Encouraging a Generation of Tremor Researchers: Macdonald Critchley’s Paper on Essential Tremor

Critchley M. Observations on essential (heredofamilial) tremor. Brain 1949;72(Pt. 2):113–139.

Our choice for the most influential and important contribution of the second half of the last century about essential tremor (ET) is Professor Macdonald Critchley’s paper published 1949 in Brain on “Observations on essential (heredofamilial) tremor”.

The simple reason is that it summarizes for the first time the clinical presentation of this very common condition and discusses the related contemporary knowledge. Thereby, he has laid the foundation for clinical tremor research starting in the 1970-ies of the last century.

Macdonald Critchley (1900–1997) has been the prototype of a British Neurology Professor of the past century (Fig. 1). Andrew Lees, one of his pupils at Queen Square Hospital in London, described him as “ascetic yet charismatic, tall and always impeccably dressed” and that alcohol withdrawal can worsen tremor. The pharmacological effect of alcohol on GABA-receptors as the pathophysiological background was unclear at that time. The publication describes the great influence of external factors such as fatigue or extreme temperatures on tremor severity as well as the ability of some patients to temporarily check tremor...” and that alcohol withdrawal can worsen tremor. The pharmacological effect of alcohol on GABA-receptors as the pathophysiological background was unclear at that time. The publication describes the great influence of external factors such as fatigue or extreme temperatures on tremor severity as well as the ability of some patients to temporarily check tremor...”

Interestingly, Critchley separates essential tremor into mild high frequency tremor (resembling thyrotoxic or psychogenic tremor), medium frequency tremor (resembling Parkinsonian tremor) and even low-frequency intention tremor. Charles D. Marsden later adapted this subdivision into his clinical classification of the variants of essential tremor which is nowadays no longer used.

With regard to additional signs and symptoms, Critchley did not yet separate essential from other forms of tremor including dystonic tremor but described many subtle accompanying symptoms including that alcohol withdrawal can worsen tremor. The pharmacological effect of alcohol on GABA-receptors as the pathophysiological background was unclear at that time. The publication describes the great influence of external factors such as fatigue or extreme temperatures on tremor severity as well as the ability of some patients to temporarily check tremor...”

*Correspondence to: Prof. Dr. Günther Deuschl, Department of Neurology, Christian-Albrechts-University, Arnold-Heller-Straße 3, 24105 Kiel, Germany; E-mail: g.deuschl@neurologie.uni-kiel.de

[The copyright line for this article was changed on 26 October 2021, after original online publication.]

IN FOCUS ON: Critchley M. Observations on essential (heredofamilial) tremor. Brain 1949;72(Pt. 2):113–139.
symptoms in patients with ET and introduced them as "other involuntary movements" like choreiform contractions of the face or head or facial twitching. Nowadays, these particular soft signs are frequently recognized within the context of the special syndrome ETplus. Despite the frequent misunderstanding of this novel concept (ETplus) as a disease entity instead of a syndrome, these signs and symptoms have regained scientific interest as they may indicate special variants with possibly different disease courses and various underlying etiologies. Interestingly, the notion that ET can develop into another disorder (e.g., Parkinson’s) was already propagated by Critchley.

The paper does not explicitly mention non-motor symptoms as part of the clinical presentation of ET, but extensively quotes other neurologists who reported that ET-patients are often clinically presenting with a névrose trémulante (C. Achard) or psychiatric degeneration associated with a neuropathic stock (F. Raymond). Pelnar believed that ET-patients were characterized by irritability, anxiety, shyness eccentricity, irresolution and other neurotic, hysterical and psychotic traits. Nowadays, we can only speculate that these figurative descriptions are summarizing the average personality profile of ET-patients which has more recently been captured in recent studies as a tender-minded and harm-avoiding behavior. This symptom complex is nowadays mostly interpreted as a consequence of slight cerebellar abnormalities in ET and is currently discussed as the cerebellar cognitive affective syndrome.

Regarding etiology, Critchley’s paper nicely describes the obvious hereditary nature of ET with dominant inheritance pattern. Interestingly, the "phenomenon of anticipation" is proposed for ET meaning that the condition manifests earlier in life of every successive generation—a finding which has not been confirmed by modern genetics. With the rise of genetic sciences at the end of the last century there was a clear hope that the mystery of the origin of ET will be lifted in short time. Meanwhile, experts are struck by the lack of positive genetic findings despite intense research.

