The sites of novelty activation in the present study that overlapped with similar sites in the earlier auditory sentence study[1] are shown in Table 2. These comprised Sylvian and opercular regions bilaterally, as well as the right auditory/visual association cortex (area 37).

Other novelty activations, not further discussed here, occurred in insular cortex bilaterally (representative pixels 38, -14, 12, Z-score = 2.65, and -40 -14 12, Z = 3.00), in the sulcal region between the right medial and inferior temporal gyrus (54 - 46 8, Z = 2.33), right inferior temporal gyrus (54 -46 -4, Z = 3.00), sulcal region between left inferior temporal gyrus and fusiform gyrus (-44 -14 -20, Z = 3.73), lenticular nucleus (putamen and globus pallidus, -26 -10 -4, Z = 1.93), as well as some other areas.

Familiarity activations (higher blood flow associated with the viewing of old than new pictures) were largely confined to a band-like strip in the right dorsolateral prefrontal cortex, the left and right cingulate region up to the supplementary motor cortex, and the left medial retrosplenial/parietal region. The right-frontal familiarity activation is in line with earlier similar retrieval-related PET findings, as summarized in the hemispheric encoding/retrieval asymmetry (HERA) model.8

Discussion

Novelty is a biological concept. A physical stimulus itself is neither novel nor non-novel. It is only the organism's previous experience with it that determines its status. Novelty can be thought of as the differential response of a biological memory system to a stimulus depending upon the relation between incoming and previously stored information. At the level of PET analysis, the differential response, which probably comprises a number of neurocognitive processes ('attention,' 'vigilance,' 'search,' 'decision-making,' 'categorization,' and the like), can be tracked through novelty activations as defined. Our data suggest that novelty is registered by the brain in widespread cortical and subcortical regions. We think of these regions as components of novelty encoding networks of the brain. They are differentially involved in detecting novel stimuli and encoding the appropriate information in memory.[1,8]

The highly selective novelty activation of the right limbic lobe, in the absence of any similar activation on the left, confirms the role of these structures in material-specific and task-specific cognitive information processing, at least for information which is primarily visual or spatial in nature.[9,10] The activation also validates the PET technique as capable of detecting changes in blood flow in relatively small subcortical structures, including the hippocampus. The scarcity of hippocampal activations in most other PET studies thus seems to be attributable to the cognitive and behavioral tasks that have been analyzed, rather than the anatomical and physiological properties of the hippocampus as such.

The novelty activations we observed in the right limbic system fit well with evidence from single-unit recording studies in nonhuman primates. Wilson and his colleagues have located neurons differentially responsive to the recency of prior presentation of pictures and objects in the perirhinal cortex,[11] as well as the basal forebrain area[12], although no hemispheric asymmetry has been noted. A small proportion of neurons even responded more vigorously to novel stimuli than to stimuli encountered more than 24 h previously. Neurons responsive to familiarity and recency have also been found in the orbital frontal regions (Fraser Wilson, personal communication, June 1994).

Lesion research with subhuman primates[13] has established the involvement of limbic structures in picture recognition. Other evidence concerning the role of prefrontal and cingulate regions in novelty responding can be seen in neurocognitive analyses of attention[14], supervisory processes[15], and short-term memory.[16] Medial temporal lobe, medial diencephalic, and basal forebrain regions are known to subserve processes responsible for converting perceptual inputs into more permanent storage of episodic information.[6]

The distribution of activation illustrated by the data in Table 1 is the end product of the PET-analysis and does not reveal anything about the temporal sequencing of the activation. Thus it is not known whether all activity occurred more-or-less simultaneously, or whether there was a time-related shift from the prefrontal to the central limbic regions or vice versa. One possible assumption is that during cognitive activity there is a continuous interchange between these regions, along the lines suggested by Dennett and Kinsbourne,[17] who postulated the existence of 'drafts' in the brain which code and re-code incoming information. Such drafts in the medial temporal lobe, the medial diencephalic region, and the prefrontal regions could provide the information for the decision as to whether incoming information needs to be encoded for long-term storage. It may involve other structures as well, such as the putamen, which showed blood flow changes in our study and which has been noted by others.[18,19]

