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Where the imaginal appears real: A positron emission tomography study of auditory hallucinations

(reality monitoring/anterior cingulate/hypnosis/attention/affect)

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ABSTRACT **An auditory hallucination shares with imaginal hearing the property of being self-generated and with real hearing the experience of the stimulus being an external one. To investigate where in the brain an auditory event is "tagged" as originating from the external world, we used positron emission tomography to identify neural sites activated by both real hearing and hallucinations but not by imaginal hearing. Regional cerebral blood flow was measured during hearing, imagining, and hallucinating in eight healthy, highly hypnotizable male subjects prescreened for their ability to hallucinate under hypnosis (hallucinators). Control subjects were six highly hypnotizable male volunteers who lacked the ability to hallucinate under hypnosis (nonhallucinators). A region in the right anterior cingulate (Brodmann area 32) was activated in the group of hallucinators when they heard an auditory stimulus and when they hallucinated hearing it but not when they merely imagined hearing it. The same experimental conditions did not yield this activation in the group of nonhallucinators. Inappropriate activation of the right anterior cingulate may lead self-generated thoughts to be experienced as external, producing spontaneous auditory hallucinations.**

An auditory hallucination has elements of both imaginal and real hearing. It shares with imaginal hearing the property of being self-generated and with real hearing the experience of the stimulus being an external one. As put by Bentall (1), "hallucinators mistake their own internal, mental, or private events for external, publicly observable events." Indeed, hallucinations can be viewed as a failed instance of source monitoring, which refers to processes involved in making attributions about origins of mental contents (2). Although a variety of processes are likely involved in such reality monitoring, a number of investigators have argued for the existence of a fundamental neural process that "tags" a percept as originating either externally or internally (2–5).

The present study addressed the question of what brain regions are involved in distinguishing whether an auditory event originates from the external world or not. In other words, where in the brain is a hallucination processed specifically like a real external stimulus? For this purpose, we examined whether there exist neural sites activated by both real hearing and hallucinations but not by imaginal hearing. We measured regional cerebral blood flow with positron emission tomography to compare the relative brain maps of hearing, imagining, and hallucinating. To obtain subjects capable of hallucinating during a positron emission tomography scan, we prescreened healthy male volunteers for high hypnotizability and the ability to hallucinate under hypnosis.

METHODS

Procedures. Changes in regional cerebral blood flow (rCBF) were measured in eight male volunteers under four conditions: at rest, while listening to a taped message, while imagining hearing the taped message, and while hallucinating hearing the taped message. This was followed by a repetition of the four conditions in reversed order. The taped message was the sentence "The man did not speak often, but when he did, it was worth hearing what he had to say." It was said in a nonemotional tone by a male voice in ≈5 s. The same sentence was said *de novo* approximately every 10 s for 2.5 min (slight changes in intonation and timing between repetitions were expected to sustain attention to the recording). Throughout the session, subjects were under hypnosis and lay in the tomograph with eyes covered. For the baseline condition, they were instructed to lay quietly, think of nothing, and let their minds be blank. For the hearing condition, they were told that the tape recorder would be played and were instructed to pay attention to the voice message on the tape. For the imagining condition, they were told that the tape would not be turned on and instead they were to imagine "as vividly as possible, hearing the same man's voice repeating the same phrase over and over again." Finally, for the hallucinating condition, they were instructed identically as for the hearing condition, but the tape recorder was not played (the sound of activating the tape recorder was made, however). After each condition, subjects rated the "externality" and the "clarity" of the sound they heard. Subjects made externality ratings on a scale of 1–10 to indicate the extent to which they experienced the sound source as entirely inside their own head (rating of 1) vs. entirely external (rating of 10). Similarly, for clarity, a rating of 1 indicated that the sound was virtually inaudible, and a 10 indicated that it was "clear and vivid—as real as real." Start and end of conditions were signaled to the subject by a finger snap. The study was approved by the McMaster University Ethics Committee and the University of Waterloo Office of Human Research.

