

Conceptual Processing during the Conscious Resting State: A Functional MRI Study

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Abstract

■ Localized, task-induced decreases in cerebral blood flow are a frequent finding in functional brain imaging research but remain poorly understood. One account of these phenomena postulates processes ongoing during conscious, resting states that are interrupted or inhibited by task performance. Psychological evidence suggests that conscious humans are engaged almost continuously in adaptive processes involving semantic knowledge retrieval, representation in awareness, and directed manipulation of represented knowledge for organization, problem-solving, and planning. If interruption of such “conceptual” processes accounts for task-induced deactivation, tasks that also engage these conceptual processes should not cause deactivation. Furthermore, comparisons between conceptual and nonconceptual tasks should show activation during conceptual tasks of the same brain areas that are “deactivated” relative to rest.

To test this model, functional magnetic resonance imaging data were acquired during a resting state, a perceptual task, and a semantic retrieval task. A network of left-hemisphere polymodal cortical regions showed higher signal values during the resting state than during the perceptual task but equal values during the resting and semantic conditions. This result is consistent with the proposal that perceptual tasks interrupt processes ongoing during rest that involve many of the same brain areas engaged during semantic retrieval. As further evidence for this model, the same network of brain areas was activated in two direct comparisons between semantic and perceptual processing tasks. This same “conceptual processing” network was also identified in several previous studies that contrasted semantic and perceptual tasks or resting and active states. The model proposed here offers a unified account of these findings and may help to explain several unanticipated results from prior studies of semantic processing. ■

INTRODUCTION

Like other human biological structures, the human brain developed over evolutionary time to solve species-specific, recurring problems in the ancestral environment (Barkow, Cosmides, & Tooby, 1992; Donald, 1991). The general function of the brain is to process information, as is apparent in our considerable abilities to discriminate, recognize, categorize, and otherwise respond to external sensory stimuli. In addition to these problems related to sensory data, the human brain evolved to solve certain classes of problems over a longer time scale and independent of external sensory stimulation (Gibson & Ingold, 1993; Hebb, 1954; Miller, Galanter, & Pribram, 1960; Newell & Simon, 1972). The design and creation of tools, for example, depends on a neural system capable of “internally representing” specific scenarios for which the tool is being created as well as a specific plan that will bring about its creation. These simulated goals and plans further depend on internal stores of knowledge about the world because a given tool will be designed for a specific category of activities (hunting, not grooming) involving a specific class of things (land animals, not

fish), and the plan for creating the tool will reference specific, efficacious motor sequences (sharpening, not crushing) involving specific categories of preferred materials (tree limbs, not rocks). The occurrence of creative behaviors like tool-making thus implies that there are systems in the human brain capable of retrieving and representing previously learned information, generating specific goals defined in terms of this information, and formulating complex sequences of motor acts designed to attain these goals, all quite independent of external sensory stimulation.

Psychological research suggests that such internalized activities comprise a surprisingly large part of the information processing performed by humans during daily existence. William James observed that human awareness is a stream of continuous mental experiences that bear no necessary relationship to external events (James, 1890). Depriving the brain of external sensory information further stimulates the occurrence of internally generated neural activity (Solomon et al., 1961; West, 1962). Studies of subjects who were asked to report thought content at random intervals during controlled laboratory conditions and daily activities demonstrate that there is

continuous shifting of attention between externally and internally generated sources of information and that thought content becomes increasingly unrelated to external events as these external events become more static and predictable (Antrobus, Singer, & Greenberg, 1966; Pope & Singer, 1976). Conversely, the performance of difficult perceptual and short-term memory tasks suppresses internally generated phenomena, indicating a direct competition between exogenous and endogenous signals for attentional and executive resources (Antrobus, 1968; Antrobus et al., 1966; Filler & Giambra, 1973; Giambra, 1995; Pope & Singer, 1976; Segal & Fusella, 1970; Teasdale et al., 1995; Teasdale, Proctor, Lloyd, & Baddeley, 1993). Internally generated processes are extremely adaptive because they allow the organism to address unresolved problems over long periods of time. Accordingly, internally generated thoughts unrelated to external events are further stimulated by prior exposure of the subject to ambiguous, horrific, or unresolved situations (Antrobus et al., 1966; Horowitz, 1975; Klinger, 1978; Pope & Singer, 1976; Singer, 1993).

Although these psychological data imply the existence of neural activity related to ongoing thought, little systematic study of this type of activity has been undertaken. One essential question is whether subjectively experienced phenomena are to some degree associated with neural activity in specific brain areas. Thoughts experienced by awake, resting humans are characterized by information retrieval and problem-solving processes (e.g., internal monologue, imagery, deduction, inference, planning), and it is conceivable that the neural activity responsible for these processes arises in brain regions known to support such functions, such as the prefrontal and posterior association cortex (Damasio, 1989; Goldman-Rakic, 1987; Knight & Grabowecy, 1995; Stuss & Benson, 1986). An alternative possibility is that the neural activity underlying such phenomena is nonlocalized, unorganized, random, or negligible. An understanding of such issues is critical for the design and interpretation of functional neuroimaging studies, which commonly employ a resting state or a state involving highly predictable sensory stimulation as a putative neutral baseline (Eulitz et al., 1994; Herholz et al., 1994; Kawashima et al., 1993; Mazoyer et al., 1993; Tamas, Shibasaki, Horikoshi, & Ohye, 1993; Wise et al., 1991; Yetkin et al., 1995). If localized neural activity related to thinking and problem-solving regularly occurs during resting states, such activity might be expected to disguise activation from thinking and problem-solving tasks when resting is used as a baseline for comparison. Furthermore, interruption of processes ongoing during resting would result in decreased neural activity in brain regions where such processes were localized. Such phenomena could in some instances account for the “deactivation” that has been reported in association with various sensory processing tasks (Shulman et al., 1997).

