Differentiating Ictal Panic With Low-Grade Temporal Lobe Tumors From Psychogenic Panic Attacks

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ABSTRACT

Objective: Indolent low-grade temporal lobe tumors may present with ictal panic that may be difficult to differentiate from psychogenic panic attacks. The current study aims to demonstrate the differences between the two disorders and help physicians generate a diagnostic paradigm.

Method: This was a retrospective study of 43 patients who underwent a temporal lobectomy between 1981 and 2008 for the treatment of intractable temporal lobe epilepsy secondary to low-grade neoplasms at Rush University Medical Center. A total of 10 patients in this group presented with ictal panic who were previously being treated for psychogenic panic attacks. Medical records were reviewed for age at seizure onset, duration of symptoms, lateralization of the epileptogenic zone, pathological diagnosis, and postsurgical seizure outcome according to the modified Engel classification.

Results: Neuropathologic findings of the 10 tumors were pleomorphic xanthoastrocytoma, ganglioglioma, oligodendroglioma, and dysembryoplastic neuroepithelial. The mean age of the patients undergoing surgery was 28 years (range, 15–49). The mean duration of panic symptoms prior to surgery was 9.8 years (range, 3–23). All patients had unprovoked ictal panic. None had symptoms suggestive of a brain tumor, such as signs of increased intracranial pressure or any focal neurologic deficit. In 5 of the patients, other symptoms associated with the ictal panic, including unusual sounds, nausea, automatism, uprising gastric sensation, and déjà vu were identified. Gross total resection of the lesion resulted in improved seizure outcome in all patients undergoing surgery. Patient follow-up was, on average, 7.4 years (range, 2–14) from time of surgery.

Conclusions: Although similar, ictal panic from epilepsy and classic panic attacks are clinically distinguishable entities with different modalities of treatment. A careful history may help differentiate patients with ictal panic from those with psychogenic panic attacks and determine for which patients to obtain neuroimaging studies.

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Although most brain tumors present with specific neurologic signs and symptoms, they may present with neurobehavioral or psychiatric symptoms. In fact, up to 80% of partial seizures of mesial temporal lobe origin or mesial frontal origin can begin with a variety of psychiatric symptoms.[1–9] Only 3% of patients hospitalized for psychiatric illness harbor intracranial lesions.[1] However, suspicion of a brain tumor is typically triggered by the report of neurologic symptoms (eg, headaches, seizures, weakness) but rarely, if ever, by the presence of psychiatric symptomatology.

Panic attack is a commonly encountered psychiatric diagnosis, with a prevalence of nearly 2%.[10] Previously published case series have described patients with partial seizures misdiagnosed as panic attacks.[10–13] Panic attacks can be easily confused with partial seizures of temporal lobe origin associated with mesial temporal sclerosis, other structural lesions (eg, brain tumor), or cryptogenic temporal lobe epilepsy (TLE).[7,10,13–21] Indeed, it is not uncommon for physicians to mistreat patients with seizures of the mesial temporal lobe as psychogenic panic attacks for years.[6,14,21] This notion has been supported by some studies of patients with temporal lobe epilepsy describing fear auras during the ictal stage. In most of these patients, the right temporal lobe was the source of these seizures, with the vast majority of them containing a structural lesion.[11,12,22] Additionally, patients with epilepsy presenting with ictal panic may have a higher prevalence of panic disorder interictally compared to the general population (6% vs 2%).[23]

Clinically, ictal panic and panic attacks can be distinguished with a careful history and, in particular, the duration, severity, timing, and autonomic findings of the attacks.[24–27] Additionally, psychogenic panic attacks rarely present after 30–35 years of age and generally occur by the mid- to late-20s.[28]

In this article, we present a series of 10 patients with low-grade temporal lobe tumors who presented with 3–26 years of ictal panic initially treated as panic attacks who all had improved seizure control after surgical resection of the tumor and the epileptogenic zone.