Subjects. Subjects were selected from male students at the University of Waterloo prescreened on the Harvard Group Scale of Hypnotic Susceptibility, Form A (6), and the Waterloo–Stanford Group C Scale of Hypnotic Susceptibility (WSGC) (7). Those scoring at least 8 on both scales were administered an individual clinical evaluation with a variety of hypnotically suggested hallucinations (music, voices, singing) to verify the subjective vividness and perceived reality of hallucinations. The selected subjects who were hallucinators

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Abbreviation: rCBF, regional cerebral blood flow.

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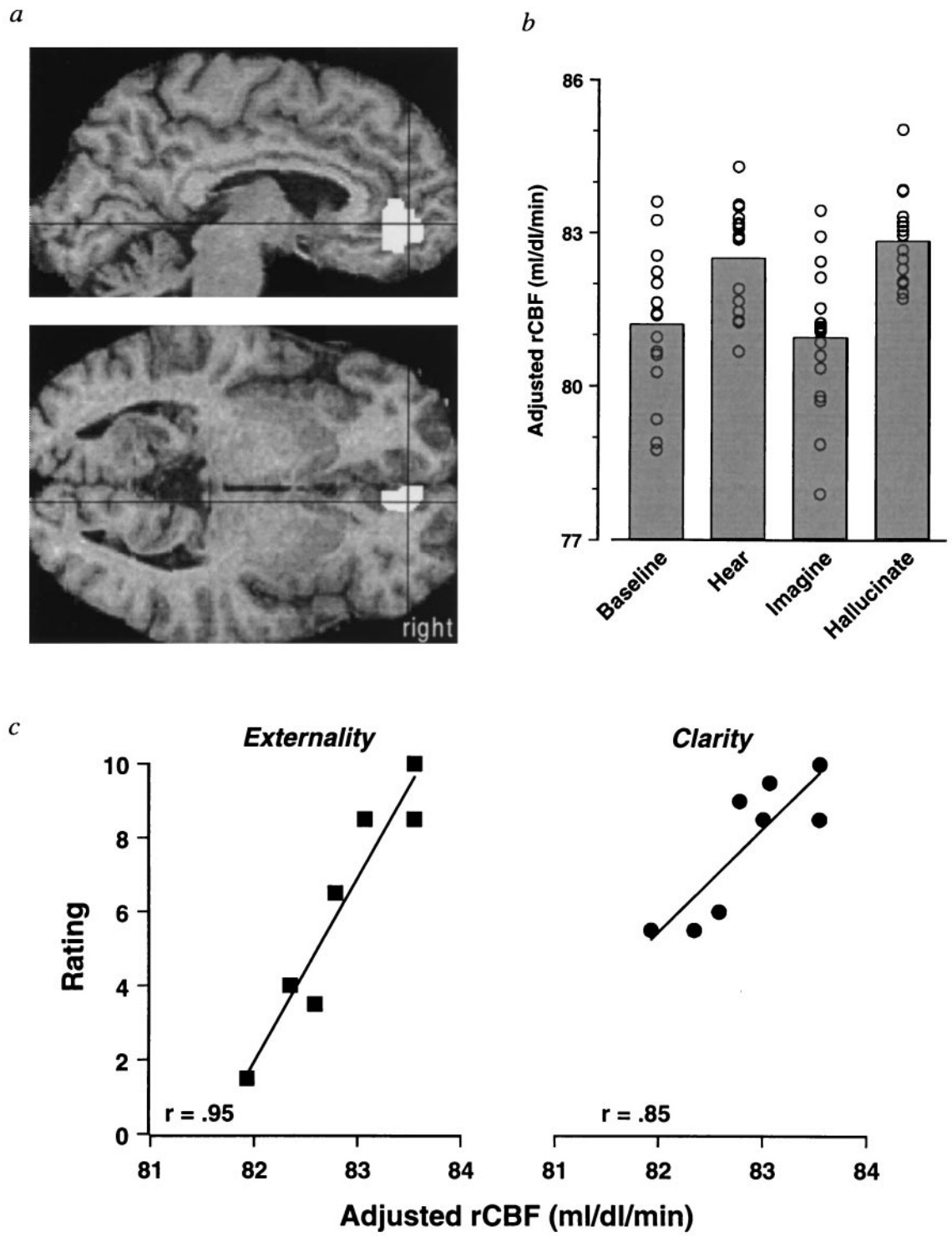