A major obstacle to resolving such issues is the inability

to characterize objectively the mental state of subjects at rest. The present study is an attempt to partly circumvent the need for such a method by measuring brain activation during rest and during several contrasting activation states. One of these contrasting states, a tone-monitoring task, was designed explicitly to interfere with the occurrence of ongoing thought processes by requiring subjects to continuously monitor sensory information and hold this information in working memory. Pilot testing was conducted to verify that this task suppresses thought phenomena relative to a resting state. We then used functional magnetic resonance imaging (fMRI; Sanders & Orrison, 1995) to compare levels of brain activation during the resting state, the tone monitoring task, and a semantic retrieval task (Table 1) in 30 normal subjects. These data enabled identification of brain regions that are more active during the resting state than in either one or both of the active task conditions. The hypothesis that there are processes ongoing during rest that involve semantic retrieval and knowledge utilization leads to two clear predictions concerning these data. First, areas showing deactivation (relative to the resting state) during the tone-monitoring task should not show comparable deactivation during the semantic retrieval task. Deactivation during the tone task is hypothesized to occur because the task interferes with semantic processes ongoing during rest in specific brain areas. In contrast, the semantic retrieval task engages these same areas in processes similar to those ongoing during rest and so should not cause deactivation. Because these areas are hypothesized to participate in processes involving knowledge retrieval and utilization, the second prediction is that these same brain areas should show activation in any contrast between a task involving semantic processing and a task involving non-semantic processing. We tested the second prediction by contrasting the semantic retrieval task with the tone-monitoring task and with a more closely matched non-

Table 1.

<i>Condition</i>	<i>Instructions</i>
Rest	Remain still with eyes closed.
Tones	Listen to sequences of low (L) and high (H) tones (example: L-L-H-L). Respond when a sequence has two high tones (example: L-H-L-L-H).
Semantic	Listen to names of animals (example: squirrel). Respond when a named animal is found in the United States and is used by people (example: cow).
Phonetic	Listen to CV syllable triplets (example: pa-da-su). Respond when a triplet contains both the consonant /b/ and the consonant /d/.

semantic task involving detection of target phonemes in speech sounds. Activation data for the semantic-tone contrast were reported previously (Binder et al., 1997) and are briefly summarized here to permit a direct comparison with the other results.

RESULTS

Pilot Study: Task-Unrelated Thoughts During Rest and the Tone Task

All subjects learned the tone task easily. Performance was uniformly very good, averaging 98.6% correct. All 14 subjects reported the occurrence of task-unrelated thoughts (TUTs) more frequently at the end of rest periods than at the end of tone task periods. The mean proportion of TUT responses associated with rest was 0.628 ($SD = 0.217$) and with tone task periods was 0.114 ($SD = 0.103$), a difference that was highly significant ($df = 13$, paired $t = 9.89$, $p < 0.000001$).

fMRI Task Performance

All subjects learned the tasks easily and tolerated the scanning procedure well. Performance on the tone task was uniformly good, with subjects attaining a mean score of 98.3% correct (range: 89 to 100%) when the tone task was paired with rest, and 98.8% correct (range: 94 to 100%) when the tone task was paired with the semantic task. Subjects also performed well in discriminating targets from distractors on the semantic task, with a mean score of 92.1% correct (range: 72 to 98%) when the semantic task was paired with rest, 92.6% correct (range: 73 to 100%) when the semantic task was paired with the tone task, and 91.4% correct (range: 75 to 100%) when the semantic task was paired with the phonetic task. Accuracy on the phonetic task averaged 91.6% correct (range: 77 to 100%).

Rest Compared with the Tone Task

The tone task produced activation in a bilateral network of auditory, attentional, working memory, and motor systems in comparison to the resting state. As reported previously (Binder et al., 1997), these areas included the superior temporal auditory cortex, supramarginal gyrus, premotor cortex, supplementary motor area, anterior cingulate, anterior insula, dorsolateral prefrontal cortex, cerebellum, putamen, and thalamus. These activations were predominantly bilateral, although there was modest right-hemisphere dominance in prefrontal, middle temporal, and supramarginal regions.

In contrast, several cortical areas were significantly more active during the resting state than during the tone task. As shown in red-yellow in Figure 1, these included the angular gyrus, the posterior cingulate/retrosplenial

area, dorsal prefrontal cortex in the superior frontal gyrus, a ventromedial frontal region including the rostral anterior cingulate (ventral to the genu of the corpus callosum) and neighboring orbital frontal cortex, the posterior parahippocampus, and the inferior frontal gyrus (pars triangularis). In some areas this resting state activation occurred bilaterally but was always considerably stronger and more extensive in the left hemisphere. Stereotaxic coordinates for the centers of mass of these sites are listed in Table 2.

Rest Compared with the Semantic Task

The semantic task produced activation compared with rest in many of the same bilateral regions activated by the tone task. Shown in blue in Figure 2, these sites included the superior temporal auditory cortex, premotor cortex, caudal anterior cingulate, anterior insula, dorsolateral prefrontal cortex, cerebellum, putamen, and thalamus. Additional small activation foci were observed in the left inferior frontal gyrus, left intraparietal sulcus, and left superior frontal gyrus (Figure 2).

In contrast to the previous comparison between resting and the tone task, there were very few significant areas of activation during the resting state compared with the semantic task (red-yellow areas, Figure 2). Only one of the sites listed in Table 2, the right posterior cingulate, showed greater activation during rest than during the semantic task. Other areas listed in Table 2 thus showed similar levels of activity during the resting and semantic task states.

Semantic Task Compared with the Tone Task

Two observations made thus far have relevance for an interpretation of the resting state. First, the left hemisphere regions listed in Table 2 are more active during the resting state than during the tone task. Second, these areas have roughly similar signal levels during the resting and semantic task states. From these observations, it follows that these areas should also show activation during the semantic task relative to the tone task.

As anticipated, nearly all of the areas activated by the resting state relative to the tone task (Table 2) were also activated by the semantic task relative to the tone task (red-yellow areas, Figure 3; see Binder et al., 1997, for a more detailed discussion of regions activated by this task comparison). Areas activated in both comparisons included the left angular gyrus, left posterior cingulate/retrosplenial region, left dorsal prefrontal cortex, and left parahippocampus (compare Figures 1 and 3). The exception to this rule was the left rostral cingulate/orbital frontal region (approximately Brodmann's areas 11, 12, ventral 32, and 47), which showed relative activation in the rest-tone comparison but not in the semantic-tone comparison. This region also did not show

Table 2. Location of brain activation foci showing higher levels of blood oxygenation at rest than during the tone task (Rest-Tone) and higher levels during the semantic task than during the phonetic task (Semantic-Phonetic). Foci were defined as contiguous groups of voxels passing a significance criterion of $p < 10^{-7}$. Gyral/sulcal descriptions and stereotaxic coordinates refer to the atlas of Talairach and Tournoux (1988). Approximate cytoarchitectonic labels follow the nomenclature of Brodmann (1994/1909).

