

The “forced normalisation” of Landolt – an EEG phenomenon?

■ I. W. Mothersill, S. Ried

Swiss Epilepsy Centre

Summary

Mothersill IW, Ried S. The “forced normalisation” of Landolt – an EEG phenomenon? Arch Neurol Psychiatr 1998;149:264–67.

With the introduction of clinical electroencephalography (EEG) it was hoped that there was finally a tool available with which it would be possible to quantify the therapeutic success, or the lack of it, in the treatment of patients with epilepsy. It was soon, however, seen that the EEG could become normal not only as expected after treatment with antiepileptic drugs but also through changes in the psychological state of the patient at the time of recording. This normalisation of the EEG reminded Landolt of previous patients with epilepsy who had had normal EEGs in connection with psychotic states. This in turn led him to the observation of “epileptics who must have a pathological EEG in order to be mentally sane”, this he termed “forced normalisation” which he then defined. This definition focussed on the EEG. Is then the “forced normalisation” of Landolt an EEG phenomenon which can be precisely defined?

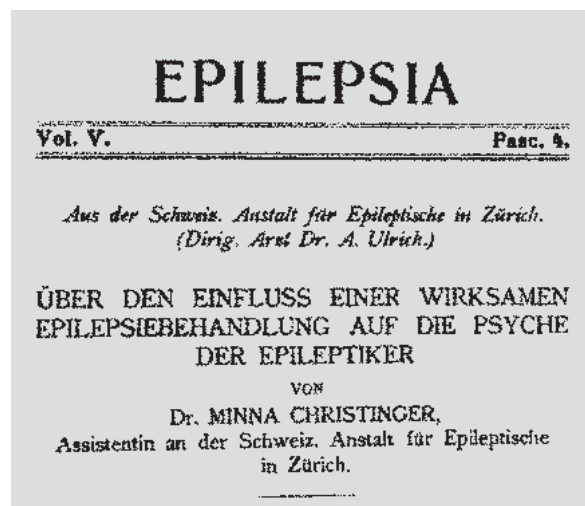
Keywords: EEG; forced normalisation; psychosis

The association between seizure freedom and the occurrence of psychic symptoms or changes in the mental state has long been known, terms such as “transformed epilepsy” were introduced as early as 1875 [1]. In a publication devoted to this problem Christinger [2] compared seizure disorders to morphine dependency and recommended that in risk patients, those with pre-existing neurotic or psychic symptoms, the seizures should be reduced very slowly in order to avoid a deterioration of the mental state.

Correspondence:
Ian William Mothersill, Sibylle Ried,
Swiss Epilepsy Centre,
Bleulerstrasse 60,
CH-8008 Zürich

Figure 1

Title page of Christinger’s publication from 1914.



Landolt shifted the emphasis away from seizure freedom and to the normalisation of the electroencephalographic (EEG) findings and in 1958 he wrote “... there would seem to be epileptics who must have a pathological EEG in order to be mentally sane ...” [3]. Landolt called these changes in the EEG which were associated with alterations of the mental state of the patients “forced normalisation” which he defined as “the phenomenon characterised by the fact that the EEG becomes more normal or entirely normal as compared with previous and subsequent EEG findings” [3]. Was this a precise electro-clinical definition, an EEG phenomenon, or just a description of the relationship between the EEG and the clinical changes he observed? In an attempt to clarify this question we examined the case histories and EEG findings of the first patients described by Landolt.

The introduction of clinical EEG at the Swiss epilepsy centre in the Spring of 1948, where Landolt worked at the time, opened new possibilities concerning the diagnosis and therapy control of patients with epilepsy. Landolt showed a very early interest in the relations between clin-

ical findings, not only somatic, but also the psychological state of the patient, and EEG changes.

It was generally accepted at this time that the EEG of epileptic patients, who were correctly and adequately treated, could become normal and that in most cases there was a good correlation between the normalisation of the EEG and a decrease in seizure frequency. The EEGs shown in Figures 2 and 3 were used by Landolt to illustrate the effects of antiepileptic drugs (AED) on the pathological EEG [4] where he wrote "the disappearance of the absences can be followed in the EEG".

Figure 2
EEG before therapy.