FIG. 1. Anterior cingulate region activated in the group of hallucinators by both hearing and hallucinating conditions. (*a*) Projections on sagittal (upper) and transverse (lower) MRI templates of the region identified by the combination of four contrasts: the conjunction of two orthogonal contrasts (threshold, $P = 0.001$), hallucinate vs. baseline, and hearing vs. imagining, masked with two other orthogonal contrasts (threshold, $P = 0.05$), hearing vs. baseline, and hallucinate vs. imagining. The combination of these contrasts (with either pair masked by the other pair) isolates a significant region ($P = 0.009$, voxel level significance) that is activated by both hearing and hallucinating compared with both imagining and baseline conditions. This region of 207 voxels lies in the right ventral anterior cingulate, and its maximum ($z = 4.60$) is located at {6,48,0} (16); the crosshairs are located at these coordinates. (*b*) The adjusted rCBF response at {6,48,0} for each condition. The rCBF response is adjusted to an arbitrary mean of 50 ml/dl/min. Note the parallel rCBF changes during the hearing and hallucinating conditions. Subjects contributed two replications of each condition. (*c*) Correlations between the adjusted rCBF response at {6,48,0} and ratings of externality and clarity of the heard voices during the hallucinating condition. The average rCBF response and the average ratings of the two hallucinating conditions are plotted. The externality rating for one subject was unavailable.

[mean age = 21 yr, range = 19–24 yr; five right-handed according to modified Annett handedness questionnaire (8), one left-handed, and two not assessed) were highly hypnotizable (mean hypnotizability score = 10.9), passed the auditory hallucination item on the WSGC, and were consistently capable of vivid hallucinations in the clinical evaluation. Approx-

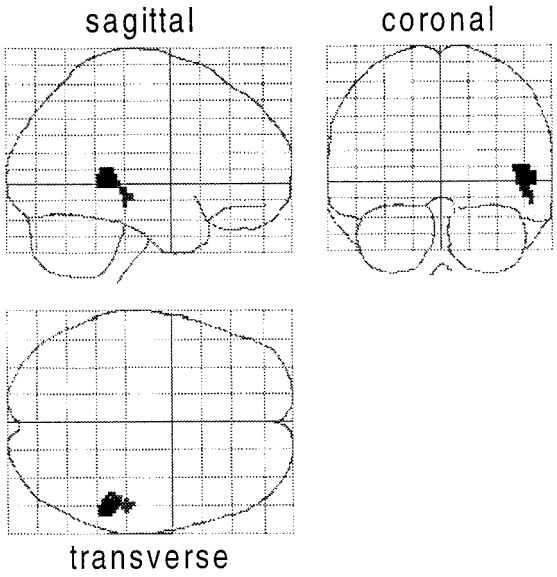

FIG. 2. Auditory association cortex activated in the group of nonhallucinators by both hearing and hallucinating conditions. Orthogonal projections of the region identified by the combination of four contrasts: the conjunction of two orthogonal contrasts (threshold, $P = 0.001$), hallucinate vs. baseline, and hearing vs. imagining, masked with two other orthogonal contrasts (threshold, $P = 0.05$), hearing vs. baseline, and hallucinate vs. imagining. The identified region lies in the right Brodmann area 22, and its maximum ($z = 4.44$, 73 k, $P = 0.02$ voxel level significance) is located at {52,-38,4} (16).

imately 4% of highly hypnotizable subjects are able to hallucinate (9, 10). The nonhallucinators who were selected for the study (mean age = 21 yr, range = 19–24; five right-handed, one not assessed) were screened in the same manner as the hallucinators and were equally highly hypnotizable (mean hypnosis score = 10.5) except that they failed the auditory hallucination item on the WSGC and consistently failed to produce hallucinations in the clinical evaluation as well as in the positron emission tomography scanner (mean rating of clarity of heard voices = 2). In the experiment, the recording was played through a speaker placed on a stand ≈1 m in front and at 45° to the left of the subject's ear. Before the start of the experiment, subjects were familiarized with the experimental procedure, they listened to the tape for two repetitions of the sentence, and then they were administered a brief, standardized hypnotic induction and were positioned in the tomograph.

