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Disease
Systematic review

Citation classics in epilepsy

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Abstract

BACKGROUND: The impact of a scientific article is proportional to the citations it has received. In this study, we set out to identify the most cited works in epileptology in order to evaluate research trends in this field. METHODS: According to the Web of Science database, articles with more than 400 citations qualify as "citation classics". We conducted a literature search on the ISI Web of Science bibliometric database for scientific articles relevant to epilepsy. RESULTS: We retrieved 67 highly cited articles (400 or more citations), which were published in 31 journals: 17 clinical studies, 42 laboratory studies, 5 reviews and 3 classification articles. Clinical studies consisted of epidemiological analyses (n=3), studies on the clinical phenomenology of epilepsy (n=5) – including behavioral and prognostic aspects – and articles focusing on pharmacological (n=6) and non-pharmacological (n=3) treatment. The laboratory studies dealt with genetics (n=6), animal models (n=27), and neurobiology (n=9) – including both neurophysiology and neuropathology studies. The majority (61%) of citation classics on epilepsy were published after 1986, possibly reflecting the expansion of research interest in laboratory studies driven by the development of new methodologies, specifically in the fields of genetics and animal models. Consequently, clinical studies were highly cited both before and after the mid 80s, whilst laboratory researches became widely cited after 1990. CONCLUSIONS: Our study indicates that the main drivers of scientific impact in the field of epileptology have increasingly become genetic and neurobiological studies, along with research on animal models of epilepsy. These articles are able to gain the highest numbers of citations in the time span of a few years and suggest potential directions for future research.

Keywords

Epilepsy; Bibliometrics; Citation classics; Impact

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Introduction

The science of bibliometrics, defined as the study and analysis of citation indexes, has led to the development of various metrics to assess the directions of rapidly evolving research fields, such as basic and clinical epileptology [1]. Bibliometric analyses have taken advantage of the availability of dedicated tools, such as the Science Citation Index, which was first developed in 1962 at the Institute of Scientific Information with the purpose of maintaining a systematic ongoing measurement of the scientific impact of research articles [2].

The purpose of this study was to identify the core works in the scientific literature on epilepsy, i.e. works that have made significant contributions and are driving or have driven the research and practice in the field of epileptology. For the scope of the present study, the impact of an article was measured as the number of citations that article has received from other scientific papers (citation count). By identifying these works, it is possible to see how the field has developed, what clinical areas have been researched most, how previous and current research has shaped our understanding of epilepsy and what directions future research is likely to take.

Methods

We conducted a literature search on the ISI Web of Science bibliometric database for scientific articles relevant to epilepsy, using the keywords "epilep*" or "seizure*" in the title. The search, which was performed on January 30, 2012, generated 95,764 articles published between January 1898 and January 2012 (the asterisk was included as a wild card character). We subsequently focused our analysis to "citation classics", which for the purpose of our study were defined as articles which received 400 or more citations [3]. This search methodology was consistent with recent works conducted in other neurological conditions (e.g. Parkinson disease [4] and Tourette syndrome [5]) and in the overall neurosurgical literature [6-8]. In the following sections, parenthetical numbers (...) refer to the rank of the relevant articles as per Table I.

Results

Sixty-seven citation classics in epilepsy were identified, spanning six decades (1946-2005). The number of citations received by the articles ranged from 402 to 3,279 (Table I).

Rank	Article	Cites
1	Racine RJ. Modification of seizure activity by electrical stimulation. 2. Motor seizure. *Electroencephalogr Clin Neurophysiol* 1972; 32: 281-94	3,279
2	Bancaud J, Henriksen O, Rubiodonnadieu F, et al. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981; 22: 489-501	1,410
3	Morgan JI, Cohen DR, Hempstead JL, et al. Mapping patterns of c-fos expression in the central nervous system after seizure. *Science* 1987; 237: 192-97	1,338
4	Ben-Ari Y. Limbic seizure and brain damage produced by kainic acid: mechanisms and relevance to human temporal lobe epilepsy. *Neuroscience* 1985; 14: 375-403	1,249
5	Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Eng J Med* 2000; 342: 314-9	1,000

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Rank	Article	Cites
6	Parent JM, Yu TW, Leibowitz RT, et al. Dentate granule cell neurogenesis is increased by seizures and contributes to aberrant network reorganization in the adult rat hippocampus. *J Neurosci* 1997; 17: 3727-38	966
7	Nibuya M, Morinobu S, Duman RS. Regulation of BDNF and TRKB mRNA in rat brain by chronic electroconvulsive seizure and antidepressant drug treatments. *J Neurosci* 1995; 15: 7539-47	962
8	Shoffner JM, Lott MT, Lezza AMS, et al. Myoclonic epilepsy and ragged-red fiber disease (MERRF) is associated with a mitochondrial-DNA transfer RNALys mutation. *Cell* 1990; 61: 931-7	919
9	Margerison JH, Corsellis JA. Epilepsy and temporal lobes. A clinical, electroencephalographic and neuropathological study of brain in epilepsy, with particular reference to temporal lobes. *Brain* 1966; 89: 499-530	827
10	Mattson RH, Cramer JA, Collins JF, et al. Comparison of carbamazepine, phenobarbital, phenytoin, and primidone in partial and secondarily generalized tonic clonic seizures.*N Eng J Med* 1985; 313: 145-51	775
11	Tanaka K, Watase K, Manabe T, et al. Epilepsy and exacerbation of brain injury in mice lacking the glutamate transporter GLT-1. *Science* 1997; 276: 1699-702	758
12a	Sloviter RS. Decreased hippocampal inhibition and selective loss of interneurons in experimental epilepsy. *Science* 1987; 235: 73-6	741
12b	Erickson JC, Clegg KE, Palmiter RD. Sensitivity to leptin and susceptibility to seizures of mice lacking neuropeptide Y. *Nature* 1996; 381: 415-8	741
14	Engel J. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. *Epilepsia* 2001; 42: 796-803	732
15	Tecott LH, Sun LM, Akana SF, et al. Eating disorder and epilepsy in mice lacking 5-HT2C serotonin receptors. *Nature* 1995; 374: 542-6	727
16	Hauser WA, Kurland LT. Epidemiology of epilepsy in Rochester, Minnesota, 1935 through 1967. *Epilepsia* 1975; 16: 1-66	724
17	Sutula T, Cascino G, Cavazos J, et al. Mossy fiber synaptic reorganization in the epileptic human temporal-lobe. *Ann Neurol* 1989; 26: 321-30	717
18	Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota- 1935-1984. *Epilepsia* 1993; 34: 453-68	706
19	Slater E, Beard AW. Schizophrenia-like psychoses of epilepsy. 1. Psychiatric aspects. *Br J Psychiatry* 1963; 109: 95-112	669
20	Wiebe S, Blume WT, Girvin JP, et al. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Eng J Med* 2001; 345: 311-8	664
21	Steinlein OK, Mulley JC, Propping P, et al. A missense mutation in the neuronal nicotinic acetylcholine-receptor alpha-4 subunit is associated with autosomal-dominant nocturnal frontal-lobe epilepsy. *Nature Genetics* 1995; 11: 201-3	622
22	Florhenr P. Psychosis and temporal lobe epilepsy – a controlled investigation. *Epilepsia* 1969; 10: 363-95	610
23	Lothman EW, Collins RC. Kainic acid-induced limbic seizures – metabolic, behavioral, electroencephalographic and neuropathological correlates. *Brain Research* 1981; 218: 299-318	597
24	Singh NA, Charlier C, Stauffer D, et al. A novel potassium channel gene, KCNQ2, is mutated in an inherited epilepsy of newborns. *Nature Genetics* 1998; 18: 25-9	587
25	Wallace RH, Wang DW, Singh R, et al. Febrile seizures and generalized epilepsy associated with a mutation in the Na+-channel beta 1 subunit gene SCN1B. *Nature Genetics* 1998; 19: 366-70	586
26	Taylor DC, Falconer MA, Bruton CJ, et al. Focal dysplasia of cerebral cortex in epilepsy. *J Neurol Neurosurg Psychiatry* 1971; 34: 369-87	581
27	Ben-Ari Y, Tremblay E, Riche D, et al. Electrographic, clinical and pathological alterations following systemic administration of kainic acid, bicuculline or pentetrazole-metabolic mapping using the deoxyglucose method with special reference to the pathology of epilepsy. *Neuroscience* 1981; 6: 1361-91	568