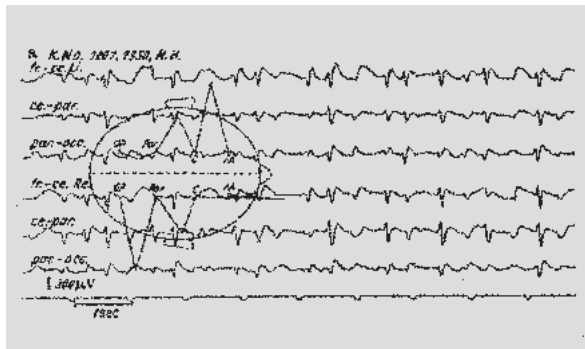
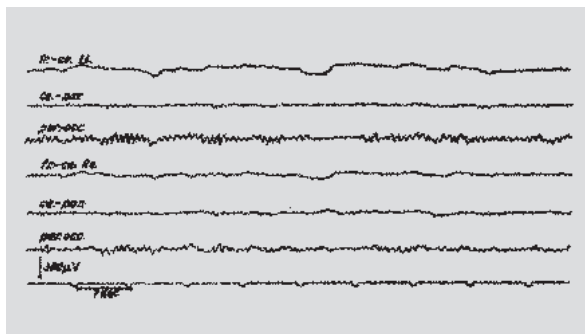
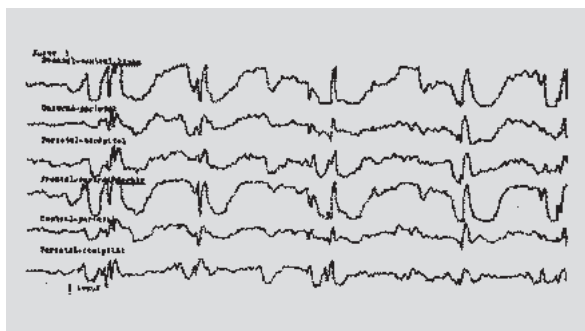


Figure 3
After therapy with antiepileptic drugs.



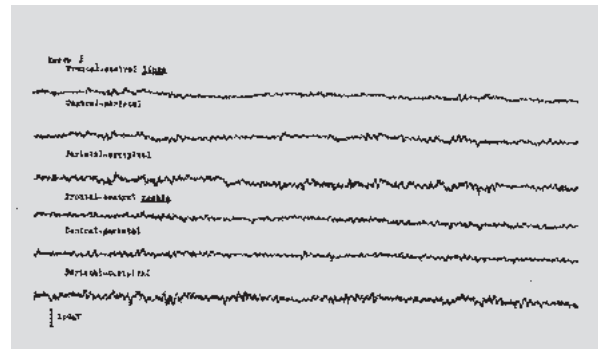
In 1952 Landolt made one of his most important observations, namely that there was a striking connection between the mental disposition of the patient at time of recording and the EEG manifestations, suggesting that a given mental disposition can lead to a normalisation of the cerebral electrical activity. Figures 4 and 5 illustrate the EEG findings of the first patient in which Landolt observed this phenomenon.

Figure 4
EEG recorded when the patient was in a friendly and relaxed mood, showing frequent series of bilateral spikes-and-waves.



The next EEG was recorded without the patient being forewarned. At first he refused to cooperate, was extremely exasperated and trembled with rage at what he called inconsiderate and inhuman treatment. The EEG failed to reveal any spikes-and-waves even during 3 minutes of hyperventilation. With the exception of a few scattered theta waves, the EEG was normal. There had been no change of medication made since the previous recording.

Figure 5
EEG recorded when the patient was extremely exasperated. No spikes-and-waves were registered, the EEG was normal.



In order to confirm these findings, Landolt repeated the recordings three times under the same conditions. The results were the same each time i.e. a relaxed patient correlating with a pathological EEG, and an angry patient correlating with a normal EEG.

This, at the time, surprising discovery, that the EEG could become normal not only as expected after AED therapy but also through changes in the psychological state of the patient, led Landolt to a reappraisal of the role of the EEG in the diagnosis and therapy. He warned that the diagnostic value of the EEG may differ with changes in the patient's mental condition. Later he wrote "if serial EEG recordings are to have any value at all the psychological state of the patient has to be taken into account, ... and the recording should be performed under the same conditions, under the same circumstances and with the patient being in the same state of mind. Whoever performs EEG recordings should not just be content with the technical aspects but also has to continuously and exactly observe the patient" [4]: factors which have remained valid until today.