Measurement of rCBF. rCBF was measured with a Siemens/CTI (Knoxville, TN) ECAT 953/31 scanner according to the method of Lammertsma *et al.* (11). In brief, six frames at 30 s/frame were acquired beginning 30 s before administering a bolus injection of 15 mCi of $H_2{}^{15}O$ through an indwelling venous catheter in the arm opposite to the position of the audio speaker. Start of injection coincided with start of condition. Integrated counts per pixel over the middle 2 min were used as a measure of rCBF. Correction for attenuation was made by performing a transmission scan with an exposed $^{68}Ge/^{68}Ga$ external rod source before each session. Images were reconstructed by using a Hann filter (cut-off frequency 0.5) giving a transaxial resolution of 6 mm full width at half maximum. The reconstruction matrix was 128 × 128 pixels, each 2.05 × 2.05 mm.

The method used in assessing statistically significant changes between conditions was that of Statistical Parametric Mapping (SPM) developed by Friston and colleagues (12–15). Image normalization was performed by using SPM94 software, and statistical analysis was performed with SPM96 (Wellcome Department of Cognitive Neurology, London, England). A multisubject with replication design was used as was an ANCOVA for global normalization. The threshold for significant voxels was set at $P = 0.001$. The regional distributions of the supra threshold elements are displayed in Figs. 1–3, and their neuroanatomic locations are identified with reference to the atlas (16). The smoothed voxel size (k) is ≈8.5 × 9.4. × 4.9 mm.

RESULTS AND DISCUSSION

To localize regions activated by hearing and hallucinating but not by imagining, we identified significant voxels for which both hearing and hallucinating conditions were different from both baseline and imagining conditions. These voxels were contained in a region of the right anterior cingulate encompassing the Talairach (16) coordinates {6,48,0} (Fig. 1*a*). During hallucination, the adjusted blood flow at these coordinates was elevated above baseline to the same extent as during hearing whereas imagining did not increase rCBF compared with baseline (Fig. 1*b*). In addition, there was a strong positive correlation between the rCBF response during the hallucination condition and the subjects' ratings of externality ($r = 0.95, P < 0.001$, two-tailed) and a similar correlation with the ratings of clarity of the heard voice ($r = 0.85$, $P = 0.008$; Fig. 1*c*).

We also tested in the same experimental design six subjects who were equally highly hypnotizable but who lacked the ability to hallucinate. The same combination of four contrasts revealed that, unlike the hallucinators, the nonhallucinators did not show a significant right anterior cingulate activation. The difference between the two groups at this location ({6, 48,0}) was statistically significant ($z = 1.75$, $P = 0.04$). These results suggest that activation of the right anterior cingulate is crucially related to the experience of the hallucination.

However, the nonhallucinators did show significant activation for this combination of four contrasts in one region, namely, the auditory association cortex (Brodmann area 22; {52, −38, 4}; Fig. 2), and differed significantly from the hallucinators at this coordinate ($z = 1.77, P = 0.038$). Although it is not readily apparent why nonhallucinators differed from the hallucinators in the pattern of activation of the auditory association cortex, this difference between the groups indicates that activation of the auditory cortex alone is insufficient for the experience of a hallucination. This suggestion is supported by the comparisons of hearing vs. hallucination for hallucinators and nonhallucinators (Fig. 3*a*). The extent of activation for hearing over hallucination was substantially greater for the hallucinators than the nonhallucinators, encompassing a much wider region of the temporal lobes (≈2,700 voxels in hallucinators vs. 350 voxels in nonhallucinators). Thus, with regard to auditory cortex activation, hallucination is less similar to hearing in the hallucinators than in the nonhallucinators.

Not only was the brain response of hallucinators and nonhallucinators different during the hallucination task, but it was also different during hearing. Brain activation during hearing compared with baseline included more extensive regions in the hallucinators than in the nonhallucinators, including the right rostral anterior cingulate (Fig. 3*b*). The pattern of brain activation during hearing in the highly hypnotizable nonhallucinators closely resembled the pattern observed in unselected nonhypnotized subjects studied previously (17). Thus, hallucinators appear to process auditory events more extensively, suggesting that these individuals are distinct from the general population in a number of ways. Other studies report that highly hypnotizable individuals who show the same capacity to hallucinate under hypnosis as our subjects did are acutely sensitive to sensory stimuli. Moreover, they are unique in fantasizing vividly through much of their everyday life and often feel their fantasies to be real and external (10, 18).