Atlas Structure at Center of Mass	Approximate Brodmann's Areas	Center of Mass Coordinates						Separation Distance (cm)
		Rest-Tone			Semantic-Phonetic			
		<i>x</i>	<i>y</i>	<i>z</i>	<i>x</i>	<i>y</i>	<i>z</i>	
L. angular gyrus	39	-43	-70	+26	-45	-71	+31	0.5
L. posterior cingulate	23, 29-31	-9	-55	+24	-8	-55	+15	0.9
L. dorsal prefrontal cortex	8, 9, 10	-20	+30	+44	-17	+27	+48	0.6
L. parahippocampal gyrus	36	-26	-35	-12	-26	-35	-16	0.4
L. rostral cingulate sulcus	12, 32	-9	+34	-7				
L. orbital sulcus	11, 47	-26	+28	-8				
R. posterior cingulate	23, 30, 31	+9	-53	+23				
L. inferior frontal gyrus	45	-51	+26	+14				

significant activity differences in the rest-semantic comparison, suggesting an absolute level of activity during the semantic task that was intermediate between the resting and tone task conditions.

Semantic Task Compared with the Phonetic Task

If the left-hemisphere regions listed in Table 2 are active during the resting state because they are engaged in semantic processing, then contrasts between semantic and nonsemantic tasks should reveal relative activation in these same regions. Although these regions were activated in the semantic-tones comparison (Figure 3), the semantic and tones tasks differ in ways other than the requirement for semantic processing. The semantic-phonetic task comparison was intended to identify activation related more specifically to semantic processing.

As shown in Figure 4 and Table 2, the areas activated by the semantic task relative to the phonetic task were nearly identical to those activated during rest relative to the tones task (Figure 1). The main exception was again the left rostral cingulate/orbital frontal region, which showed relative activation in the rest-tone comparison but not in the semantic-phonetic comparison.

DISCUSSION

These experiments indicate a network of brain areas that are more active during a conscious resting state than during a tone-monitoring task (Table 2, Figure 1). Expressed in other terms, these areas are “deactivated” by

the tone task. In contrast, these same areas appear to remain active during a semantic retrieval task. The sites showing this response pattern are polymodal and amodal association cortices, predominantly in the left hemisphere. Perhaps most strikingly, this same network of areas was identified by comparing the semantic retrieval task with a phonetic task. In the following paragraphs we offer a theoretical framework designed to account for these phenomena and for a variety of unanticipated results from previous functional neuroimaging studies.

“Conceptual” Processing during the Conscious Resting State

A basic tenet of the model to be presented is that the conscious resting state is not a state of neural inactivity. In addition to the brainstem homeostatic systems that regulate basic body functions, ongoing neural activity occurs at the cortical level and can be readily detected by electroencephalographic methods. Cerebral blood flow and metabolism vary across different regions of the cortex during resting states, being somewhat greater in the medial occipital, medial parietal, and dorsal prefrontal areas (Frackowiak, Lenzi, Jones, & Heather, 1981; Gur et al., 1995; Roland, 1993). Although this variation is probably due in part to regional differences in synaptic density and other structural factors, the “hyperfrontality” reported to occur during rest in early xenon cerebral blood flow studies (Ingvar, 1975) is greatest when both auditory and visual stimulation are minimized (Mazziotta, Phelps, Carson, & Kuhl, 1982), suggesting that intrinsic

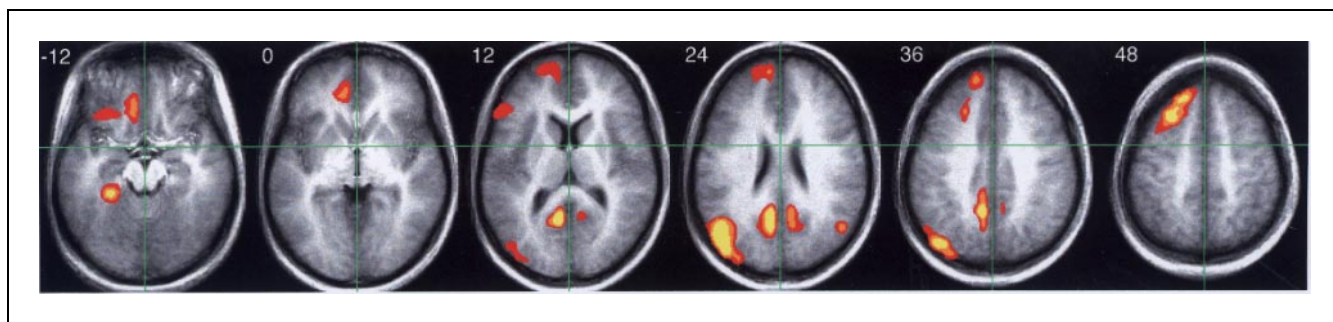


Figure 1. Rest minus Tones. Regions of significant activation difference ($p < 0.00001$) are shown in red-yellow superimposed on averaged anatomical brain images in axial orientation. Stereotaxic x and y axes are shown in green, and z coordinates are given above each image. The left hemisphere is on the reader's left. Areas more active during rest include the left parahippocampus ($z = -12, 0$), orbital frontal and rostral-ventral anterior cingulate cortex ($z = -12, 0$), left > right angular gyrus ($z = 12, 24, 36$), left > right posterior cingulate/retrosplenial cortex ($z = 12, 24, 36$), and left dorsal prefrontal cortex ($z = 12, 24, 36, 48$).

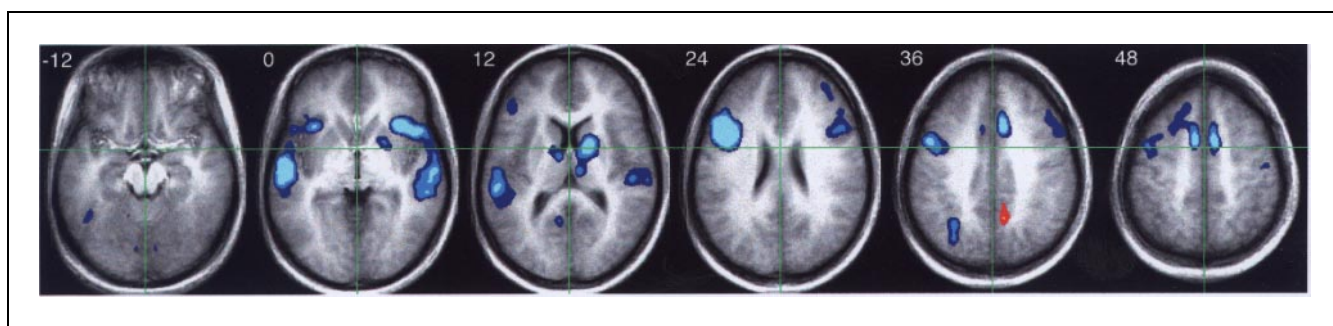


Figure 2. Rest minus Semantic. Only a small focus in the right posterior cingulate gyrus ($z = 36$) is more active during rest than during the semantic task. Areas that are more active during the semantic task are shown using the blue-cyan color scale.