Regarding pathology, inconsistencies are reported with some cases of basal ganglia or cerebellar abnormalities but normal findings in most other cases. Critchley therefore concluded "that it cannot be claimed that our knowledge of the pathology … is much advanced…". It remains somewhat frustrating that this conclusion has not changed substantially until today: Current pathological studies are controversial as one group found a Purkinje-cell loss in the cerebellum which could not be reproduced by two other groups. Critchley’s considerations on the "nature" of essential tremor are of particular interest. He initiates the discussion by putting ET into an almost philosophical perspective: “A life-long monosymptomatic affection can scarcely be regarded as falling within the province of a morbid entity, any more than any other inborn and inherited peculiarity of physique or coloring and elsewhere "In its nature as a constitutional monosymptomatic peculiarity it can scarcely be regarded as a "disease" and some medical men may never have been confronted with an example.' This view is true in the sense that most patients with ET do not seek the help of physicians as observed in cross-sectional studies. But on the other hand, a significant proportion of these patients do have a severe handicap and benefit medical or even neurosurgical interventions.

At Critchley’s time two pathogenetic interpretations of the condition were proposed. Lazar S. Minor (Vilnius/Moscow (Paris/Berlin, 1855–1942), proposed that ET is characterized by a "status macrobioticus multiparus," a triad of tremor, longevity and fecundity, which he observed in his patients. Critchley was not convinced and discussed the controversial literature. Since then, there are two studies reporting that ET families and early-onset ET patients have a longer life expectancy but larger series are lacking. On the contrary, several studies have shown on group level that at least elderly...
ET-patients suffer from more cognitive deficits than controls. Those are usually mild and the profile of their dementia may be related to the cerebellar disturbance which was suggested first for motor symptoms of ET and later for cognitive disturbances presumably corresponding to the "cognitive affective syndrome" of Schmahmann. Today, essential tremor is sometimes referred to as a "neurodegenerative disease" and is put on par with Alzheimer’s or Parkinson’s disease. Given the obviously different course of these conditions and the lack of consented data, Critchley would certainly have been skeptical of such interpretations.

On the contrary, Critchley discussed the concept of ET as “a degenerative disorder associated with a neuropathic family taint.” This is not corresponding to our present understanding of neurodegeneration but meant the occurrence of other neuropsychiatric signs and symptoms in the patients and their families like the occurrence of "nervousness," "anxiety states," "epilepsies" which were believed to be hereditary until the 1950-ies. In his figurative language he considered ET as an “instance of an unmasking of an inherent property of neurocellular activity, as the result of some constitutional defect in the usual controlling mechanism.” The pathogenesis was thereby interpreted as a loss of a control mechanism. Despite the common complaint of tremor he did clearly separate Parkinson’s disease from ET.

This brief summary of Critchley’s contribution shows how much was already known about this mysterious syndrome in 1950. His merit was a brilliant summary of the knowledge until then. We also can see how much has been added since then. PubMed teaches us that since 1950 more than 2500 papers have been published on ET and fundamental additions have been made in the past 70 years. When reading it carefully it reminds us of core questions for this syndrome which should guide our research.

Acknowledgments

We thank the National Hospital Archives for allowing us to reproduce the painting of M. Critchley. Open Access funding enabled and organized by Projekt DEAL.

Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the first draft, B. Review and Critique.

F.B.: 1A, 1B, 3A
C.R.B.: 1A, 3B
A.L.: 1C, 3B
G.D.: 1A, 1B, 1C, 3B

Disclosures

Ethical Compliance Statement: This work did not require the approval of an institutional review board or informed patient consent. The author confirms that he has read the Journal’s position on issues involved in ethical publication and affirms that this work is consistent with those guidelines.

Funding Sources and Conflicts of Interest: No specific funding was received for this work. The authors have no conflicts of interest relevant to this work.

Financial Disclosures for the Previous 12 Months: FB and CRB report no conflicts of interest. GD reports personal fees from Boston Scientific, Cavion, Aleva, Functional Neuronmodulation and Thieme publishers.

Fabian Buechele MD,1 Christian R. Baumann MD, PhD,1,6
Andrew Lees MD, PhD,2 Günther Deuschl MD, PhD1,3
1Department of Neurology, University Hospital Zürich, University of Zürich, Zurich, 2University College London; and Reta Lila Weston Institute of Neurological Studies, London, United Kingdom;
3Department of Neurology, Universitätsklinikum Schleswig-Holstein, Kiel Campus, Christian-Albrechts University, Kiel, Germany