Our finding that the anterior cingulate is a neuroanatomic substrate associated with hallucinations raises a hypothesis

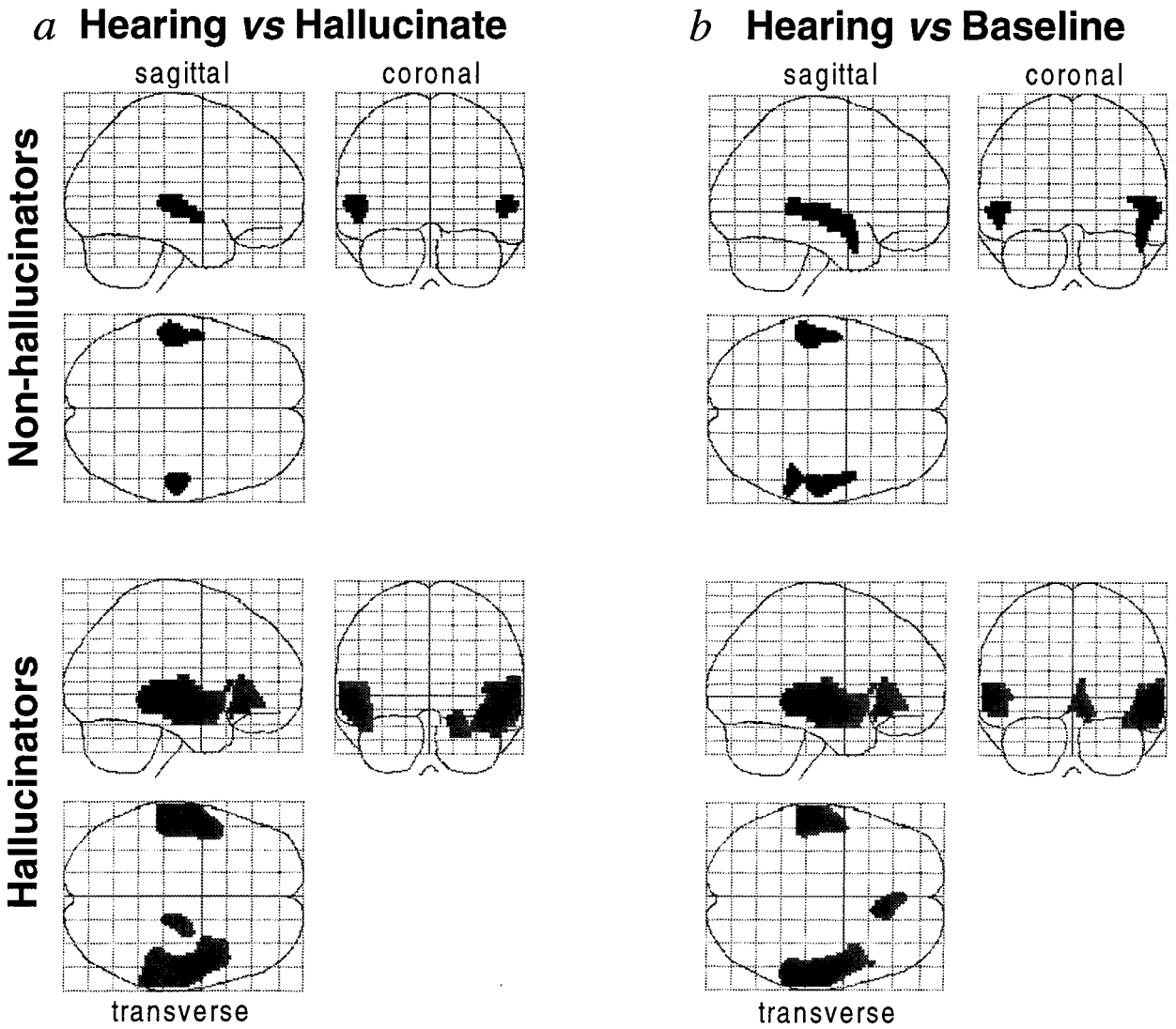

FIG. 3. Cerebral regions significantly activated (threshold, $P = .001$) in nonhallucinators (upper) and hallucinators (lower). (*a*) Regions activated during the hearing condition compared with the hallucinate condition. In nonhallucinators, the maxima of significant foci were located at: {−54, −22, 4} ($z = 4.82$, 236 k, $P = 0.004$), {54, −20, 4} ($z = 4.04$, 111 k, $P = 0.089$). In the hallucinators, significant areas of activation were: {52, −6, −8} ($z = 6.06$, 1579 k, $P < 0.001$), {−52, −2 −8} ($z = 5.45$, 1007 k, $P < 0.001$), and {18, −16, −20} ($z = 3.71$, 171 k, $P = 0.075$ cluster level significance). (*b)* Regions activated during the hearing condition compared with baseline. In nonhallucinators, significant foci were located at: {−54, −22, 0} ($z = 4.29$, 220 k, $P = 0.037$), and {54, −18, 0} ($z = 4.18$, 382 k, $P = 0.012$ cluster level significance). In the hallucinators, significant areas of activation were: {64, −30, −4} ($z = 5.71$, 1347 k, $P < 0.001$), {−58, −26, 0} ($z = 5.00$, 556 k, $P = .002$), and {10, 30, −12} ($z = 4.14$, 228 k, $P = 0.042$ cluster level significance). Unless noted otherwise, P values refer to significance at the voxel level.

concerning how such experiences may be produced. The rostral division of the anterior cingulate has been implicated in modulating autonomic activity associated with affect, consistent with extensive anatomic connections with limbic structures including the amygdala (19). The anterior cingulate also is thought to be part of an "anterior attentional system" (20, 21), consistent with extensive cortical connections including the prefrontal cortex and the auditory association cortex (22, 23). Recently, Ballard *et al.