METHOD

This was a retrospective study of 43 patients who underwent a temporal lobectomy for the treatment of intractable temporal lobe epilepsy secondary to low-grade neoplasms (World Health Organization grade I or II). The Rush Surgical Epilepsy Database was queried to identify all patients with chronic medically intractable epilepsy who underwent resection of the temporal lobe between 1981 and 2008 at Rush University Medical Center, Chicago, Illinois. Over 500 patients were identified. Of these patients, 43 had low-grade tumors in the temporal lobe. Those patients who presented with ictal panic and previous treatment for panic attacks (totaling 10 patients) were included in this study. These patients had been diagnosed with ictal panic using continuous video electroencephalogram (EEG) monitoring by epileptology specialists at our institution. Medical

Clinical Points

- Because of the similarities between ictal panic from epilepsy and classic panic attacks, it may be difficult for clinicians to distinguish ictal panic from panic attacks.
- Making the distinction between ictal panic and panic attacks is important because the treatment for each type of panic is different.
- Ictal panic from epilepsy should be suspected in patients with atypical symptoms of panic attacks such as déjà vu, lack of response to traditional psychiatric treatment, or neurologic signs or symptoms.

records were reviewed for age at seizure onset, duration of symptoms, lateralization of the epileptogenic zone, pathological diagnosis, and postsurgical seizure outcome. Postoperative seizure outcome was categorized using the modified Engel classification,[29] which is the accepted standard classification system used to describe postoperative outcome in patients undergoing epilepsy surgery and consists of the following: IA: no seizures, no auras; IB: only auras; II: 2 seizures/year; III: > 90% seizure reduction; IVA: < 90% seizure reduction; IVB: unchanged; and IVC: worse. This study was approved by the Institutional Review Board of Rush University Medical Center.

RESULTS

The demographics and clinical data of the 10 patients are summarized in Table 1. Neuropathologic findings of the tumors included pleomorphic xanthoastrocytoma (PXA) in 3 cases, ganglioglioma (GG) in 4 cases, oligodendroglioma in 2 cases, and dysembryoplastic neuroepithelial tumor (DNET) in 1 case. The mean age of the patients undergoing surgery was 28 years (range, 15–49). The mean duration of panic symptoms prior to surgery was 9.8 years (range, 3–23). All patients had unprovoked ictal panic per continuous video EEG monitoring and their epileptologists. Some had been misdiagnosed as panic attacks and were refractory to medical management. Additionally, none had symptoms suggestive of a brain tumor, such as signs of increased intracranial pressure (eg, vomiting, headaches, altered mental status) or any focal neurologic deficit (eg, weakness, sensory deficits). In 5 of the patients, other symptoms were identified that were associated with the ictal panic, including unusual sounds, nausea, automatism, uprising gastric sensation, and déjà vu. Six patients presented with complex-partial seizures and 3 with simple-partial seizures. One patient had years of complex-partial seizures and eventually presented with a generalized seizure. Five tumors were in the left temporal lobe and 5 were in the right. The frequency and duration of ictal panic as well as postsurgical seizure outcome appears in Table 1. Gross total resection of the lesion resulted in improved seizure outcome in all of the patients who underwent surgery. Eight patients experienced remission of their ictal panic (Engel I), while the remaining 2 patients achieved an Engel class II and III outcome, respectively. Patient follow-up was, on average, 7.4 years (range, 2–14) from time of surgery.

DISCUSSION

Brain tumors more often present with signs and symptoms of elevated intracranial pressure rather than psychiatric symptoms. In 1963, Hobbs[5] noted that in psychiatric admissions, the incidence of brain tumors was only 0.1%. Keschner and colleagues[30] first described in 1938 a series of 530 patients with brain tumors in which 18% presented with neuropsychiatric ailments. In that series, brain tumors presented with depression, mania, anxiety, cognitive changes, psychosis, and personality changes. In 1951, Papez and Bateman[31] noted psychiatric illness arising from epileptic lesions, tumors, strokes, and arteriovenous malformations involving the temporolimbic system. In a literature review by Madhusoodanan et al,[8] the authors found 66 case reports of patients with brain tumors initially presenting with psychiatric manifestations. The group concluded there was no correlation between psychiatric symptoms and tumor location or tumor histology. The temporal lobe is involved with memory and emotion and is involved in 22% of intracranial tumors. Patients with tumors in this region have been shown to present with personality changes, mania, hallucinations, amnesia, and anxiety.