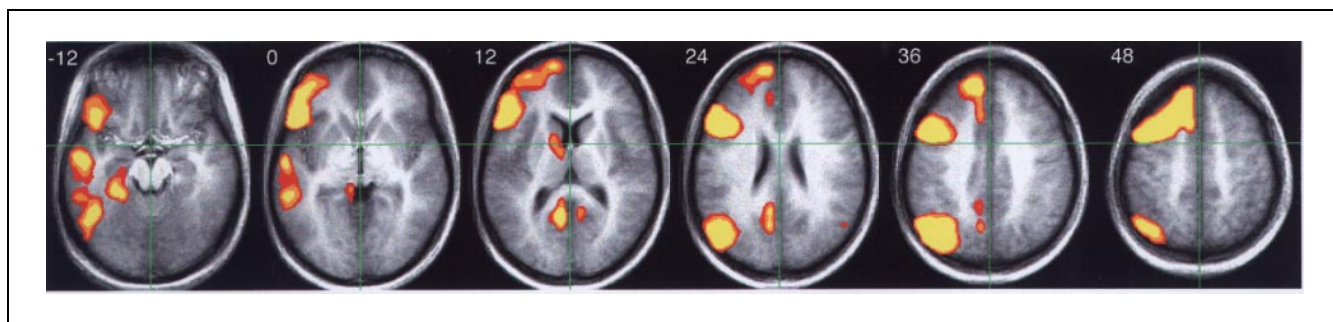


Figure 3. Semantic minus Tones. Like rest, the semantic task activates the parahippocampus, angular gyrus, posterior cingulate/retrosplenial cortex, and dorsal prefrontal cortex in the left hemisphere relative to the tone task (see Binder et al., 1997, for a presentation of these data in sagittal orientation).

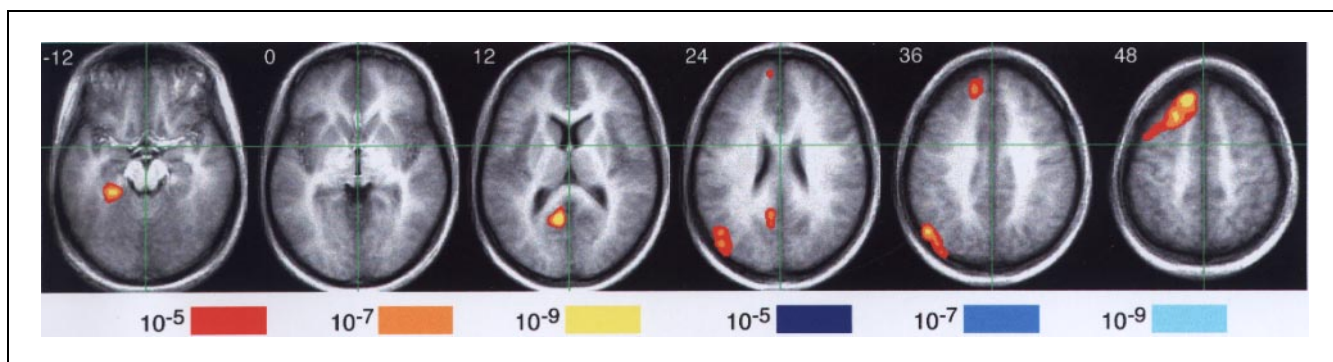


Figure 4. Semantic minus Phonetic. The semantic task also activates parahippocampus, angular gyrus, posterior cingulate/retrosplenial cortex, and dorsal prefrontal cortex in the left hemisphere relative to the phonetic task.

functional processes may also affect blood flow and metabolism at rest (Ingvar, 1979; Roland, 1993).

Although it is clear that neural activity occurs during rest, the purpose and significance of this activation are far from certain. One possibility is that resting neural activity is “noncomputational” (i.e., this activity does not represent information processing). According to this view, neural activity tends toward a minimal (but nonzero) tonic firing rate during rest (referred to as spontaneous, intrinsic, or background activity), presumably reflecting random inputs from other neurons, intrinsic physiological constraints on minimal levels of metabolic activity, or other unknown factors. An alternative possibility is that resting state neural activity is at least partly computational and that information processing occurs at rest that is in some way advantageous or essential for the organism. These processes might be available or unavailable to awareness and might include such tasks as monitoring body and limb positions, processing sensory and autonomic signals arising within the body, keeping track of the passage of time, planning future behaviors, or keeping an episodic memory record. These contrasting views of spontaneous activity lead to correspondingly different views of “deactivation” relative to rest. Under the first view, deactivation relative to rest is a special case in which neural activity, already at or near minimal “background” levels, is further suppressed, for example, by active inhibition, slow-wave sleep, or anesthesia. In contrast, deactivation relative to rest occurs in the second case because organized processes ongoing during rest are interrupted or interfered with. These views of spontaneous neural activity are not mutually exclusive, and each might be useful for describing resting activity in different brain regions. The model considered here makes specific reference to the second type of spontaneous activity in explaining activations during the resting state relative to the tone task.