* (24) argued that an attentional system creates a momentary coordinate system for computing stimulus location. This computational frame of reference to external space reflects the subject's current intentions. Our instructions in the hallucination condition pointed the subject's attention to external space. Consequently, the self-generated event in the hallucinators may have been interpreted in the external frame of reference and thus was experienced as real.

Considering that activation of the rostral anterior cingulate also is implicated in modulating affect (19), we propose that the attention of hallucinators is more affect-laden than that of nonhallucinators. Furthermore, when attention is more affect-laden, self-generation of the expected auditory event is more likely to occur.

The activity of the anterior cingulate in schizophrenic patients is correlated with measures of auditory hallucination (25–27). Although the coordinates identified in these patients are somewhat more dorsal than the site identified in our study, the hallucinations studied here may nonetheless share mechanisms with those of schizophrenia. At a conceptual level, schizophrenic hallucinations have been attributed to a disturbance in the neural circuitry of the language system (25, 26, 28, 29), to a defect in the self-monitoring of inner speech (3, 30, 31) or perception of cognitive effort (32), and to a deficient metacognitive "reality discrimination" skill (1). The notion advanced here, however, emphasizes a mismatch between externally directed attention and internally generated events. Such a mechanism may be relevant also to auditory hallucinations of schizophrenia, as we suggest for the mechanism of hypnotic hallucinations.