Partial seizures mimicking psychogenic panic attacks pose a diagnostic challenge to the medical community, raising the question of the need to obtain neuroimaging in the psychiatric population. Typical symptoms of panic disorder include anxiety, fear, derealization, palpitations, depersonalization, diaphoresis, autonomic changes, and a sense of impending doom. These symptoms may also present in patients with epilepsy, known as ictal panic or fear. Ictal panic is a manifestation of either partial seizures or auras in complex partial seizures and are more commonly found in seizure foci located in the temporal lobe.[2,32] The *DSM-IV* describes panic attacks as a discrete period of intense fear or discomfort in which 4 or more specific symptoms develop abruptly and reach a peak within 10 minutes.[33(p395)] Although similar, ictal panic as a result of partial seizures and psychogenic panic attacks are clinically different and can be distinguished based on a thorough history.[24,26] Ictal panic generally lasts less than 30 seconds, unless it progresses into a complex partial or secondarily generalized seizure, which may last on average 90 seconds. Panic attacks, however, are much longer in duration and, on average, last 5–20 minutes.[26] Additionally, the panic episodes occurring during ictal panic are mild in contrast to the "impending doom" experienced in patients with panic attacks, which can eventually lead to agoraphobia.[27] Other characteristics of ictal panic are that it may occur during times of both sleep and wakefulness, and it is a stereotypical paroxysmal event with respect to duration and symptoms. In contrast, panic attacks tend to occur in awake patients and may or may not be stereotypical, and can be triggered by stressful situations.[25,26] It is also evident that autonomic

Table 1. Low-Grade Temporal Lobe Tumor Characteristics

Patient	Age, y	Pathology	Grade[a]	Side	Duration of Fear Symptom, y	Preoperative Seizures	Postsurgical Engel Classification	Seizure Type	Symptom
1	26	PXA	II	R	10	15/mo	IA	CP + SP	Fear, nausea
2	17	Ganglioglioma	I	L	3	2/d	IA	SP	Fear, depersonalization
3	19	Ganglioglioma	I	R	6	2/wk	IA	SP	Fear, buzzing sound
4	30	Oligodendroglioma	II	L	7	2/d	IA	CP + SP	Fear
5	36	Oligodendroglioma	II	R	18	2/mo	IA	CP + SP to generalized	Fear
6	20	PXA	II	L	5	20/d	IB	CP + SP	Fear
7	29	PXA	II	L	15	1/mo	IA	CP + SP	Fear
8	49	Ganglioglioma	I	L	23	4/mo	II	CP + SP	Fear, automatism
9	36	DNET	I	R	5	4/wk	IA	SP	Fear, auditory hallucination, déjà vu
10	15	Ganglioglioma	I	R	6	3/wk	III	CP + SP	Fear, uprising sensation in stomach

[a]Based on World Health Organization grade I or II.
Abbreviations: CP = complex-partial seizure, DNET = dysembryoplastic neuroepithelial tumor, L = left temporal lobe, PXA = pleomorphic xanthoastrocytoma, R = right temporal lobe, SP = simple-partial seizure.

symptoms occur in both panic attacks and ictal panic. Autonomic manifestations of both include hyperventilation, tachycardia, hypertension, palpitations, and chest pain. However, paroxysmal salivation, derealization, déjà vu, jamais vu, and depersonalization are pathognomonic of mesial temporal epilepsy.[24,26] Psychogenic panic attacks rarely present after 35 years of age and generally occur in late adolescence or early adulthood. In contrast, ictal panic can occur at any age and should be suspected in patients older than 30 years who are experiencing new onset of panic symptoms.

In 1962, Roth and Harper[34] hypothesized that the temporal lobe was the source of phobia and anxiety in patients experiencing depersonalization-derealization as a result of partial seizures. Hobbs[5] described the similarity between complex partial seizures and the condition "phobic-anxiety-depersonalization." This notion has been supported by the observation that up to 15% of patients with temporal lobe epilepsy describe ictal panic.[35] In fact, fear is the most common emotion during focal discharge of the temporal lobe, with anxiety or attacks often being the only clinical finding observed in temporal lobe epilepsy. Furthermore, direct brain stimulation of the anteromedial temporal lobe and limbic structures, including the amygdala and hippocampus, has been shown to elicit a sense of fear.[36,37] Gloor et al[38] used temporal depth recordings to localize the origin of such fear response to the amygdala, but not the hippocampus. Animal models have also suggested the role of the amygdala in panic attacks—the central nucleus has been shown to be responsible for arbitrating both fear and anxiety in animal models of anxiety, and stimulation of the central nucleus generates fear-like responses.[39]