The idea that limbic and neocortical regions interact in novelty detection and ensuing engram formation fits well with Warrington and Weiskrantz's[20] analysis of anterograde amnesia as a syndrome of 'disconnection' of the limbic and frontal lobes, and an extension of this view by Hodges and McCarthy[21]. The concept of the limbic/neocortical network is further buttressed by (i) neuro-pathological findings of degenerative changes in the ipsilateral thalamus and the putamen after temporal lobectomies,[22] (ii) the ideas on visual representation expressed by Roland and Gulyas[23] on the basis of their PET data, and (iii) recent results of blood flow changes in normal subjects engaged in memorizing a word list.[18]

Much more restricted evidence of the involvement of the limbic system was observed in a previous study[1] in which rCBF was observed through PET while subjects listened to new and old sentence-like constructs. Thus it looks as if the limbic system represents a component of a largely nonlinguistic (visual/spatial) novelty encoding network.

The other cluster of novelty activations observed in this study, summarized in Table 2, however, were common to both studies. Further research will have to be conducted to delineate the generality of these observations. Tentatively, however, it is possible to entertain the hypothesis that the brain regions onto which visual/pictorial and auditory/linguistic novelty responses converged (Table 2) represent components of a more general transmodal novelty encoding network. Recent PET evidence with pain stimulation is consistent with this view.[24]

The interactive network that includes the limbic system (Table 1) and the cortical sensory integration areas (Table 2) for the pictorial information is noteworthy because, as far as we know, it has no reported precedents. The cortical components of this associative network belong to higher-order integration cortex[25]. Neurological cases have thrown little light on the functions of these regions. Analogies drawn from animal work are helpful but cannot tell the whole story, because some of these regions (area 37) either do not exist in most mammals or have undergone considerable change during evolution (Sylvian and insular areas). It is possible, therefore, that the novelty encoding network in which these regions participate has properties that makes some of its operations uniquely human.

Conclusion

The PET data reported and discussed here point to certain regions of the brain as specifically involved in responding to novel incoming information. The evidence suggests that some of these regions, such as the right limbic system, may respond to novelty in a single modality, whereas others, such as temporal/parietal cortical regions, may react to novelty transmodally. Because novel incoming information is preferentially encoded for memory storage, we conclude that these regions can be viewed as components of widespread novelty encoding networks. The networks include unimodal information-specific modules as well as transmodal ones that operate at a higher level of cognitive abstraction. The novelty encoding networks serve as a gateway to memory storage.

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Table 1. Regions in the limbic system showing significantly higher blood flow during the viewing of novel pictures than pictures seen 24 hours previously.

Region	Coordinates, mm			
	x	y	z	Z-score
Hippocampal formation	26	-12	-20	3.64
	26	-20	-16	2.82
	28	-20	-12	2.76
	26	-32	-8	2.73
	26	-34	-4	2.88
Parahippocampal gyrus	22	-38	0	2.85
	14	-38	8	2.07
	10	-40	4	3.22
	10	-38	0	2.85
Medial dorsal thalamus	2	-18	16	2.43
	4	-22	12	1.68
Medial prefrontal cortex	2	34	-12	3.72
	4	50	12	1.81
Medial orbitofrontal cortex	-4	12	-16	3.02
Anterior cingulate/ medial prefrontal cortex	2	46	0	2.83
	-2	44	-4	3.53
	0	44	-8	3.19

Table 2

Brain regions and stereotaxic coordinates (mm) of novelty activation peaks observed in two tasks: Viewing new visual pictures and listening to new auditory sentences. Control tasks consisted in viewing familiar pictures and listening to familiar sentences, respectively. All peaks are situated either in the region of the Sylvian fissure, the insula, and the temporal and parietal opercula, or in area 37.

	Visual Pictures				Auditory Sentences			
	x	y	z	Z-score	x	y	z	Z-score
Left Sylvian/Insular/Opercular								
	-52	-28	20	3.40	-56	-28	20	2.10
	-50	-8	-8	2.59	-50	-12	-8	2.64
Right Sylvian/Insular/Opercular								
	46	-4	-12	2.45	42	-6	-12	3.61
	46	-6	-8	2.14	44	-8	-8	3.44
Right Inferior Temporal Gyrus (area 37)								
	42	-60	0	1.73	44	-58	0	3.14