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Rank	Article	Cites
28	Sloviter RS. Calcium-binding protein (Calbindin-D28k) and parvalbumin immunocytochemistry-localization in the rat hippocampus with specific reference to the selective vulnerability of hippocampal-neurons to seizure activity. *J Comp Neurol* 1989; 280: 183-96	563
29	Bear DM, Fedio P. Quantitative-analysis of interictal behavior in temporal-lobe epilepsy. *Arch Neurol* 1977; 34: 454-67	561
30a	Turski WA, Cavalheiro EA, Scwarz M, et al. Limbic seizures produced by pilocarpine in rats: behavioural, electroencephalographic and neuropathological study. *Behavioural Brain Research* 1983; 9: 315-35	547
30b	Gall CM, Isackson PJ. Limbic seizures increase neuronal production of messenger-RNA for nerve growth-factor. *Science* 1989; 245: 758-61	547
32	Charlier C, Singh NA, Ryan SG, et al. A pore mutation in a novel KQT-like potassium channel gene in an idiopathic epilepsy family. *Nature Genetics* 1998; 18: 53-5	544
33	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: 129-44	536
34	de Lanerolle NC, Kim JH, Robbins RJ, et al. Hippocampal interneuron loss and plasticity in human temporal-lobe epilepsy. *Brain Research* 1989; 495: 387-95	529
35	Qian Z, Gilbert ME, Colicos MA, et al. Tissue-plasminogen activator is induced as an immediate early gene during seizure kindling and long-term potentiation. *Nature* 1993; 361: 453-7	525
36	Isackson PJ, Huntsman MM, Murray KD, et al. BDNF messenger-RNA expression is increased in adult-rat forebrain after limbic seizures: temporal patterns of induction distinct from NGF. *Neuron* 1991; 6: 937-48	521
37	Molyneux AJ, Kerr RSC, Yu LM, et al. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. *Lancet* 2005; 366: 809-17	520
38	Goddard GV. Development of epileptic seizures through brain stimulation at low intensity. *Nature* 1967; 214: 1020-1	516
39	Biervert C, Schroeder BC, Kubisch C, et al.A potassium channel mutation in neonatal human epilepsy. *Science* 1998; 279: 403-6	514
40	Ernfors P, Bengzon J, Kokaia Z, et al. Increased levels of messenger-RNAs for neurotrophic factors in the brain during kindling epileptogenesis. *Neuron* 1991; 7: 165-76	496
41	Chae T, Kwon YT, Bronson R, et al. Mice lacking p35, a neuronal specific activator of Cdk5, display cortical lamination defects, seizures, and adult lethality. *Neuron* 1997; 18: 29-42	495
42	Zwillich CW, Sutton FD, Neff TA, et al. Theophylline-induced seizures in adults: correlation with serum concentrations. *Ann Intern Med* 1975; 82: 784-7	492
43	Falconer MA, Serafetinides EA, Corsellis JAN. Etiology and pathogenesis of temporal lobe epilepsy. *Arch Neurol* 1964; 10: 233-48	481
44a	Fletcher CF, Lutz CM, OSullivan TN, et al. Absence epilepsy in tottering mutant mice is associated with calcium channel defects. *Cell* 1996; 87: 607-17	480
44b	Bengzon J, Kokaia Z, Elmer E, et al. Apoptosis and proliferation of dentate gyrus neurons after single and intermittent limbic seizures. *Proc Natl Acad Sci U S A* 1997; 94: 10432-7	480
46	Matsumoto H, Marsan CA. Cortical cellular phenomena in experimental epilepsy: interictal manifestations. *Experimental Neurology* 1964; 9: 286-304	478
47	Toman JEP, Swinyard EA, Goodman LS. Properties of maximal seizures, and their alteration by anticonvulsant drugs and other agents. *J Neurophysiol* 1946; 9: 231-9	470
48	Nadler JV. Kainic acid as a tool for the study of temporal-lobe epilepsy. *Life Sciences* 1981; 29: 2031-42	469
49	Sperk G. Kainic acid seizures in the rat. *Progress of Neurobiology* 1994; 42: 1-32	467