Focal seizures may generate autonomic symptoms similar to those seen in panic attacks—tachycardia, hypertension, hyperventilation, etc. Studies in animals and humans have shown that the right hemisphere may play a role in controlling heart rate and blood pressure, a phenomena described as "sympathetic lateralization." Using hemispheric inactivation by injecting intracarotid amobarbital in 15 patients with intractable epilepsy, Hilz et al[40] demonstrated lateralization of sympathetic function to the right and parasympathetic function to the left, an idea that was proposed by several authors earlier.[41–43] The principal location involved in autonomic regulation is believed to be the insular cortex.[44] Additionally, modalities such as positron emission tomography (PET) and single photon emission computed tomography (SPECT) scans have implicated the right parahippocampal gyrus in the origin of anxiety during epileptic attacks.[45,46] With this in mind, the spread of seizure activity from right mesial temporal structures to the insular region can possibly generate both the aura of fear and the autonomic findings associated with panic attacks. In our series of 10 patients, we did not find a preference for right-sided lateralization. In fact, 5 patients presented with left-sided temporal lesions. This discrepancy has been a subject of debate in the past, with some authors arguing against the lateralization of autonomic control.[47] Further studies are necessary to determine whether there is indeed sympathetic lateralization in the limbic structures. Our series would argue against lateralization of panic auras to the right hemisphere.

A review of the literature describes a number of patients with partial seizures as a consequence of a brain lesion initially misdiagnosed as panic disorder.* The right temporal lobe was found to be the major source of these seizures, with many of them containing a structural lesion (ie, tumor, vascular lesion, mesial temporal sclerosis). The 2 largest published series are those compiled by Tassinari et al[49] and Sazgar et al,[12] both describing lesions in the right temporal lobe as the cause of epileptic seizures manifesting as panic attacks (Table 2). Tassinari's series consisted of 7 patients,[49] while Sazgar's described 5 patients.[12] Both groups showed an improvement in seizure frequency in patients who either were switched to antiepileptic medications or underwent resection of their lesions. The benefit of surgery in curing these seizures was also apparent in small case series, including 1 by Filley and Kleinschmidt-DeMasters[4] that showed nearly 88% improvement or resolution of neurobehavioral syndromes. In the present series, we noted

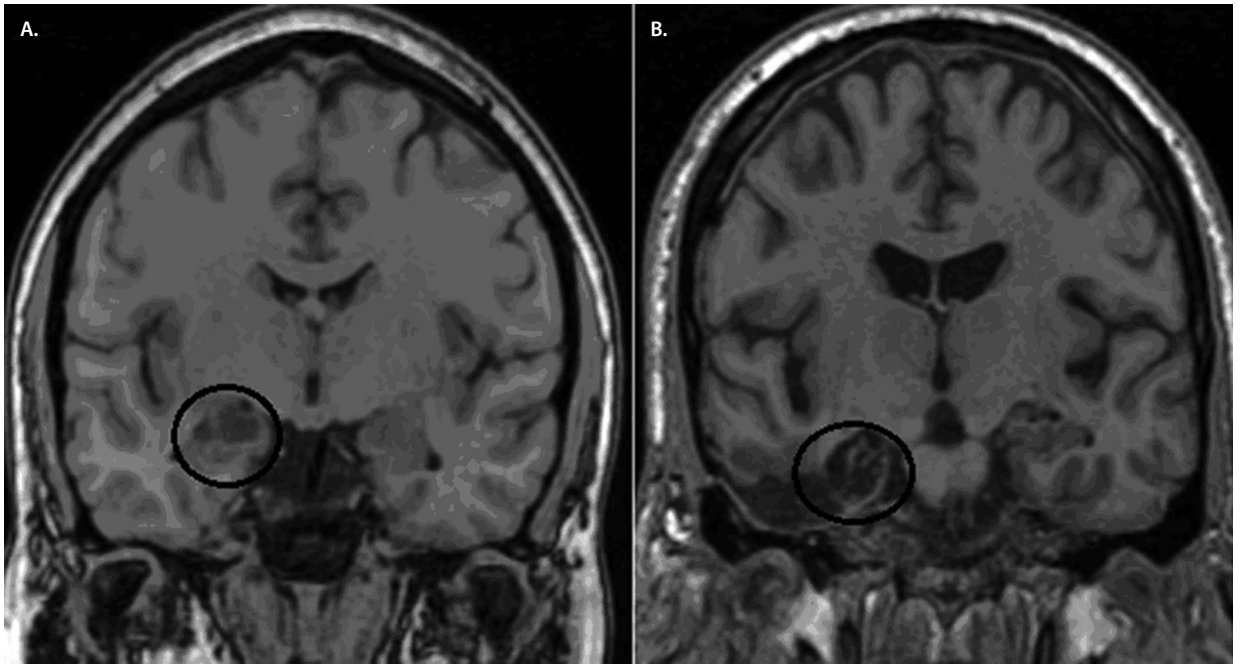
*References 10, 12, 14–17, 19, 20, 38, 47, 48.