A second tenet of the model involves a distinction between two very general classes of brain function that will be called *perceptual* and *conceptual*. As defined here, perceptual functions are those concerned with sources of information external to the brain and include sensory processing systems as well as the attentional control systems that modulate sensory processing. Conceptual functions are those concerned with sources of information within the brain and include long-term memory (i.e., knowledge) stores as well as the retrieval, representation, and manipulation systems that allow use of this information. Similar dichotomies based on a distinction between external and internal information sources have been articulated often in the past (Aurell, 1979; Hebb, 1954; James, 1890; Miller et al., 1960; Picton & Stuss, 1994; Pope & Singer, 1976; Posner, 1994; West, 1962). Interactions between external and internal sources of information are probably commonplace during perception (Hochberg, 1981; McClelland & Rumelhart, 1981; Miller et al., 1960; Neisser, 1967; Shepard,

1984; Yates, 1985), making the distinction between perceptual and conceptual processes relative rather than absolute. The distinction is of interest because behavioral tasks can be substantially weighted toward engaging either perceptual or conceptual functions. In operational terms, a perceptual task is one in which the required response is based on information physically represented in the sensory stimulus. For example, one perceptual task used in this study required detection of two occurrences of a change in frequency of tone stimuli. A conceptual task is one in which the required response cannot be determined from the physical features of the sensory stimulus alone but is based on previously learned information arbitrarily associated with the stimulus.

Because conceptual functions operate on internal sources of information, we assume that such functions can and do occur in the absence of external information. For example, conscious resting subjects frequently experience thoughts (consisting variously of mental images, auditory verbal images, “ideas,” and other similar phenomena) that are relatively unrelated to external perceptual events. In the pilot study conducted here, subjects reported such phenomena at the conclusion of a 15- to 24-sec period of rest on 62.8% of queries; very similar results were obtained by other investigators (Antrobus, 1968; Teasdale et al., 1995, 1993). The supposition that these phenomena reflect processing of internal sources of information does not imply that such processing is “spontaneous” or “indeterminate” in a philosophical sense or that such processing has no origin in the environment or in behavioral adaptation (Skinner, 1975). On the contrary, the adaptive significance of such phenomena is difficult to deny: By storing, retrieving, and manipulating internal information, we organize what could not be organized during stimulus presentation, solve problems that require computation over long periods of time, and create effective plans governing behavior in the future. These capabilities have surely made no small contribution to human survival and the invention of technology.

Given that there are limits on the processing capacity of the brain, however, it is reasonable to assume that perceptual and conceptual functions often compete for attentional and processing resources (Pope & Singer, 1976). For example, the need to process external stimuli takes precedence in many situations and “interrupts the train of thought.” Conversely, highly predictable or irrelevant external stimuli are frequently ignored while mentally pursuing the solution to a pressing problem. This competition for resources was investigated experimentally several decades ago by Antrobus and colleagues. Subjects performed perceptual signal detection tasks of various kinds and were asked to report the occurrence of thoughts unrelated to performance of the task. By manipulating the characteristics of the signal detection task, it was shown that the likelihood of experiencing a

task-unrelated thought was predictably decreased by increasing the rate of perceptual information processed during the task (Antrobus, 1968; Antrobus et al., 1966; Giambra, 1995; Pope & Singer, 1976). Subsequent investigators demonstrated that task-unrelated thoughts are also less likely to occur when the task requires maintenance of sensory information in a short-term store and when the task is less practiced (Filler & Giambra, 1973; Teasdale et al., 1995, 1993).

On the basis of these considerations, we propose that the brain areas identified in Table 2 and in Figure 1 are involved in “conceptual” functions operating on internal stores of information. These areas are active during conscious resting states and are engaged in such processes as retrieval of information from long-term memory, information representation in conscious awareness in the form of mental images and thoughts, and manipulation of this information for problem-solving and planning. These conceptual functions are interrupted or attenuated when subjects perform the tone-monitoring task, leading to a reduction in neural activity and accompanying reduction of fMRI signal in these areas. The model also explains why this network of regions was not identified in the rest-semantic comparison (Figure 2). The semantic retrieval task, although highly formalized and unnatural, engages some of the same conceptual functions that we propose are active during the resting state involving retrieval, representation, and utilization of internal sources of information. Because the brain areas performing these functions are active during both the resting and the semantic tasks, they are observed in the rest-tone comparison (Figure 1) and in the semantic-tone comparison (Figure 3) but not in the rest-semantic comparison (Figure 2). In addition to parsimoniously accounting for these observations, the model is neuroanatomically acceptable in that the identified regions comprise a network of areas that are relatively distant (as measured by cortico-cortical connections) from primary sensory areas (Felleman & Van Essen, 1991; Jones & Powell, 1970; Mesulam, 1985) and could thus be expected to participate primarily in conceptual rather than perceptual functions, in the sense outlined above.

This model also predicts the rather nonintuitive finding that subtraction of a tone-monitoring task from rest yields the same group of activation foci as subtraction of a phonetic perceptual task from a semantic retrieval task (Table 2, Figures 1 and 4). The semantic and phonetic tasks are relatively closely matched in that both employ speech stimuli and require phonetic perception and make similar (if not identical) demands on attentional, working memory, and motor response systems. Performance accuracy on the two tasks was nearly identical. The tasks differ primarily in terms of conceptual processing: stimuli in the semantic task have considerable semantic value, whereas those in the phonetic task have much less, and the semantic task requires retrieval of this stored information, whereas the phonetic task

does not. Subtraction of the phonetic from the semantic task thus identifies areas that are likely to be important in processing internal sources of information. These areas are virtually identical to those showing deactivation relative to rest, supporting the view that these areas are actively engaged in a similar type of processing during the resting state.

Independent support comes from other functional imaging studies contrasting conceptual and perceptual tasks, as these are defined here. Such comparisons are not common because most studies employing conceptually weighted tasks used resting or similar states (such as fixation or passive stimulation) as a baseline or compared tasks with similar perceptual and conceptual weightings. Two published studies, however, included strongly weighted conceptual-perceptual contrasts. Démonet et al. (1992) compared a semantic retrieval task similar to the one used here with a phonetic perceptual task similar to the phonetic task used here, with the goal of isolating brain areas involved specifically in semantic processing. Price et al. (1994) compared reading real words aloud to a perceptual task requiring detection of vertically oriented lines in a string of nonsense characters. Although seemingly very different, both of these comparisons identified the same left-hemisphere network of regions listed in Table 2: the angular gyrus, dorsal prefrontal cortex, posterior cingulate, and ventral temporal cortex. In each case these were the four most prominent cortical activations, and in each case the peak activation coordinates were within 2 cm of those listed in Table 2, despite considerable differences in methodology across the three studies (see Table 3). These studies thus independently and unintentionally identified the same network of brain areas. The conceptual/perceptual distinction outlined above predicts this convergence and provides an initial theoretical framework for interpreting many other studies that showed activation of a subset of this network (Bookheimer, Zeffiro, Blaxton, Gaillard, & Theodore, 1995; Bottini et al., 1994; Damasio, Grabowski, Tranel, Hichwa, & Damasio, 1996; Frith, Friston, Liddle, & Frackowiak, 1991; Raichle et al., 1994; Price, Wise, & Frackowiak, 1996; Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996; Warburton et al., 1996).