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Rank	Article	Cites
50	Babb TL, Kupfer WR, Pretorius JK, et al. Synaptic reorganization by mossy fibers in human epileptic fascia-dentata. *Neuroscience* 1991; 42: 351-63	465
51	Tsirka SE, Gualandris A, Amaral DG, et al. Excitotoxin-induced neuronal degeneration and seizure are mediated by tissue-plasminogen activator. *Nature* 1995; 377: 340-4	461
52	Sloviter RS. Epileptic brain-damage in rats induced by sustained electrical-stimulation of the perforant path. 1. Acute electro-physiological and light microscopic studies. *Brain Research Bulletin* 1983; 10: 675-97	457
53	Mattson RH, Cramer JA, Collins JF. A comparison of valproate with carbamazepine for the treatment of complex partial seizures and secondarily generalized tonic clonic seizures in adults. *N Eng J Med* 1992; 327: 765-71	451
54	Babloyantz A, Destexhe A. Low-dimensional chaos in an instance of epilepsy. *Proc Natl Acad Sci U S A* 1986; 83: 3513-7	444
55a	Racine RJ. Modification of seizure activity by electrical stimulation. 1. After-discharge threshold. *Electroencephalogr Clin Neurophysiol* 1972; 32: 269-79	436
55b	Engel J. Current concepts: surgery for seizures. *N Eng J Med* 1996; 334: 647-52	436
57	Brodie MJ, Richens A, Yuen AWC. Double-blinded comparison of lamotrigine and carbamazepine in newly-diagnosed epilepsy. *Lancet* 1995; 345: 476-9	427
58	During MJ, Spencer DD. Extracellular hippocampal glutamate and spontaneous seizure in the conscious human brain. *Lancet* 1993; 341: 1607-10	422
59	Sperk G, Lassmann H, Baran H, et al. Kainic acid-induced seizures: neurochemical and histopathological changes. *Neuroscience* 1983; 10: 1301-15	419
60	Houser CR, Miyashiro JE, Swartz BE, et al. Altered patterns of dynorphin immunoreactivity suggest mossy fiber reorganization in human hippocampal epilepsy. *J Neurosci* 1990; 10: 267-82	417
61	Dent CE, Richens A, Rowe DJF, et al. Osteomalacia with long-term anticonvulsant therapy in epilepsy. *BMJ* 1970; 4: 69-72	416
62	Mody I, Lambert JDC, Heinemann U. Low extracellular magnesium induces epileptiform activity and spreading depression in rat hippocampal slices. *J Neurophysiol* 1987; 57: 869-88	410
63	Woodbury LA, Davenport VD. Design and use of a new electroshock seizure apparatus, and analysis of factors altering seizure threshold and pattern. *Arch Int Pharmacodyn Ther* 1952; 92: 97-107	405
64a	Nelson KB, Ellenberg JH. Prognosis in children with febrile seizures. *Pediatrics* 1978; 61: 720-7	404
64b	Daumas-Duport C, Scheithauer BW, Chodkiewicz JP, et al. Dysembryoplastic neuroepithelial tumor: a surgically curable tumor of young patients with intractable partial seizures. Report of thirty-nine cases. *Neurosurgery* 1988; 23: 545-56	404
66	Hauser WA, Annegers JF, Kurland LT. Prevalence of epilepsy in Rochester, Minnesota 1940-1980. *Epilepsia* 1991; 32: 429-45	403
67	Dingledine R, McBain CJ, McNamara JO. Excitatory amino-acid receptors in epilepsy. *Trends in Pharmacological Sciences* 1990; 11: 334-8	402

Table I. Articles on epilepsy with more than 400 citations, ranked by number of citations received

Among the citation classics, there were 17 clinical studies, including 3 epidemiological studies, 5 studies on clinical phenomenology, 6 on pharmacological therapies, and 3 on non-pharmacological therapies. Also captured by the search were 42 laboratory studies, which included 9 articles on the neurobiology of epilepsy, 27 studies on animal models and 6 genetic studies. Finally, 5 review papers and 3 articles on the classification of epilepsy were identified (Table II).

		Clinical					Laboratory			
		Classification	Epidemiology	Phenomenology*	Pharmacological therapy	Non-pharmacological therapy	Genetics	Animal models	Neurobiology**	Review
Journal										
Total	67	3	3	5	6	3	6	27	9	5
Epilepsia	6	2	3	1	-	-	-	-	-	-
Nature	5	-	-	-	-	-	-	5	-	-
Science	5	-	-	-	-	-	1	4	-	-
N Eng J Med	5	1	-	-	2	1	-	-	-	1
Neuroscience	4	-	-	-	-	-	-	2	1	1
Nature Genet	4	-	-	-	-	-	4	-	-	-
Lancet	3	-	-	-	1	1	-	-	1	-
J Neurosci	3	-	-	-	-	-	-	2	1	-
Neuron	3	-	-	-	-	-	-	3	-	-
Cell	2	-	-	-	-	-	1	1	-	-
Brain Res	2	-	-	-	-	-	-	1	1	-
Electroencephalogr Clin Neurophysiol	2	-	-	-	-	-	-	2	-	-
J Neurophysiol	2	-	-	-	1	-	-	1	-	-
Ann Neurol	2	-	-	1	-	-	-	-	1	-
Arch Neurol	2	-	-	1	-	-	-	-	1	-
PNAS	2	-	-	-	-	-	-	1	1	-
Pediatrics	1	-	-	1	-	-	-	-	-	-
Br J Psychiatry	1	-	-	1	-	-	-	-	-	-
J Comp Neurol	1	-	-	-	-	-	-	1	-	-
Ann Int Med	1	-	-	-	1	-	-	-	-	-
Behav Brain Res	1	-	-	-	-	-	-	1	-	-
Brain	1	-	-	-	-	-	-	-	1	-
J Neurol Neurosurg Psychiatry	1	-	-	-	-	-	-	-	1	-
Exp Neurol	1	-	-	-	-	-	-	1	-	-
Brain Res Bull	1	-	-	-	-	-	-	1	-	-
Prog Neurosci	1	-	-	-	-	-	-	-	-	1
BMJ	1	-	-	-	1	-	-	-	-	-
Neurosurgery	1	-	-	-	-	1	-	-	-	-
Trends Pharmacol Sci	1	-	-	-	-	-	-	-	-	1
Archives Internationales de Pharmacodynamie et de Therapie	1	-	-	-	-	-	-	1	-	-
Life Sciences	1	-	-	-	-	-	-	-	-	1