This "normalisation" of the EEG reminded him of previous patients with epilepsy who had had normal EEGs in connection with a psychotic state. The following EEGs illustrate the findings from one of these patients.

Figure 6
EEG recorded with the patient in his habitual psychological (normal) state.

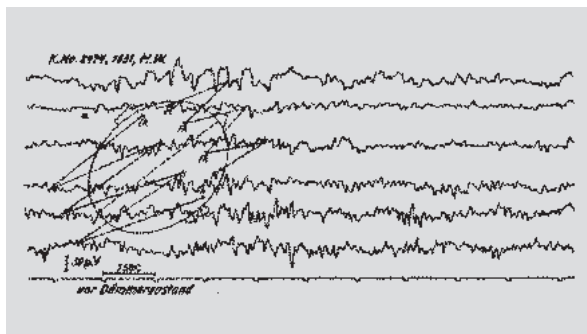


Figure 7
EEG recorded during a psychotic state.

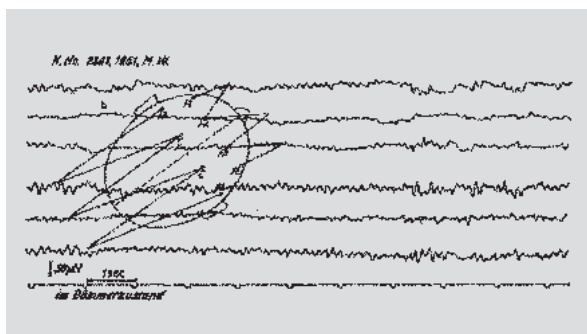
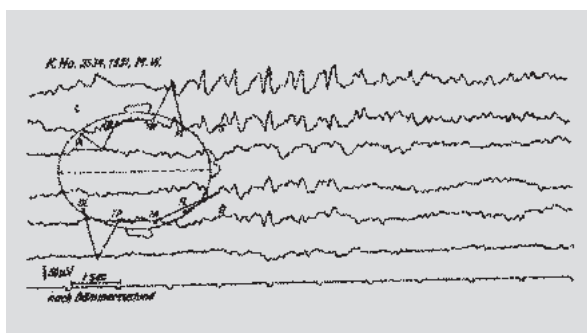


Figure 8
Recorded after all AEDs had been discontinued, with the exception of phenytoin which was reintroduced 1 day before recording.



Landolt observed similar findings in a total of 47 patients and interpreted these as follows. “Thus these cases reveal an unmistakable correlation between the course of the psychotic process and the changes in the EEG, in that the paroxysmal focus which is active before and after the twilight state dissolves during this twilight state, and often so completely that the record is normalised. In other words, and putting it more crudely, there would seem to be epileptics who must have a pathological EEG in order to be mentally sane, and who enter a twilight state or become productively psychotic during a certain produced or spontaneously occurring EEG normalisation and whatever it is that underlies this.” [3]

This normalisation, first described in 1953, was considered to be “an excessive reaction of the normal cerebral tissue to a usually circumscribed cerebrophysiological pathological condition at the expense of the mental condition, and therefore giving a forced impression” [3]. Forced normalisation was then defined by Landolt as

“the phenomenon characterised by the fact that, with the occurrence of psychotic states, the EEG becomes more or entirely normal as compared to previous and subsequent EEG findings» [3]. These findings have, over the years, led to many questions being asked.

Do these EEG changes relate to a specific pathological process causing the change in mental state or are they merely a reflection of this state?

There have been many hypotheses forwarded over the years as to the possible underlying mechanism causing forced normalisation. In an overview Wolf reported on as many as 11 possible mechanisms [5].

The aetiology is therefore most likely heterogeneous, the different clinical symptoms presented, the fact that it can occur in different epilepsy syndromes, and most importantly the EEG changes which are not an “abnormal” normalisation which can be defined in terms of topography, reactivity frequency, etc., such as seen in the so-called alpha coma, suggest that the changes in the EEG seen during forced normalisation are a reflection of the mental state of the patient. In other words the mind is affecting the EEG and most probably not changes in the EEG affecting the mind.

Was the EEG recorded by chance during a phase of relative inactivity and the changes seen purely coincidental or due to inadequate sampling?