Table 2. Literature Review of Brain Neoplasms Causing Ictal Fear

Report	Patients, n	Right Temporal	Lesion Type
Ghadirian et al,[11] 1986	1	1	Meningioma
Alemayehu et al,[10] 1995	2	0	Astrocytoma in both
Tassinari et al,[49] 2000	7	7	2 mesiotemporal sclerosis, 2 cavernomas, 2 tumors, 1 cerebral lupus
Sazgar et al,[12] 2003	5	5	4 mesiotemporal sclerosis, 1 ganglioglioma
Present study, 2013	10	5	3 PXA, 4 ganglioglioma, 2 oligodendroglioma, 1 DNET

Abbreviations: DNET = dysembryoplastic neuroepithelial tumor, PXA = pleomorphic xanthoastrocytoma.

Figure 1. Preoperative (A) and Postoperative (B) Magnetic Resonance Image of Right Temporal Lesion[a]



[a]Circles identify a tumor in the amygdala (A) and the postoperative resection cavity (B).

a cure rate of 70%, with improved seizure frequency in the remaining 30% (Table 1).

The pertinent question that arises is, "Which patients presenting with psychiatric symptoms warrant magnetic resonance imaging, given the cost limitations and practicality of imaging all such patients?" Psychogenic panic attacks rarely present after 35 years of age and generally occur by the mid- to late-20s. Also, as described above, several clinical differences do exist between ictal panic and panic attacks. In light of these findings, authors have argued that neuroimaging should be implemented in older patients, generally 35–40 years of age or older, presenting with a new psychiatric diagnosis or in those resistant to pharmacologic treatment.[4,50] In so doing, the possibility of an anatomic lesion that may be causing these attacks may be found, and the benefit of implementing proper antiepileptic therapy and/or subsequent surgery to cure the partial seizures would be warranted (Figure 1). In light of the literature, our series consists of a much younger age group, with a mean age of 28 years and only 4 patients older than 30 years. We also observed several other manifestations of temporal lobe seizures in several of the patients in our series, including an uprising feeling in the stomach, nausea auras, and déjà vu. Our series differs from all previous published reports in that only low-grade temporal tumors were evaluated with clear localization to the temporal lobe and it is the largest series of its kind. These tumors tend to present in young adults and do not display symptoms of mass effect—headaches, nausea, vomiting, altered mental status, etc. Additionally, we did not evaluate patients with vascular lesions or mesial temporal sclerosis. Although neuroimaging is not likely to be implemented on a routine basis due to its high cost, we suggest that it should be considered in any patient with atypical symptoms of panic attacks, such as déjà vu; lack of response to traditional psychiatric treatment; or any additional neurologic signs or symptoms that may suggest a lesion as a cause of epilepsy.

Several limitations are evident in our study. These include the retrospective nature of the study, the relatively small number of patients in the series, and the lack of a control group. Nonetheless, this is the largest case series to date describing low-grade cerebral tumors presenting with ictal fear.

CONCLUSION

In conclusion, indolent low-grade temporal lobe tumors may present with ictal panic that may be difficult

to differentiate from psychogenic panic attacks. This is especially true in cases in which there is a lesion with little mass effect and no neurologic symptoms. However, a careful history may help differentiate patients with ictal panic from those with psychogenic panic attacks.