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		Clinical					Laboratory			
		Classification	Epidemiology	Phenomenology*	Pharmacological therapy	Non-pharmacological therapy	Genetics	Animal models	Neurobiology**	Review
Year of publication										
1946-1950	1	-	-	-	1	-	-	-	-	-
1951-1955	1	-	-	-	-	-	-	1	-	-
1956-1960	0	-	-	-	-	-	-	-	-	-
1961-1965	3	-	-	1	-	-	-	1	1	-
1966-1970	4	-	-	1	1	-	-	1	1	-
1971-1975	5	-	1	-	1	-	-	2	1	-
1976-1980	2	-	-	2	-	-	-	-	-	-
1981-1985	10	1	-	1	1	-	-	5	-	2
1986-1990	12	-	-	-	-	1	1	5	4	1
1991-1995	14	-	2	-	2	-	1	6	2	1
1996-2000	12	1	-	-	-	-	4	6	-	1
2001-2005	3	1	-	-	-	2	-	-	-	-
Cites										
401-450	14	-	1	1	2	1	-	4	3	2
451-500	14	-	-	-	3	-	-	7	2	2
501-550	10	-	-	1	-	1	2	5	1	
551-600	7	-	-	1	-	-	2	3	1	-
601-650	2	-	-	1	-	-	1	-	-	-
651-700	2	-	-	1	-	1	-	-	-	-
701-750	7	1	2	-	-	-	-	3	1	-
751-800	2	-	-	-	1	-	-	1	-	-
801-900	1	-	-	-	-	-	-	-	1	-
901-1000	4	1	-	-	-	-	1	2	-	-
1001-1100	0	-	-	-	-	-	-	-	-	-
1101-1200	0	-	-	-	-	-	-	-	-	-
1201-1300	1	-	-	-	-	-	-	-	-	1
1301-1400	1	-	-	-	-	-	-	1	-	-
1401-1500	1	1	-	-	-	-	-	-	-	-
<1500	1	-	-	-	-	-	-	1	-	-

Table II. Breakdown of citation classics in epilepsy by research topics, 5-year epochs, and citation counts

* Includes behavioural aspects and prognosis

** Includes neurophysiology and neuropathology

Clinical studies

Epidemiological studies

There were three articles on epidemiological aspects of epilepsy (16, 18, 66). They were all part of the community study based in Rochester, Minnesota, USA.

Phenomenological studies

Four out of the five articles on the clinical phenomenology of epilepsy looked at behavioral aspects and psychopathology (19, 22, 29, 33), with focus on temporal lobe epilepsy. The other study explored the long-term prognosis of children with febrile seizures (64a).

Pharmacological therapy

There were six articles on medical therapies for epilepsy (10, 42, 47, 53, 57, 61). Half of them were studies comparing carbamazepine with other drugs (10, 53, 57). Of the remaining articles, one looked at the correlation between theophylline-induced seizures and serum concentration of antiepileptic drugs (42) and the other two evaluated the effects of anticonvulsant therapies (47, 61).

Non-pharmacological therapy

Among the citation classics, we identified three articles on non-pharmacological treatments for epilepsy (20, 37, 64b). One study focused on surgery for temporal-lobe epilepsy (20); one looked at the effects that neurosurgical clipping and endovascular coiling have on seizures in patients with ruptured intracranial aneurysms (37); the last one evaluated the surgical treatment of dysembryoplastic neuroepithelial tumors in patients with intractable partial seizures (64b).

Laboratory studies

Genetics

All six genetic studies were about the role of mutations in epilepsy (8, 21, 24, 25, 32, 39): three of these drew attention to the potassium channel gene (24, 32, 39), one was about the link between myoclonic epilepsy and ragged-red fiber disease and a mitochondrial-DNA transfer RNALys mutation (8); one identified the relationship between a missense mutation and autosomal-dominant nocturnal frontal-lobe epilepsy (21); the last one focused on the association between febrile seizures/generalized epilepsy and a genetic mutation affecting sodium channels (25).

Animal models

There were twenty-seven studies involving animal models of epilepsy. Eight of these mentioned the use of electrical stimulation (1, 6, 12a, 28, 35, 38, 52, 55a), with two exploring how seizure activity can be modified by electrical stimulation (1, 55a). Another study focused on the design and use of an electroshock apparatus, as well as factors altering seizure threshold and pattern (63). Two studies looked at the link between seizures and feeding behavior (12b, 15). There was one study that showed the relationship between absence epilepsy in mice and calcium channel defects (44a). Four studies focused on limbic seizures (30a, 30b, 36, 44b) with two evaluating the changes in messenger-RNA production (30b, 36), one about apoptosis and proliferation of dentate gyrus neurons (44b) and the other one investigating limbic seizures by using pilocarpine models (30a). There were two other studies focusing on messenger-RNA, including one on the regulation of BDNF and TRKB messenger-RNA in rat-brain (7), and one on messenger-RNA levels during kindling epileptogenesis (40). Four studies focused on chemically-inducing seizures (3, 27, 51, 59). Moreover, one study evaluated the different aspects of kainic acid-induced limbic seizures (23) and another drew attention to extracellular magnesium and its association with epileptiform activity and spreading depression in rats (62). Finally, two studies looked at epilepsy at a cortical cellular level (41, 46), and one study concentrated on epilepsy and brain injury in mice lacking a glutamate transporter (11).

Neurobiology

Nine studies investigated the neurobiological aspects of epilepsy, including both neuropathology (9, 17, 26, 34, 43, 50, 58, 60) and neurophysiology (9, 54) approaches.

Review articles

Five reviews were identified (4, 48, 49, 55b, 67), with two of these referring to both kainic acid and temporal-lobe epilepsy (4, 48). Other reviewed topics included kainic acid seizures in the rat model (49), epilepsy surgery (55b) and excitatory amino-acid receptors in epilepsy (67).

Classification articles

We found three articles on the classification of epilepsy (2, 5, 14). This includes one about the identification of refractory epilepsy (5). Of the remaining two, one evaluated a proposed diagnostic scheme for people with epilepsy (14) and the other refers to a proposal for a revised classification of epilepsy (2).

Journals and years of publication

As seen in Table III, the journals were ranked using the ISI Journal Citation Reports 2010 Journal Impact Factor (JIF) in order to explore when and where the highest cited articles on epilepsy were published, and to ascertain whether there was a link between journals and article types.

According to Table IV, the highest impact journals were those with a JIF > 21.95, i.e. those that were in the top 1% of a rank of 821 journals in the subject categories of Behavioral sciences, Clinical neurology, Medicine: general and internal, Medicine: research and experimental, Multidisciplinary sciences, Neurological sciences, Psychiatry and Psychology. The journals in the top 10% of this rank (JIF 5.20-21.95) were classed as high impact, whilst the journals in the top 33% (JIF 2.70-5.20) were classed as medium impact. Using this classification, we found that 24 articles appeared in the highest impact journals, 19 in the high impact journals, 19 in the medium impact journals and 5 in journals with JIF below 2.70. There was a broad range of publication years from 1946-2005, with only 21% of the articles appearing before 1976, 18% appearing from 1976 to 1985, 39% appearing from 1986 to 1995 and 22% appearing after 1996. The majority of articles (56%) were published between 1986 and 2000.