Landolt was aware of the variability of bio-electrical phenomena, and recognised the difficulty of demonstrating the change in the EEG from pathological to normal necessary for the identification of forced normalisation. He stated that this can only be attained by recording EEGs as frequently as possible e.g. several times a day [3].

This would rule out the problem of under-sampling.

Is forced normalisation a drug-specific reaction?

The publications of Landolt show that he did not consider the occurrence of forced normalisation to be related to any specific side effect of AEDs. This even though he initially assumed that the psychotic state in one of his patients was a negative side effect of hydantoin therapy. In the case history he wrote “twilight state as an effect of hydantoin?”. He excluded this by stopping all AEDs, waiting until the twilight state disappeared, then re-introducing all previous AEDs with the exception of hydantoin; 5 days later the patient was once again in a twilight state. Landolt concluded in the case history “at least it has been shown that the hydantoin therapy was not responsible”. The occurrence of forced

normalisation under different drugs with different mechanisms of action, phenurone [6], phenytoin and primidone [7], valproic acid, carbamazepine [8], and vigabatrin [9], supports Landolt's original assumption that forced normalisation is a result of effective therapy and not a drug-specific reaction.

Were the EEG changes due to increased arousal caused by excitation?

Landolt tried to meet this criticism by stating that these states could arise from mental excitation, but this would never be a primary cause, and was only secondary to some underlying pathological process [10].

This question has, however, not been satisfactorily answered and for example sleep EEGs which could help in clarifying this point have, to our knowledge, not been performed in these patients.

Is, in conclusion, the forced normalisation of Landolt an EEG phenomenon? If we expect EEG phenomena to be precisely definable and homogeneous, then it is not. Fenwick who was for a long time sceptical as to the existence of forced normalisation recently made the following very apt concluding statement, "... the original observation of Landolt was prescient. He accurately predicted and started to characterise the very close relationship that there is between behaviour, seizures, and EEG activity. Used this way, forced normalisation describes a real phenomenon; the phenomenon of EEG change in some mental states. I am thus pleased to admit and accept that forced normalisation as defined by Landolt does exist" [11].

References

- 1 Sampt P. Epileptische Irreseinformen. *Arch Psychiatr* 1875;5:393-444.
- 2 Christinger M. On the influence of an effective epilepsy treatment on the psyche of epileptics. *Epilepsia* 1914;15.
- 3 Landolt H. Serial electroencephalographic investigations during psychotic episodes in epileptic patients and during schizophrenic attacks. In: Lorentz de Haas AM (editor). *Lectures on Epilepsy*. Amsterdam: Elsevier; 1958.
- 4 Landolt H. Die Bedeutung der Elektroenzephalographie für die Behandlung der Epilepsie. *Nervenarzt* 1957;28:170-6.
- 5 Wolf P. Acute behavioural symptomatology at disappearance of epileptiform EEG abnormality. Paradoxical or "forced normalisation". In: Smith D, Treiman D, Trimble MR (editors). *Adv Neurol* Vol. 55 New York: Raven Press; 1991. p. 127-42.
- 6 Gibbs FA. Ictal and non-ictal psychiatric disorders in temporal lobe epilepsy. *J Nerv Ment Dis* 1951;113:522-8.
- 7 Wolf P. The prevention of alternative epileptic psychosis in outpatients. In: Janz D (editor). *Epileptology*. Stuttgart: Thieme; 1976. p. 75-9.
- 8 Pakalnis A, Drake JK, Kellum JB. Forced normalisation: Acute psychosis after seizure control in seven patients. *Arch Neurol* 1987;44:289-92.
- 9 Sander JWAS, Hart YM, Trimble MR, Shorvon SD. Vigabatrin and psychosis. *J Neurol Neurosurg Psychiatr* 1991;54:435-9.
- 10 Landolt H. Petit Mal; Temporallappenepilepsie; epileptische Dämmerzustände mit Verstimmungen. In: Schulte W (editor). *Epilepsie und ihre Randgebiete*. München: Lehmann; 1964. p. 33-58.
- 11 Fenwick P. Does forced normalisation exist and how relevant is it to the psychiatrist?. In: Trimble MR, Schmitz B (editors). *Forced normalisation and alternative psychoses of epilepsy*. Petersfield UK, Bristol PA, USA: Wrightson; 1998. p. 209-20.