The areas associated here with conceptual processing during rest are also essentially identical to those shown recently by Shulman et al. (1997) to deactivate during a variety of visual tasks relative to passive visual stimulation and fixation. As with the other studies detailed in Table 3, the major foci identified by Shulman et al. are in the caudal inferior parietal lobe, posterior cingulate/precuneus, dorsal prefrontal cortex, and ventral temporal lobe, again with left-hemisphere predominance. One problem for the model presented here is that the areas identified by Shulman et al. also showed deactivation during several word retrieval tasks, including a verb generation and a word-stem completion task. Because the responses in these tasks depend on internal informa-

Table 3. Comparison of Brain Activation Foci from Démonet et al. (1992) and Price et al. (1994) with the Rest-Tone Foci Identified in the Present Study (Table 2)

Structure	Location from Démonet et al.			Distance from Rest focus in Table 2 (cm)	Location from Price et al.			Distance from Rest focus in Table 2 (cm)
	x	y	z		x	y	z	
L. angular gyrus	-48	-56	+28	1.5	-36	-56	+16	1.9
L. posterior cingulate	-2	-60	+24	0.9	-10	-44	+40	1.9
L. dorsal prefrontal	-20	+30	+40	0.4	-14	+20	+52	1.4
L. ventral temporal	-40	-38	-16	1.5	-36	-24	-12	1.5

tion stores, both tasks require a degree of conceptual processing, as defined here. Although this result may indicate a need for modification or refinement of the model, two points deserve comment. First, the word retrieval tasks used by Shulman et al. make relatively focused demands on retrieval of lexical (word level) information. As such, these tasks may engage internal information processing systems much less extensively than do the more complex conceptual processes postulated to occur during rest, leading to a degree of task-induced deactivation. The second point is that, consistent with the model presented here, these areas have *not* shown task-induced deactivation in other studies employing language tasks (Bookheimer et al., 1995; Frith et al., 1991; Howard et al., 1992), including one previous study of word generation (Frith et al., 1991). Resolution of these inconsistencies will require further study and replication. Direct comparisons between lexical and semantic retrieval tasks could help to refine further the conceptual-perceptual distinction underlying the model presented here.

Implications for Functional Neuroimaging

The hypothesis of conceptual processing at rest has some interesting and ubiquitous implications for the interpretation of functional imaging data. If semantic retrieval, representation, and information manipulation processes occur during conscious resting states, studies aimed at detecting these processes may lack sensitivity when employing rest as a comparison condition. The elegant study by Wise et al. (1991) illustrates this problem perhaps most clearly. In this study no differences in activation pattern were found between these three comparisons: (1) listening to nonsense speech versus rest, (2) semantically categorizing pairs of meaningful nouns versus rest, and (3) semantically categorizing verb-noun pairs versus rest. Contrary to original expectations, all three subtractions activated exactly the same superior temporal (auditory) areas bilaterally, despite seeming differences in semantic task requirements, particularly be-

tween the word tasks (2 and 3) and the nonsense speech task (1). The resting state model presented here accounts for such a finding in either of two ways. First, use of a resting baseline in each comparison would disguise areas involved in conceptual functions such as retrieval and manipulation of semantic information. If the main differences between the word and nonsense speech tasks involve such processes, these differences would have been obscured in each case by subtracting the resting state activity. By logical extension of the argument, however, the passive nonsense speech task (task 1) is similar to rest in that few resources need be diverted to perceptual functions at the expense of conceptual functions. According to the current model, conceptual functions would thus have been ongoing even during task (1), and there would consequently not have been major differences along the conceptual/perceptual dimension between the three tasks to begin with.

Conceptual processing can be expected to occur not only during resting states but also during states similar to rest, such as fixation and passive presentation. Stated more generally, there probably exists a continuum between rest, during which conceptual processing occurs relatively continuously, and engagement in a difficult perceptual task that greatly suppresses conceptual processing. The probability of identifying areas involved in conceptual processing will thus partly depend on the degree to which this type of processing is absent during the comparison task. Variables that control conceptual processing during a given task are likely to be the same variables that control task-unrelated thought frequency, such as stimulus presentation rate, working memory load, and task familiarity. Other factors could include perceptual discriminability, response rate, target or "odd-ball" rate, and linguistic properties of the stimuli. Clearly much work is needed to clarify the precise relationships between these task variables and the magnitude of task-induced deactivation observed relative to rest.

Ventromedial Frontal Activation

Activity in the rostral-ventral anterior cingulate and orbital frontal cortex followed a different pattern from the other left-hemisphere areas identified in Table 2. Activity in this region was greater in the resting state than in the tone task (Figure 1) but, unlike the other areas, was not greater in the semantic task than the tone task (Figure 3) nor greater in the semantic task than the phonetic task (Figure 4). Activity in this region thus appears to reflect a processing component that is relatively unique to the resting state. This region is probably distinct from activation foci in the anterior cingulate cortex reported previously during attentional and motor tasks because these foci were all well above the intercommissural line, generally 3.0 to 5.5 cm dorsal and caudal to the ventromedial frontal foci in Table 2 (Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991; Murtha, Chertkow, Beauregard, Dixon, & Evans, 1996; Pardo, Pardo, Janer, & Raichle, 1990; Paus, Petrides, Evans, & Meyer, 1993; Petersen, Fox, Posner, Mintun, & Raichle, 1988).

A characteristic that distinguishes the resting state from the semantic task is that the conceptual processing proposed to occur during rest is self-initiated. Unlike the semantic task, in the resting state there is no external stimulus that prompts or directs the processes of retrieving, representing, and manipulating internal information. One hypothesis consistent with these results is that the angular gyrus, dorsal prefrontal, posterior cingulate, and ventral temporal sites listed in Table 2 are involved in retrieval, representational, and manipulative aspects of conceptual processing—processes that also occur during the semantic task—whereas the ventromedial frontal region acts in some way to *initiate* these processes during the resting state.