Journal	Articles	JIF (2010)
N Eng J Med	5	53.48
Nature Genet	4	36.38
Nature	5	36.10
Lancet	3	33.63
Cell	2	32.40
Science	5	31.38
Ann Intern Med	1	16.73
Neuron	3	14.03
BMJ	1	13.47
Trends Pharmacol Sci	1	11.05
Ann Neurol	2	10.75
Prog Neurobiol	1	9.97
PNAS	2	9.77
Brain	1	9.23
J Neurosci	3	7.27
Arch Neurol	2	7.11
Br J Psychiatry	1	5.95
Pediatrics	1	5.39
J Neurol Neurosurg Psychiatry	1	4.79
Exp Neurol	1	4.44
Epilepsia	6	3.96
J Comp Neurol	1	3.77
Behav Brain Res	1	3.39
Neurosurgery	1	3.30
Neuroscience	4	3.22
J Neurophysiol	2	3.11
Electroencephalogr Clin Neurophysiol	2	2.79
Brain Res	2	2.62
Brain Res Bull	1	2.50
Life Sciences	1	2.45
Archives Internationales de Pharmacodynamie et de Therapie	1	0.77

Table III. Journals in which citation classics on epilepsy were published, with 2010 impact factors (JIF, source: ISI Journal Citation Reports)

	JIF < 2.70	JIF=2.70-5.20	JIF=5.21-21.95	JIF > 21.95	Total
Year of publication					
Total articles	5	19	19	24	67
1946-1950	-	1	-	-	1
1951-1955	1	-	-	-	1
1956-1960	-	-	-	-	0
1961-1965	-	1	2	-	3
1966-1970	-	1	2	1	4
1971-1975	-	4	1	-	5
1976-1980	-	-	2	-	2
1981-1985	3	5	1	1	10
1986-1990	1	3	4	4	12
1991-1995	-	3	4	7	14
1996-2000	-	-	3	9	12
2001-2005	-	1	-	2	3
Type of study					
Classification	-	2	-	1	3
Clinical: epidemiology	-	3	-	-	3
Clinical: phenomenology*	-	1	4	-	5
Clinical: pharmacological therapy	-	1	2	3	6
Clinical: non-pharmacological therapy	-	1	-	2	3
Lab: genetics	-	-	-	6	6
Lab: animal models	3	8	6	10	27
Lab: neurobiology**	1	2	5	1	9
Reviews	1	1	2	1	5
Cites					
401-450	1	5	5	3	14
451-500	2	3	6	3	14
501-550	1	1	2	6	10
551-600	1	3	1	2	7
601-650	-	1	-	1	2
651-700	-	-	1	1	2
701-750	-	3	1	3	7
751-800	-	-	-	2	2
801-900	-	-	1	-	1
901-1000	-	-	2	2	4
1001-1100	-	-	-	-	0
1101-1200	-	-	-	-	0
1201-1300	-	1	-	-	1
1301-1400	-	-	-	1	1
1401-1500	-	1	-	-	1
>1500	-	1	-	-	1

Table IV. Year of publication, topic and number of citations of the epilepsy citation classics as related to impact of journal (2010 JIF, from ISI Citation Reports. JIF > 21.95 corresponds to top 1%, JIF 5.20-21.95 corresponds to the top 10% excluding the top 1% and JIF 2.70-5.20 corresponds to the top 33% excluding the top 10%)

* Includes behavioral aspects and prognosis

** Includes neurophysiology and neuropathology

Clinical studies

Epilepsia, the *New England Journal of Medicine* and *Lancet* accounted for 53% of all clinical studies captured by the search. It is worth noting that these three journals, together with *Nature*, *Science*, *Nature Genetics*, *Cell*, the *Annals of Internal medicine* and *Neuron* – all journals that have an impact factor greater than 14.00 – accounted for 42% of all the citations classics. *Epilepsia* and the *New England Journal of Medicine* published 41% of all clinical studies. The three articles on the epidemiological aspects of epilepsy were all published by *Epilepsia*. A third of the articles regarding both pharmacological and non-pharmacological therapy were published by the *New England Journal of Medicine*. Significantly, all the phenomenological studies appeared between 1963 and 1988; the two thirds of the articles on pharmacological therapy appeared between 1946 and 1985; whilst all the three studies captured by the search on non-pharmacological therapy (focusing on sophisticated neurosurgical techniques) appeared in journals in 1988, 2001, and 2005.

Laboratory studies

Nature Genetics, Science and *Nature* published a third of all laboratory studies. *Nature Genetics* published 67% of all genetics studies. *Nature* and *Science* published 33% of animal model studies, with 5 articles for *Nature* and 4 articles for *Science*, respectively. Papers in the Neurobiology category were equally distributed between journals and published from 1964 to 1993. All six genetics studies appeared after 1990 and, in particular, four in 1998. The largest number of articles regarding animal models were published between 1981 and 1997, specifically 10 in the 80s and 12 in the 90s, accounting for 81% of all the articles published on this topic and reflecting the surge of interest in animal models during the last two decades of the past century. We did not find, however, any citation classics in this field after 1997, even though they represent 64% of all laboratory studies.

Review articles

Neuroscience published the first most cited article among reviews and the fourth most cited article of all citation classics. The five reviews found in our search appeared from 1981 to 1996.

Classification articles

Epilepsia published two out of the three articles that were captured and the one that holds the second rank in our search. The other article one was published by the *New England Journal of Medicine*. Two papers appeared fairly recently, in 2000 and 2001. The most cited paper, however, was published in 1981.

Discussion

According to our study, the most highly cited articles on epilepsy dealt with animal models (electrical stimulation, chemically-induced seizures, the relationship between seizures and feeding behavior, the regulation of BDNF and TRKB messenger-RNA in the rat brain, etc.), classification of epileptic seizures and identification of refractory epilepsies, a review about limbic seizure and brain damage produced by kainic acid, genetic and neurobiological studies. As a top article in our rank we found a study using an animal model to explore how seizure activity can be modified by electrical stimulation.

Sources of the citation classics

The 67 articles captured by our search appeared in 31 different journals. Six journals published more than 4 highly cited articles each: *Epilepsia* (n=6), the *New England Journal of Medicine* (n=5), *Nature* (n=5), *Science* (n=5), *Nature Genetics* (n=4), *Neuroscience* (n=4), accounting for the 43% of all the citation classics. About half (48%) of all articles were published in journals with a JIF > 10.00; 17% in jour-

nal with a JIF between 9.97 and 5.39; 25% in journal with a JIF between 4.79 and 3.11; 10% in journal with a JIF between 2.79 and 0.77.