References

1. Critchley M. Observations on essential (heredofamial) tremor. Brain 1940;72(Pt. 2):113–139.
2. Lees A. In memoriam-Macdonald Critchley 2nd January 1900 15th October 1997 Bristol nether Stowey. Asq Neuropsiquiatr 1998;56(4):865–867.
3. Critchley M. The neurology of old age. Lancet 1931;217:1119–1127.
4. Das Zittern PJ. Seine Erscheinungsformen, seine Pathogenese und klinische Bedeutung. Berlin: Julius Springer; 1913.
5. Jung R. Physiologische Untersuchungen über den Parkinsonsyndrom und andere Zitterformen beim Menschen. Zeh ges Neurol und Psychiat 1941;173:283–332.
6. Wällner M, Hanchar HJ, Olsen R.W. Low dose acute alcohol effects on GABAa receptor subtypes. Pharmacol Ther 2006;112(2):513–528.
7. Marsden CD. Origins of normal and pathologic tremor. In: Findley LJ, Capaldeo R, eds. Movement Disorders: Tremor. London: Macmillan Press; 1984:37–84.
8. Bhatia KP, Bain P, Bajaj N, et al. Consensus Statement on the classification of tremors. From the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord 2018;33(1):75–87.
9. Louis ED, Bares M, Benito-Leon J, et al. Essential tremor plus: a controversial new concept. Lancet Neurol 2020;19(3):266–270.
10. Beckstepe J, Govert F, Balint B, et al. Exploring interrater disagreement on essential tremor using a standardized tremor elements assessment. Mov Disord Clin Pract 2021;8(3):371–376.
11. Fearon C, Espay AJ, Lang AE, et al. Soft signs in movement disorders: friends or foes? Journal of neurology. Neurosur Psychiatry 2019;90(8):961–962.
12. Lorenz D, Schwieger D, Moses H, Deuschl G. Quality of life and personality in essential tremor patients. Mov Disord 2006;21(8):1114–1118.
13. Thenganatt MA, Louis ED. Personality profile in essential tremor: a case-control study. Parkinsonism Relat Disord 2012;18(9):1042–1044.
14. Troster AI, Wood SP, Fields JA, et al. Neuropsychological deficits in essential tremor: an expression of cerebell-balano-cortical pathophysiology? Eur J Neurol 2002;9(2):143–151.
15. Tio M, Tan EK. Genetics of essential tremor. Parkinsonism Relat Disord 2016;22(suppl 1):S176–S178.
16. Kuhlenbaumer G, Hopfner F, Deuschl G. Genetics of essential tremor: meta-analysis and review. *Neurology* 2014;82(11):1000–1007.

17. Louis ED, Faust PL. Purkinje cell loss in essential tremor. *Mov Disord* 2014;29(10):1329–1330.

18. Rajput AH, Adler CH, Shill HA, Rajput A. Essential tremor is not a neurodegenerative disease. *Neurodegener Dis Manag* 2012;2(3):259–268.

19. Shill HA, Adler CH, Sabbagh MN, et al. Pathologic findings in prospectively ascertained essential tremor subjects. *Neurology* 2008;70(16 Pt 2):1452–1455.

20. Benito-Leon J, Bermejo-Pareja F, Morales JM, Vega S, Molina JA. Prevalence of essential tremor in three elderly populations of Central Spain. *Mov Disord* 2003;18(4):389–394.

21. Dogu O, Sevim S, Camdeviren H, et al. Prevalence of essential tremor: door-to-door neurologic exams in Mersin Province, Turkey. *Neurology* 2003;61(12):1804–1806.

22. Jankovic J, Beach J, Schwartz K, Contant C. Tremor and longevity in relatives of patients with Parkinson’s disease, essential tremor, and control subjects. *Neurology* 1995;45(4):645–648.

23. Deuschl G, Petersen I, Lorenz D, Christensen K. Tremor in the elderly: essential and aging-related tremor. *Mov Disord* 2015;30(10):1327–1334.

24. Bermejo-Pareja F. Essential tremor—a neurodegenerative disorder associated with cognitive defects? *Nat Rev Neurol* 2011;7(5):273–282.

25. Deuschl G, Wenzelburger R, Loffler K, Raethjen J, Stolze H. Essential tremor and cerebellar dysfunction clinical and kinematic analysis of intention tremor. *Brain* 2000;123(Pt 8):1568–1580.

26. Singer C, Sanchez RJ, Weiner WJ. Gait abnormality in essential tremor. *Mov Disord* 1994;9(2):193–196.

27. Schmahmann JD, Sherman JC. The cerebellar cognitive affective syndrome. *Brain* 1998;121(Pt 4):561–579.

28. Louis ED, Faust PL. Essential tremor pathology: neurodegeneration and reorganization of neuronal connections. *Nat Rev Neurol* 2020;16(2):69–83.

29. Deuschl G, Ebbe R. Essential tremor—neurodegenerative or non-degenerative disease towards a working definition of ET. *Mov Disord* 2009;24(14):2033–2041.

30. de Jong H. Action tremor in Parkinson’s disease. *J Neurol Ment Dis* 1926;64:1.