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1. Bentall, R. P. (1990) *Psychol. Bull.* **107,** 82–95.
2. Johnson, M. K., Hashtroudi, S. & Lindsay, D. S. (1993) *Psychol. Bull.* **114,** 3–28.
3. Feinberg, I. (1978) *Schizophr. Bull.* **4,** 636–668.
4. Kunzendorf, R. G. (1985–1986) *Imagination Cognition Personality* **5,** 255–270.
5. Frith, C. D. & Done, D. J. (1988) *Br. J. Psychiatry* **153,** 437–443.
6. Shor, R. E. & Orne, E. C. (1962) *Harvard Group Scale of Hypnotic Susceptibility* (Consulting Psychologists Press, Palo Alto, CA).
7. Bowers, K. S. (1993) *Int. J. Clin. Exp. Hypnosis* **61,** 35–46.
8. Briggs, P. F. & Nebes, R. D. (1975) *Cortex* **11,** 230–238.
9. Hilgard, E. R. (1965) *Hypnotic Susceptibility* (Harcourt, Brace & World, New York).
10. Wilson, S. C. & Barber, T. X. (1983) in *Imagery: Current Theory, Research, and Application*, ed. Sheikh, A. A. (Wiley, New York), pp. 340–387.
11. Lammertsma, A. A., Cunningham, V. J., Deiber, M. P., Heather, J. D., Bloomfield, P. M., Nutt, J. G., Frackowiak, R. S. J. & Jones, T. (1990) *J. Cereb. Blood Flow Metab.* **10,** 675–686.
12. Friston, K. J., Frith, C. D., Liddle, P. F. & Frackowiak, R. S. J. (1991) *J. Cereb. Blood Flow Metab.* **11,** 690–699.
13. Friston, K. J., Passingham, R. E., Nutt, J. G., Heather, J. D., Sawle, G. V. & Frackowiak, R. S. J. (1989) *J. Cereb. Blood Flow Metab.* **9,** 690–695.
14. Friston, K. J., Frith, C. D., Liddle, P. F. & Frackowiak, R. S. J. (1991) *J. Comput. Assist. Tomogr.* **15,** 634–639.
15. Friston, K. J., Frith, C. D., Liddle, P. F., Dolan, R. J., Lammerstsma, A. A. & Frackowiak, R. S. J. (1990) *J. Cereb. Blood Flow Metab.* **10,** 458–466.
16. Talairach, J. & Tournoux, P. (1988) *Co-Planar Stereotaxic Atlas of the Human Brain* (Georg Thieme Verlag, Stuttgart, Germany).
17. Szechtman, H., Cleghorn, J. M., List, S., Whelton, C., Kaplan, R., Ballagh, S., Franco, S., Szechtman, B., Bowers, K., Woody, E., Firnau, G., Nahmias, C. & Garnett, E. S. (1992) *Soc. Neurosci. Abstr.* **18,** 865 (abstr.).
18. Lynn, S. J. & Rhue, J. W. (1988) *Am. Psychol.* **43,** 35–44.
19. Devinsky, O., Morrell, M. J. & Vogt, B. A. (1995) *Brain* **118,** 279–306.
20. Posner, M. J. & Petersen, SE (1990) *Annu. Rev. Neurosci.* **13,** 25–42.
21. Morecraft, R. J., Geula, C. & Mesulam, M. M. (1990) *Arch. Neurol.* **50,** 279–284.
22. Barbas, H. (1988) *J. Comp. Neurol.* **276,** 313–342.
23. Paus, T., Petrides, M., Evans, A. C. & Meyer, E. (1993) *J. Neurophysiol.* **70,** 453–469.
24. Ballard, D. H., Hayhoe, M. M., Pook, P. K. & Rao, R. P. N. (1997) *Behav. Brain Sci.*, in press.
25. Cleghorn, J. M., Garnett, E. S., Nahmias, C., Brown, G. M., Kaplan, R. D., Szechtman, H., Szechtman, B., Franco, S., Dermer, S. W. & Cook, P. (1990) *Br. J. Psychiatry* **157,** 562–570.
26. Cleghorn, J. M., Franco, S., Szechtman, B., Kaplan, R. D., Szechtman, H., Brown, G. M., Nahmias, C. & Garnett, E. S. (1992) *Am. J. Psychiatry* **149,** 1062–1069.
27. Silbersweig, D. A., Stern, E., Frith, C., Cahill, C., Holmes, A., Grootoonk, S., Seaward, J., Mckenna, P., Chua, S. E., Schnorr, L., Jones, T. & Frackowiak, R. S. J. (1995) *Nature (London)* **378,** 176–179.
28. Johnson, F. H. (1979) *The Anatomy of Hallucinations* (Nelson Hall, New York).
29. McGuire, P. K., Shah, G. M. S. & Murray, R. M. (1993) *Lancet* **342,** 703–706.
30. Frith, C. (1995) *Lancet* **346,** 615–620.
31. McGuire, P. K., Silbersweig, D. A., Wright, I., Murray, R. M., David, A. S., Frackowiak, R. S. J. & Frith, C. D. (1995) *Lancet* **346,** 596–600.
32. Hoffman, R. E (1986) *Behav. Brain Sci.* **9,** 503–546.