Similar findings come from a functional imaging study of task-unrelated thought production by McGuire, Paulesu, Frackowiak, and Frith (1996). In this study subjects were scanned while resting, speaking nonsense syllables, and reading. After each condition, subjects rated the frequency of task-unrelated thoughts they had just experienced using an arbitrary 0 to 10 scale. The analysis searched for image voxels in which activity was correlated with task-unrelated thought frequency ratings. The main foci of correlation were in the left rostral cingulate and medial prefrontal cortex. Two of the three foci ($-4,44,8$ and $-10,48,0$) were within 2 cm of the ventral anterior cingulate focus given in Table 2. A crucial point is that the tasks used by McGuire et al., involved linguistic stimuli and may therefore have engaged the retrieval, representation, and manipulation components of conceptual processing to varying degrees. This task-related conceptual processing would not be expected to correlate with task-unrelated thought frequency and therefore would not have been identified in the correlation analysis. The ventromedial frontal area identified by McGuire

et al., is therefore associated with functions specific to task-unrelated conceptual processing as distinct from task-related conceptual processing. This is essentially the same result that emerged from the present study. Taken together, these findings suggest that ventromedial frontal activity may be related rather specifically to conceptual processing initiated intrinsically rather than prompted by external stimuli.

According to this interpretation, the ventromedial frontal cortex would be predicted to show relative activation during a resting state in comparison to a perceptual task but not during a semantic task in comparison to a perceptual task. This prediction is borne out in the available studies (Démonet et al., 1992; Price et al., 1994; Shulman et al., 1997).

Left-Hemisphere Lateralization of Conceptual Processing

The proposal that there is a network of brain regions located primarily in the left hemisphere that is specialized for knowledge retrieval, problem-solving, and planning is consistent with several recent findings regarding cerebral lateralization. For example, the left hemisphere was shown to control the decision to respond in a go/no-go task (Bisiach, Mini, Sterzi, & Vallar, 1982; Vallar, Bisiach, Cerizza, & Rusconi, 1988), suggesting that it may play a dominant role in decision-making. The left hemisphere appears to be critical for generating mental images from constituent parts (Farah, Gazzaniga, Holtzman, & Kosslyn, 1985; Kosslyn, 1988; Kosslyn, Maljkovic, Hamilton, Horwitz, & Thompson, 1995), a process likely to play a role in generating plans through the conscious representation of alternative scenarios. The left hemisphere may be the site of origin of uncontrolled thoughts resulting in verbal hallucinations in schizophrenia (Barta, Pearlson, Powers, Richards, & Tune, 1990; Liddle et al., 1992; McGuire, Shah, & Murray, 1993). Perhaps most relevant are the conclusions about human cognition drawn from studies of patients with interhemispheric disconnection. In such individuals, the right hemisphere typically is devoid of language ability and is difficult to engage in any sort of task involving an overt response (Gazzaniga, 1983). When minimal language abilities are present in the right hemisphere, a variety of matching and discriminative responses can be obtained, and the right hemisphere demonstrates superiority for many visuospatial judgments (Franco & Sperry, 1977; Levy, Trevarthen, & Sperry, 1972; Nebes, 1971, 1973). Even in such cases, however, the right hemisphere appears virtually incapable of making simple inferences from sensory events based on prior experience. Shown a picture of logs and a picture of matches, for example, the left hemisphere of such patients will select a picture of a bonfire from a multiple choice display, whereas the right hemisphere is unable to demonstrate this type of

spontaneous inferential behavior (Gazzaniga, 1995; Gazzaniga & Ledoux, 1978; Gazzaniga & Smylie, 1984). Whether such organizing, differentiating, inferential, problem-solving activities are essentially linguistic or extralinguistic has been much debated (Révész, 1954; Weiskrantz, 1988). Lateralization to the language-dominant hemisphere of brain activity associated with ongoing thought, as observed here, lends some support to claims that linguistic or generative systems play a role in mediating such processes, perhaps providing a computationally efficient means of accessing, representing, and manipulating internal sources of information (Corballis, 1991; Karmiloff-Smith, 1992; Kendler & Kendler, 1962; Morris, 1946; Sapir, 1927; Vygotsky, 1962).

METHOD

Pilot Study: Task-Unrelated Thought

Subjects in the pilot study were 14 healthy adults (7 women, 7 men), ranging in age from 18 to 35 years. Subjects gave written informed consent and were paid a small hourly stipend. The study received prior approval by the Medical College of Wisconsin Human Research Review Committee.

Testing took place in a simulated magnetic resonance imaging (MRI) scanner that consisted of a sliding table, on which the subject lay supine during the study, and a tube-shaped enclosure with an inner diameter identical to the MRI scanner bore, into which the subject was slid halfway. Simulated echo-planar scanner pulses were played over a loudspeaker at the back of the enclosure at a rate of 4.8 Hz during all study conditions. The room lights were extinguished, and subjects were instructed to close their eyes during testing.

Two conditions were compared. In the rest condition, subjects heard only the simulated scanner pulses and performed no task. In the task condition, subjects performed the same tone-monitoring task used in the fMRI experiment and described previously (Binder et al., 1995). Stimuli in this task were 500- and 750-Hz tones of 150-msec duration each, separated by 250-msec inter-stimulus intervals. These were presented as sequences of three to seven tones. Subjects were required to respond by pressing a button with the left hand for any sequence containing two 750-Hz tones. Stimuli were digitally synthesized pure tones played by a computer through amplified headphones worn by the subject. Target sequences occurred randomly on 37.5% of trials. Several practice trials were given to ensure that subjects understood and could perform the task.

Prior to testing subjects were also familiarized with a definition of TUTs, using instructions modeled after those employed by previous investigators (Antrobus et al., 1966; Teasdale et al., 1993): "During the session, it is very possible that thoughts or images may enter your

mind that are not related to the tones task. For example, you may think of something that you did last night or someone you met recently or some other event that happened in the past. Or you may think of something you should do on your way home or something you need to make plans for or some other event that could happen in the future. All of these thoughts or images share in common the property of being unrelated to doing the tones task. We will call these 'task-unrelated thoughts'."

During subsequent testing, scanner pulse sounds and tones were halted abruptly after periods of the task or rest condition that varied in length from 15 to 24 sec (average 19.5 sec). Subjects were instructed to report the presence or absence of a TUT at the moment of sound interruption, using two keys operated with the right hand. This reporting procedure was practiced several times prior to testing. Twenty such TUT queries were conducted for each of the two conditions. The order of conditions was random over the 40 condition periods.

fMRI Study

Subjects

As described previously (Binder et al., 1997), subjects in the fMRI study were 30 healthy adults (15 men, 15 women), ranging in age from 18 to 29 years, with no history of neurologic, psychiatric, or auditory symptoms. All subjects indicated strong right-hand preferences (laterality quotient > 50) on the Edinburgh Handedness Inventory (Oldfield, 1971). Subjects gave written informed consent and were paid a small hourly stipend. The study received prior approval by the Medical College of Wisconsin Human Research Review Committee.