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REFERENCES

1. Andersson PG. Intracranial tumors in a psychiatric autopsy material. *Acta Psychiatr Scand*. 1970;46(3):213–224.
2. Capwell RR, Carter R. Organic anxiety syndrome secondary to metastatic brain tumor. *Psychosomatics*. 1991;32(2):231–233.
3. Dietch JT. Cerebral tumor presenting with panic attacks. *Psychosomatics*. 1984;25(11):861–863.
4. Filley CM, Kleinschmidt-DeMasters BK. Neurobehavioral presentations of brain neoplasms. *West J Med*. 1995;163(1):19–25.
5. Hobbs GE. Brain tumours simulating psychiatric disease. *Can Med Assoc J*. 1963;88:186–188.
6. Jarquin-Valdivia AA. Psychiatric symptoms and brain tumors: a brief historical overview. *Arch Neurol*. 2004;61(11):1800–1804.
7. Kellner M, Hirschmann M, Wiedemann K. Panic attacks caused by temporal tumors: an exemplary new case and a review. *Depress Anxiety*. 1996–1997;4(5):243–245.
8. Madhusoodanan S, Danan D, Moise D. Psychiatric manifestations of brain tumors: diagnostic implications. *Expert Rev Neurother*. 2007;7(4):343–349.
9. Uribe VM. Psychiatric symptoms and brain tumor. *Am Fam Physician*. 1986;34(2):95–98.
10. Alemayehu S, Bergey GK, Barry E, et al. Panic attacks as ictal manifestations of parietal lobe seizures. *Epilepsia*. 1995;36(8):824–830.
11. Ghadirian AM, Gauthier S, Bertrand S. Anxiety attacks in a patient with a right temporal lobe meningioma. *J Clin Psychiatry*. 1986;47(5):270–271.
12. Sazgar M, Carlen PL, Wennberg R. Panic attack semiology in right temporal lobe epilepsy. *Epileptic Disord*. 2003;5(2):93–100.
13. Thompson SA, Duncan JS, Smith SJ. Partial seizures presenting as panic attacks. *BMJ*. 2000;321(7267):1002–1003.
14. Brodsky L, Zuniga JS, Casenas ER, et al. Refractory anxiety: a masked epileptiform disorder? *Psychiatr J Univ Ott*. 1983;8(1):42–45.
15. Spitz MC. Panic disorder in seizure patients: a diagnostic pitfall. *Epilepsia*. 1991;32(1):33–38.
16. Deutsch SI, Rosse RB, Sud IM, et al. Temporal lobe epilepsy confused with panic disorder: implications for treatment. *Clin Neuropharmacol*. 2009;32(3): 160–162.
17. Edlund MJ, Swann AC, Clothier J. Patients with panic attacks and abnormal EEG results. *Am J Psychiatry*. 1987;144(4):508–509.
18. Gallinat J, Stotz-Ingenlath G, Lang UE, et al. Panic attacks, spike-wave activity, and limbic dysfunction: a case report. *Pharmacopsychiatry*. 2003;36(3):123–126.
19. Laidlaw JD, Khin-Maung-Zaw. Epilepsy mistaken for panic attacks in an adolescent girl. *BMJ*. 1993;306(6879):709–710.
20. Meyer MA, Zimmerman AW, Miller CA. Temporal lobe epilepsy presenting as panic attacks: detection of interictal hypometabolism with positron emission tomography. *J Neuroimaging*. 2000;10(2):120–122.
21. Mintzer S, Lopez F. Comorbidity of ictal fear and panic disorder. *Epilepsy Behav*. 2002;3(4):330–337.
22. Wall M, Tuchman M, Mielke D. Panic attacks and temporal lobe seizures associated with a right temporal lobe arteriovenous malformation: case report. *J Clin Psychiatry*. 1985;46(4):143–145.
23. Tellez-Zenteno JF, Patten SB, Jetté N, et al. Psychiatric comorbidity in epilepsy: a population-based analysis. *Epilepsia*. 2007;48(12):2336–2344.
24. Vazquez B, Devinsky O. Epilepsy and anxiety. *Epilepsy Behav*. 2003;4(suppl 4):S20–S25.
25. Craske MG, Barlow DH. Nocturnal panic. *J Nerv Ment Dis*. 1989;177(3):160–167.
26. Kanner AM. Ictal panic and interictal panic attacks: diagnostic and therapeutic principles. *Neurol Clin*. 2011;29(1):163–175, ix.
27. Henriksen GF. Status epilepticus partialis with fear as clinical expression: report of a case and ictal EEG findings. *Epilepsia*. 1973;14(1):39–46.
28. Burke KC, Burke JD Jr, Regier DA, et al. Age at onset of selected mental disorders in five community populations. *Arch Gen Psychiatry*. 1990;47(6): 511–518.