Among the top ten articles in our rank, two were published in the journal with the highest impact factor (JIF=53.48), one in a journal with JIF=32.40, two in a journal with JIF=31.38, one in a journal with JIF=9.23, one in a journal with JIF=7.27, one in a journal with JIF=3.96, one in a journal with JIF=3.22, and one in a journal with JIF=2.79. However, the two most cited articles were published in journals with JIF=2.79 and JIF=3.96, respectively. This shows that although the JIF is certainly an important element to consider when looking for citation classics, it may not be the most significant determinant for the number of citations an article receives. Moreover, the JIF of a journal can vary with time, so that articles published years or decades ago might have originally been associated with a different JIF.

Highlights of high impact work by publication eras

The results of our search show the temporal progression of research into epilepsy, with different areas being prominent in different eras. The majority of all citation classics (56%) were published between 1986 and 2000. The earliest article identified as a citation classic evaluated the effects of anticonvulsant drugs and was published in 1946. The most recent article appeared in 2005 and dealt with the effects of neurosurgical clipping and endovascular coiling on seizures in patients with ruptured intracranial aneurysms. The numbers of publications on clinical studies have remained relatively stable throughout the periods taken into consideration for the search. In contrast, with regard to the laboratory studies, a peak was found in genetic research during the 90s and in studies using animal models during the 80s and the 90s.

Comparison with other studies on citation classics in epilepsy

Our study on citations classics in epilepsy produced different results compared to another study recently published on the same topic [9]. The study by Ibrahim et al. [9] identified 89 articles which received 400 or more citations, 22 more articles than the 67 retrieved in our search. The majority of citations classics identified by us were also present in the study conducted by Ibrahim et al. [9]. Articles do not have, however, the same rank positions because of different results in the number of citations. In fact, in the study by Ibrahim et al. [9] most of these articles received a higher number of citations than we found. In addition, we captured 11 articles (i.e. 2, 37, 40, 42, 47, 52, 53, 61, 62, 63, 64b) that were not present in the list of citations classics obtained by Ibrahim et al. [9]. The comparison of these data is shown in Table V.

Rank	Rank Ibr	Article	Cites	Cites Ibr
1	1	Racine RJ. Modification of seizure activity by electrical stimulation.2. motor seizure. *Electroencephalogr Clin Neurophysiol* 1972; 32: 281-94	3,279	3,749
2		Bancaud J, Henriksen O, Rubiodonnadieu F, et al. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981; 22: 489-501	1,410	
3	4	Morgan JI, Cohen DR, Hempstead JL, et al. Mapping patterns of c-fos expression in the central-nervous-system after seizure. *Science* 1987; 237: 192-7	1,338	1,303
4	3	Ben-Ari Y. Limbic seizure and brain- damage produced by kainic acid-mechanisms and relevance to human temporal-lobe epilepsy. *Neuroscience* 1985; 14: 375-403	1,249	1,351
5	2	Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Eng J Med* 2000; 342: 314-9	1,000	1,419

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Rank	Rank Ibr	Article	Cites	Cites Ibr
6	6	Parent JM, Yu TW, Leibowitz RT, et al. Dentate granule cell neurogenesis is increased by seizures and contributes to aberrant network reorganization in the adult rat hippocampus. *J Neurosci* 1997; 17: 3727-38	966	1,162
7	5	Nibuya M, Morinobu S, Duman RS. Regulation of BDNF and TRKB messenger-RNA in rat-brain by chronic electroconvulsive seizure and antidepressant drug treatments.*J Neurosci* 1995; 15: 7539-47	962	1,193
8	9	Shoffner JM, Lott MT, Lezza AMS, et al. Myoclonic epilepsy and ragged-red fiber disease (MERRF) is associated with a mitochondrial-DNA transfer RNALys mutation. *Cell* 1990; 61: 931-7	919	961
9	14	Margerison JH, Corsellis JA. Epilepsy and temporal lobes. A clinical, electroencephalographic and neuropathological study of brain in epilepsy, with particular reference to temporal lobes. *Brain* 1966; 89: 499-530	827	822
10	15	Mattson RH, Cramer JA, Collins JF, et al. Comparison of carbamazepine, phenobarbital, phenytoin, and primidone in partial and secondarily generalized tonic clonic seizures. *N Eng J Med* 1985; 313: 145-51	775	821
11	12	Tanaka K, Watase K, Manabe T, et al. Epilepsy and exacerbation of brain injury in mice lacking the glutamate transporter GLT-1. *Science* 1997; 276: 1699-702	758	848
12a	19	Sloviter RS. Decreased hippocampal inhibition and selective loss of interneurons in experimental epilepsy. *Science* 1987; 235: 73-6	741	729
12b	16	Erickson JC, Clegg KE, Palmiter RD. Sensitivity to leptin and susceptibility to seizures of mice lacking neuropeptide Y. *Nature* 1996; 381: 415-8	741	806
14	7	Engel J. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: Report of the ILAE Task Force on Classification and Terminology. *Epilepsia* 2001; 42: 796-803	732	1,123
15	13	Tecott LH, Sun LM, Akana SF, et al. Eating disorder and epilepsy in mice lacking 5-HT2C serotonin receptors. *Nature* 1995; 374: 542-6	727	827
16	11	Hauser WA, Kurland LT. Epidemiology of epilepsy in Rochester, Minnesota, 1935 through 1967. *Epilepsia* 1975; 16: 1-66	724	854
17	23	Sutula T, Cascino G; Cavazos J, et al. Mossy fiber synaptic reorganization in the epileptic human temporal-lobe. *Ann Neurol* 1989; 26: 321-30	717	708
18	8	Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota- 1935-1984. *Epilepsia* 1993; 34: 453-68	706	996
19	21	Slater E, Beard AW. Schizophrenia-like psychoses of epilepsy. 1. Psychiatric aspects. *Br J Psychiatry* 1963; 109: 95-112	669	722
20	10	Wiebe S, Blume WT, Girvin JP, et al. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Eng J Med* 2001; 345: 311-8	664	911
21	20	Steinlein OK, Mulley JC, Propping P, et al. A missense mutation in the neuronal nicotinic acetylcholine-receptor alpha-4 subunit is associated with autosomal-dominant nocturnal frontal-lobe epilepsy. *Nature Genetics* 1995; 11: 201-3	622	724
22	25	Florhenr P. Psychosis and temporal lobe epilepsy- a controlled investigation. *Epilepsia* 1969; 10: 363-95	610	665
23	31b	Lothman EW, Collins RC. Kainic acid-induced limbic seizures – metabolic, behavioral, electroencephalographic and neuropathological correlates. *Brain Research* 1981; 218: 299-318	597	599
24	22	Singh NA, Charlier C, Stauffer D, et al. A novel potassium channel gene, KCNQ2, is mutated in an inherited epilepsy of newborns. *Nature Genetics* 1998; 18: 25-9	587	717