Task Conditions and Behavioral Measures

Task conditions during scanning included a resting state, a tone-monitoring task, a semantic decision task, and a phonetic monitoring task (Table 1). Subjects' eyes were closed, and the room lights were dimmed for all conditions. Characteristics of the auditory stimulus apparatus have been described previously (Binder et al., 1995, 1997). Stimuli and task instructions for the tone task were identical to those used in the pilot study described above. Stimuli in the semantic task were spoken English nouns designating animals (e.g., turtle). Subjects were required to respond by button press for animals they considered to be both "found in the United States" and "used by people." No animal words were used more than once during the entire scanning session. Characteristics of the tone and semantic stimuli and the rationale for task design have been described previously (Binder et al., 1995, 1997).

Stimuli in the phonetic monitoring task were spoken consonant-vowel (CV) syllables, including all combina-

tions of the consonants b, d, f, g, h, j, k, l, m, n, p, r, s, t, v, w, y, and z with the five vowels /æ/, /i/, /a/, /o/, and /u/. All syllables were edited to a duration of 400 msec. Each trial presented three CV syllables in rapid sequence (e.g., /pa dæ su/). Subjects were required to respond by button press when a triplet of CV syllables included both of the consonants /b/ and /d/.

All tasks were matched for stimulus intensity, average trial duration (3 sec), and frequency of targets (37.5% of trials). Responses consisted of a thumb press to a button device held in the left hand. Button responses produced a visual signal in the control room that was used to log performance accuracy. For the resting condition, subjects were instructed to remain relaxed and motionless with eyes closed but were given no other instructions or stimuli. Instructions and brief practice trials on each task were given prior to each functional imaging series.

Performances on the tone task and the phonetic task were scored as the proportion of correct responses. Responses on the semantic decision task were scored using response data from a group of 50 normal right-handed controls on the same stimulus sets. Items responded to with a probability greater than 0.75 by controls were categorized as targets, and items responded to with a probability less than 0.25 by controls were categorized as distractors. Performance by each subject was then scored as the proportion of correct discriminations between targets and distractors.

Image Acquisition

Scanning was conducted at 1.5 Tesla on a General Electric (GE Medical Systems, Milwaukee, WI) Signa scanner, using a three-axis local gradient coil with an insertable transmit/receive radiofrequency coil optimized for whole-brain echo-planar imaging (EPI). Padding was placed behind the neck and around the head as needed to relax the cervical spine and to pack the space between the head and inner surface of the coil. Functional imaging employed a gradient-echo EPI sequence with the following parameters: 40-msec echo time, 4-sec repetition time, 24-cm field of view, 64 × 64-pixel matrix, and 3.75 × 3.75 × 7.0-mm voxel dimensions. Between 17 and 19 contiguous sagittal slice locations were imaged, encompassing the entire brain. One hundred sequential images were collected at each of the slice locations. Each 100-image EPI series began with four baseline images (16 sec) to allow the magnetic resonance (MR) signal to reach equilibrium, followed by 96 images during which two comparison conditions were alternated for eight cycles. High resolution, T1-weighted anatomical reference images were obtained as a set of 124 contiguous sagittal slices using a 3-D spoiled-gradient-echo sequence (SPGR, GE Medical Systems, Milwaukee, WI).

Four EPI series were acquired. In each series, one of the conditions alternated eight times with one of the other conditions, with each block of each condition

lasting 24 sec. To control for the possibility that subjects might rehearse or review the semantic task during rest epochs, the first series was a resting-tone comparison that occurred before subjects had any knowledge of the semantic task. The remaining three series included a resting-semantic comparison, a semantic-tone comparison, and a semantic-phonetic comparison. The order of these three series was randomized and counterbalanced across subjects.

Image Processing and Subtraction Analysis

All EPI images were spatially coregistered using an iterative procedure that minimizes variance in voxel intensity differences between images (Cox, 1996b). For each EPI time series, *t* tests were conducted at each voxel to measure changes in signal intensity between the two alternating comparison conditions. For this analysis, one of the comparison conditions was designated the activation or “probe” condition and the other as the “control” condition. First, the final four images within each of the probe epochs were averaged to produce an image of average signal intensity values during the last 12 sec of each probe epoch. This procedure ensured that the measured values would reflect steady-state activation levels after completion of the hemodynamic response. Next, the four images obtained during control epochs immediately preceding and following each probe epoch were averaged, and a probe-control difference image was created for each of the eight activation cycles by subtracting the average control image from the corresponding average probe image (Binder et al., 1994). Finally, these mean probe-control difference values were compared, on a voxel-by-voxel basis, against a hypothetical mean of zero using pooled-variance Student *t* tests. This procedure generates statistical parametric maps (SPMs) of *t* deviates reflecting differences between probe and control states at each voxel location for each subject. These differences are referred to as “activation.”

Individual anatomical (SPGR) scans and SPMs were then projected into the standard stereotaxic space of Talairach and Tournoux (1988), using the MCW-AFNI software package (Cox, 1996a). To compensate for normal variation in anatomy across subjects (Toga et al., 1993), the unthresholded, stereotaxically resampled 3-D SPMs were smoothed slightly with a Gaussian filter of root-mean-square radius 4 mm. These datasets were then merged across subjects by averaging the *t* statistics at each voxel (Binder et al., 1997). The procedure of averaging statistics was chosen to guard against heteroscedasticity of MR signal variance among subjects that could arise, for example, from differing degrees of subject motion or tissue pulsatility, variability in global blood flow or reactivity, or scanner variability between sessions.

The maps of averaged *t* statistics were thresholded to identify voxels in which the mean change in MR signal

between comparison conditions was unlikely to be zero. The average of a set of t deviates is not a tabulated distribution. Therefore, the Cornish-Fisher expansion of the inverse distribution of a sum of random deviates was used to select a threshold for rejection of the null hypothesis (Fisher & Cornish, 1960). Only average t scores of 1.014 or greater were considered significant (voxel-wise $p < 0.00001$).

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