29. Lowe NM, Eldridge P, Varma T, et al. The duration of temporal lobe epilepsy and seizure outcome after epilepsy surgery. *Seizure*. 2010;19(5):261–263.
30. Keschner M, Bender MB, Strauss I. Mental symptoms associated with brain tumor. *JAMA*. 1938;110(10):714–718.
31. Papez JW, Bateman JF. Changes in nervous tissues and study of living organisms in mental disease. *J Nerv Ment Dis*. 1951;114(5):400–412.
32. Toni C, Cassano GB, Perugi G, et al. Psychosensorial and related phenomena in panic disorder and in temporal lobe epilepsy. *Compr Psychiatry*. 1996; 37(2):125–133.
33. Craske MG, Kircanski K, Epstein A, et al; Posttraumatic and Dissociative Disorder Work Group. Panic disorder: a review of *DSM-IV* panic disorder and proposals for *DSM-V*. *Depress Anxiety*. 2010;27(2):93–112.
34. Roth M, Harper M. Temporal lobe epilepsy and the phobic anxiety-depersonalization syndrome, 2: practical and theoretical considerations. *Compr Psychiatry*. 1962;3(4):215–226.
35. Cendes F, Andermann F, Gloor P, et al. Relationship between atrophy of the amygdala and ictal fear in temporal lobe epilepsy. *Brain*. 1994;117 (pt 4):739–746.
36. Devinsky O, Sato S, Theodore WH, et al. Fear episodes due to limbic seizures with normal ictal scalp EEG: a subdural electrographic study. *J Clin Psychiatry*. 1989;50(1):28–30.
37. Fish DR, Gloor P, Quesney FL, et al. Clinical responses to electrical brain stimulation of the temporal and frontal lobes in patients with epilepsy: pathophysiological implications. *Brain*. 1993;116(pt 2):397–414.
38. Gloor P, Olivier A, Quesney LF, et al. The role of the limbic system in experiential phenomena of temporal lobe epilepsy. *Ann Neurol*. 1982;12(2): 129–144.
39. LeDoux JE, Cicchetti P, Xagoraris A, et al. The lateral amygdaloid nucleus: sensory interface of the amygdala in fear conditioning. *J Neurosci*. 1990; 10(4):1062–1069.
40. Hilz MJ, Dütsch M, Perrine K, et al. Hemispheric influence on autonomic modulation and baroreflex sensitivity. *Ann Neurol*. 2001;49(5):575–584.
41. Zamrini EY, Meador KJ, Loring DW, et al. Unilateral cerebral inactivation produces differential left/right heart rate responses. *Neurology*. 1990; 40(9):1408–1411.
42. Yoon BW, Morillo CA, Cechetto DF, et al. Cerebral hemispheric lateralization in cardiac autonomic control. *Arch Neurol*. 1997;54(6):741–744.
43. Papez JW. A proposed mechanism of emotion: 1937. *J Neuropsychiatry Clin Neurosci*. 1995;7(1):103–112.
44. Oppenheimer SM, Gelb A, Girvin JP, et al. Cardiovascular effects of human insular cortex stimulation. *Neurology*. 1992;42(9):1727–1732.
45. O'Carroll RE, Moffoot AP, Van Beck M, et al. The effect of anxiety induction on the regional uptake of 99mTc-exametazime in simple phobia as shown by single photon emission tomography (SPET). *J Affect Disord*. 1993;28(3): 203–210.
46. Reiman EM, Raichle ME, Robins E, et al. The application of positron emission tomography to the study of panic disorder. *Am J Psychiatry*. 1986;143(4):469–477.
47. Ahern GL, Sollers JJ, Lane RD, et al. Heart rate and heart rate variability changes in the intracarotid sodium amobarbital test. *Epilepsia*. 2001;42(7):912–921.
48. Daly KA, Kushner MG, Clayton PJ, et al. Seizure disorder is in the differential diagnosis of panic disorder. *Psychosomatics*. 2000;41(5):436–438.
49. Tassinari CA, Riguzzi P, Volpi L, et al. Partial seizures misdiagnosed as panic attacks: a clue to the diagnosis of symptomatic right temporal lobe epilepsy? *Epilepsia* 2000;41(suppl 7):106.
50. Weinberger DR. Brain disease and psychiatric illness: when should a psychiatrist order a CAT scan? *Am J Psychiatry*. 1984;141(12):1521–1527.