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Rank	Rank Ibr	Article	Cites	Cites Ibr
25	17	Wallace RH, Wang DW, Singh R, et al. Febrile seizures and generalized epilepsy associated with a mutation in the Na+-channel beta 1 subunit gene SCN1B. *Nature Genetics* 1998; 19: 366-70	586	780
26	30	Taylor DC, Falconer MA, Bruton CJ, et al. Focal dysplasia of cerebral cortex in epilepsy. *J Neurol Neurosurg Psychiatry* 1971; 34: 369-87	581	602
27	33a	Ben-Ari Y, Tremblay E, Riche D, et al. Electrographic, clinical and pathological alterations following systemic administration of kainic acid, bicuculline or pentetrazole- metabolic mapping using the deoxyglucose method with special reference to the pathology of epilepsy. *Neuroscience* 1981; 6: 1361-91	568	577
28	42c	Sloviter RS. Calcium-binding protein (Calbindin-D28k) and parvalbumin immunocytochemistry- localization in the rat hippocampus with specific reference to the selective vulnerability of hippocampal-neurons to seizure activity. *J Comp Neurol* 1989; 280: 183-96	563	525
29	18	Bear DM, Fedio P. Quantitative-analysis of interictal behavior in temporal-lobe epilepsy. *Arch Neurol* 1977; 34: 454-67	561	754
30a	28	Turski WA, Cavalheiro EA, Scwarz M, et al. Limbic seizures produced by pilocarpine in rats- behavioural, electroencephalographic and neuropathological study. *Behavioural Brain Research* 1983; 9: 315-35	547	610
30b	38	Gall CM, Isackson PJ. Limbic seizures increase neuronal production of messenger-RNA for nerve growth-factor. *Science* 1989; 245: 758-61	547	554
32	27	Charlier C, Singh NA, Ryan SG, et al. A pore mutation in a novel KQT-like potassium channel gene in an idiopathic epilepsy family. *Nature Genetics* 1998; 18: 53-5	544	655
33	35	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: 129-44	536	576
34	53	de Lanerolle NC, Kim JH, Robbins RJ, et al. Hippocampal interneuron loss and plasticity in human temporal-lobe epilepsy. *Brain Research* 1989; 495: 387-395	529	506
35	33b	Qian Z, Gilbert ME, Colicos MA, et al. Tissue-plasminogen activator is induced as an immediate early gene during seizure kindling and long-term potentiation. *Nature* 1993; 361: 453-7	525	577
36	50	Isackson PJ, Huntsman MM, Murray KD, et al. BDNF messenger-RNA expression is increased in adult-rat forebrain after limbic seizures- temporal patterns of induction distinct from NGF. *Neuron* 1991; 6: 937-48	521	519
37		Molyneux AJ, Kerr RSC, Yu LM, et al. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. *Lancet* 2005; 366: 809-17	520	
38	31a	Goddard GV. Development of epileptic seizures through brain stimulation at low intensity. *Nature* 1967; 214: 1020-1	516	599
39	24	Biervert C, Schroeder BC, Kubisch C, et al.A potassium channel mutation in neonatal human epilepsy. *Science* 1998; 279: 403-6	514	684
40		Ernfors P, Bengzon J, Kokaia Z, et al. Increased levels of messenger-RNAs for neurotrophic factors in the brain during kindling epileptogenesis. *Neuron* 1991; 7: 165-76	496	
41	47	Chae T, Kwon YT, Bronson R, et al. Mice lacking p35, a neuronal specific activator of Cdk5, display cortical lamination defects, seizures, and adult lethality. *Neuron* 1997; 18: 29-42	495	523

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Rank	Rank Ibr	Article	Cites	Cites Ibr
42		Zwillich CW, Sutton FD, Neff TA, et al. Theophylline-induced seizures in adults – correlation with serum concentrations. *Ann Intern Med* 1975; 82: 784-7	492	
43	40	Falconer MA, Serafetinides EA, Corsellis JAN. Etiology and pathogenesis of temporal lobe epilepsy. *Arch Neurol* 1964; 10: 233-48	481	535
44a	41	Fletcher CF, Lutz CM, OSullivan TN, et al. Absence epilepsy in tottering mutant mice is associated with calcium channel defects. *Cell* 1996; 87: 607-17	480	534
44b	37	Bengzon J, Kokaia Z, Elmer E, et al. Apoptosis and proliferation of dentate gyrus neurons after single and intermittent limbic seizures. *Proc Natl Acad Sci U S A* 1997; 94: 10432-7	480	558
46	75	Matsumoto H, Marsan CA. Cortical cellular phenomena in experimental epilepsy- interictal manifestations. *Experimental Neurology* 1964; 9: 286-304	478	439
47		Toman JEP, Swinyard EA, Goodman LS. Properties of maximal seizures, and their alteration by anticonvulsant drugs and other agents. *J Neurophysiol* 1946; 9: 231-9	470	
48	71	Nadler JV. Kainic acid as a tool for the study of temporal-lobe epilepsy. *Life Sciences* 1981; 29: 2031-42	469	452
49	45b	Sperk G. Kainic acid seizures in the rat. *Progress of Neurobiology* 1994; 42: 1-32	467	524
50	55	Babb TL, Kupfer WR, Pretorius JK, et al. Synaptic reorganization by mossy fibers in human epileptic fascia-dentata. *Neuroscience* 1991; 42: 351-63	465	499
51	48a	Tsirka SE, Gualandris A, Amaral DG, et al. Excitotoxin-induced neuronal degeneration and seizure are mediated by tissue-plasminogen activator. *Nature* 1995; 377: 340-4	461	520
52		Sloviter RS. Epileptic brain-damage in rats induced by sustained electrical-stimulation of the perforant path.1. acute electro-physiological and light microscopic studies. *Brain Research Bulletin* 1983; 10: 675-97	457	
53		Mattson RH, Cramer JA, Collins JF. A comparison of valproate with carbamazepine for the treatment of complex partial seizures and secondarily generalized tonic clonic seizures in adults. *N Eng J Med* 1992; 327: 765-71	451	
54	26	Babloyantz A, Destexhe A. Low-dimensional chaos in an instance of epilepsy. *Proc Natl Acad Sci U S A* 1986; 83: 3513-7	444	660
55a	70	Racine RJ. Modification of seizure activity by electrical stimulation. 1. After-discharge threshold. *Electroencephalogr Clin Neurophysiol* 1972; 32: 269-79	436	456
55b	39	Engel J. Current concepts – surgery for seizures. *N Eng J Med* 1996; 334: 647-52	436	538
57	60c	Brodie MJ, Richens A, Yuen AWC. Double-blinded comparison of lamotrigine and carbamazepine in newly-diagnosed epilepsy. *Lancet* 1995; 345: 476-9	427	483
58	60b	During MJ, Spencer DD. Extracellular hippocampal glutamate and spontaneous seizure in the conscious human brain. *Lancet* 1993; 341: 1607-10	422	483
59	87	Sperk G, Lassmann H, Baran H, et al. Kainic acid-induced seizures-neurochemical and histopathological changes. *Neuroscience* 1983; 10: 1301-15	419	411
60	85	Houser CR, Miyashiro JE, Swartz BE, et al. Altered patterns of dynorphin immunoreactivity suggest mossy fiber reorganization in human hippocampal epilepsy. *J Neurosci* 1990; 10: 267-82	417	415

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Rank	Rank Ibr	Article	Cites	Cites Ibr
61		Dent CE, Richens A, Rowe DJF, et al. Osteomalacia with long-term anticonvulsant therapy in epilepsy. *BMJ* 1970; 4: 69-72	416	
62		Mody I, Lambert JDC, Heinemann U. Low extracellular magnesium induces epileptiform activity and spreading depression in rat hippocampal slices. *J Neurophysiol* 1987; 57: 869-88	410	
63		Woodbury LA, Davenport VD. Design and use of a new electroshock seizure apparatus, and analysis of factors altering seizure threshold and pattern. *Arch Int Pharmacodyn Ther* 1952; 92: 97-107	405	
64a	57	Nelson KB, Ellenberg JH. Prognosis in children with febrile seizures. *Pediatrics* 1978; 61: 720-7	404	493
64b		Daumasduport C, Scheithauser BW, Chodkiewicz JP, et al. Dysembryoplastic neuroepithelial tumor- a surgically curable tumor of young patients with intractable partial seizures- report of 39 cases. *Neurosurgery* 1988; 23: 545-56	404	
66	56	Hauser WA, Annegers JF, Kurland LT. Prevalence of epilepsy in Rochester, Minnesota 1940-1980. *Epilepsia* 1991; 32: 429-45	403	497
67	83a	Dingledine R, McBain CJ, McNamara JO. Excitatory amino-acid receptors in epilepsy. *Trends in Pharmacological Sciences* 1990; 11: 334-8	402	421

Table V. Articles on epilepsy with more than 400 citations, ranked by number of citations received – Comparison with Ibrahim et al, 2012 data (Ibr) [9]

The differences shown in Table V – especially the discrepancies in the citations number – cannot be explained by the different time of search. In fact, in the study by Ibrahim et al. [9] the search engine was accessed in November 2011, whilst in our study it was accessed in January 2012. Both searches were, therefore, carried out around the same time. Furthermore, having accessed the search engine after Ibrahim et al. [9] we should expect a higher number of citations for the same studies, but, as shown in Table V, this was not the case. In contrast, we were able to capture less citations for most articles (e.g. 1, 4, 5, 6, 7, 8, 10, 11, 12b, 14, 15, 16, 18, 19, 20, 21, 22, etc.) than Ibrahim et al. [9] did.

The differences in the two studies are likely to result from the use of two different search engines. In fact, our search was conducted on the ISI Web of Science bibliometric database, whereas Ibrahim et al. [9] used Harzing's Publish or Perish, an internet-based search engine which employs Google Scholar data to calculate its statistics. In a large-scale comparison between different search engines (i.e. Web of Science, Scopus, and Google Scholar) it was found that Google Scholar can produce more than twice as many citations as Web of Science [10]. On the other hand, Web of Science includes exclusively citations to journal articles published in ISI listed journal. Consequently, Google Scholar appears to be a more powerful engine to retrieve citations of books, book chapters, dissertations, theses, reports, conference papers, and articles published in non-ISI journal. On the contrary, Google Scholar can find less than half of the citations of the Web of Science for specific articles mostly published in scientific disciplines [11]. Moreover, Web of Science performs significantly better than Google Scholar in covering citations to articles published before 1990 [12]. In effect, 8 out of the 11 articles which we found to have more than 400 citations but were not included in citations classics by Ibrahim et al. [9] were published before 1990.

Limitations

We used a simple and reproducible methodology, following previous work on citation classics in Parkinson's disease [4] and Tourette syndrome [5]. We restricted our search strategy to articles that have

"epilep*" or "seizure*" in the title, thus potentially leading to omission of articles without either of these terms in the title, but still relevant to epilepsy. On the other hand, topic-based searches were less likely to give articles that were directly related to epilepsy as opposed to a title-based search.

Conclusions

Using a simple but systematic literature search methodology, we identified 67 articles on different aspects of epilepsy, each with at least 400 citations. These citation classics have been published in 31 scientific journals over a time span of five decades. The classification and evaluation of these articles have yielded insights into the past, present and possibly future directions of research into epilepsy. So far, the dynamic rank of the citation classics has been dominated by clinical and laboratory studies, with recent emphasis on the genetics and animal models of epilepsy. The relatively high rate of citations these articles have received in the span of a small number of years suggests that in the years to come the scientific literature on epilepsy will focus on new insights into the pathophysiology of this condition.

The review in brief	
Aim	To identify works that have made significant contributions and are driving or have driven the research and practice in the field of epileptology
Type of review	Systematic
Search of the literature	We conducted a literature search on the ISI Web of Science bibliometric database for scientific articles relevant to epilepsy, using the keywords "epilep*" or "seizure*" in the title
Conclusions	We identified 67 articles on different aspects of epilepsy, each with at least 400 citations, published in 31 scientific journals over a time span of five decades. The classification and evaluation of these articles have yielded insights into the past, present and possibly future directions of research into epilepsy
Limitations	We restricted our search strategy to articles that have "epilep*" or "seizure*" in the title, thus potentially leading to omission of articles without either of these terms in the title, but still relevant to epilepsy

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