The introduction of convulsive therapy: data contributing to the history of the treatment of schizophrenia.

The controversies surrounding Meduna’s discovery and its impact on the development of psychiatry

Thesis

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INTRODUCTION

Convulsive therapy, one of the effective biological methods for treating schizophrenia, was devised and introduced to psychiatric practice 75 years ago by a Hungarian psychiatrist, Laszlo Meduna, who was Karl Schaffer’s pupil. Electroconvulsive therapy (ECT), whereby convulsions are induced by electricity, is the developed version of Meduna’s method which is also known as chemical convulsive therapy. ECT is still a therapeutic method even though its indications have changed since the 1930s.

Effective psychotherapeutic methods were already used in treating different types of neuroses in the first decades of the twentieth century. In case of psychoses, however, therapeutic nihilism prevailed. Psychotic patients in mental institutions did not receive any treatment apart from sedation, restraint and occupational therapy. Schizophrenia was considered to be a disease of the embryonic endoderm and thus an incurable, heredo-degenerative disease – a view firmly held by the Schaffer School that was at the forefront of the brain research in Europe. None of the biological treatments – prolonged deep sleep, malaria-induced fever – used at that time met the expectations of contemporary psychiatry. In 1925, an unprecedented situation developed in the Schaffer clinic in Budapest when experienced clinicians and world-famous brain researchers became colleagues and tried to find common ground for collaboration in research and clinical practice. László Meduna’s scientific ideas were born in this inspiring professional milieu.

Meduna’s path-breaking glia research led him to conclude that an antagonism existed between the histological pictures of epilepsy and schizophrenia. Meduna also surveyed the published histological and clinical data on the subject and found information that gradually strengthened his presupposition that these two illnesses were antagonistic. Meanwhile, the Schaffer School’s once firmly held view that schizophrenia was a homogeneous, inherited endogen disease was about to dissipate. A new concept was being developed according to which a subset of schizophrenic psychoses were not ‘endogenous’ in nature and these patients might be ‘curable’. Against this background, Meduna hypothesised that the course of schizophrenia can be favourably influenced by induced epileptic seizures because of the biological antagonism between schizophrenia and epilepsy.
Following his animal experiments, Meduna found a drug suitable for inducing epileptic seizures. In January 1934, he started treating a selected group of patients with convulsive therapy induced by camphor. In his memoirs, he provided a detailed account of the spectacular cure of one of his catatonic patients, which was followed by several more patients with excellent treatment response. The initial success of convulsive treatment spread quickly, gaining a very positive reception in the scientific community all over the world.

OBJECTIVES

The objectives of this thesis are as follows.

1. To precisely elucidate the scientific background of convulsive therapy and the key professional moments preceding Meduna’s discovery.

2. To retrospectively analyse and re-evaluate Meduna’s first cohort treated with chemically induced convulsive therapy in terms of its safety and effectiveness, taking into consideration the professional and ethical context of that epoch. Meduna’s therapeutic experience is also analysed in the light of present knowledge about convulsive treatment. The thesis examines the original documents and attempts to map the details surrounding first convulsive treatments, including their frequency, safety and effectiveness.

3. To analyse the impact of convulsive therapy on the medical conceptualisation of schizophrenia.

4. To discuss the impact of the introduction of the new treatment method on the development of psychiatry, particularly biological psychiatry.

METHODS

1. First, the original documents were located in the following places: the Archives of Semmelweis University, the National the Budapest Capital Archives, the Museum and Library of Medical History, the Library and Archives of the National Institute of Psychiatry
and Neurology, and the library of the Department of Psychiatry and Neurology, and were supplemented by the recollections of Károly Schaffer’s grandchild, Dr Attila Bogsch.

2. Second, the case notes of discharged or deceased patients between 1933 and 1945 found in the Archives of National Institute of Psychiatry and Neurology were systematically examined. Only case notes containing descriptions of convulsive therapy were selected for further analysis.

3. Third, the selected case notes and the scientific literature were critically analysed.

RESULTS

Indications, course of treatment and dose titration

According to the original case reports, Meduna started simultaneous convulsive treatment on the first batch of six patients on 2 January 1934. Another five patients were included in his first series by the end of January. The first eleven patients received camphor intramuscularly to induce seizures. Convulsive treatment sessions were administered in the morning, 2-3 times a week in the 8th ward of the National Institute of Psychiatry and Neurology. The patients were observed according to standardized criteria (temperature, pulse and respiration rates, blood pressure and general and psychiatric conditions) and were documented in detail in their medical records. The total number of convulsive treatments for each patient was between 9 and 32. Ten patients were diagnosed with schizophrenia and one with “oligophrenia”, as registered in their case notes. It seems that the severity of the patients’ general and psychiatric conditions guided their selection for convulsive therapy. Prior to convulsive treatment, 9 of the 11 patients displayed various degrees of refusal of food and drink, and six needed tube feeding. It can thus be assumed that stupor was the dominant syndrome in the selection of patients.

Meduna injected 4 g of camphor into one patient in his first cohort, and having observed the patient’s reaction he halved the dose for the rest of the patients that afternoon. On the morning of the second day, after administering 8 g of camphor to the patient treated the previous morning, he witnessed two subsequent seizures. Meduna immediately suspended this patient’s treatment and in the afternoon continued convulsive therapy using half doses for the
other five patients. He did not administer camphor in a dose higher than 4-8 g in the treatment of the first 11 patients.

The effectiveness of camphor-induced convulsive therapy

Seizures occurred more than one hour after the oily dilution of camphor was given intramuscularly. Meduna only registered generalized tonic-clonic seizures (GTCS) as convulsions in the case notes and in his own notes with red pen. The 178 camphor injections during the treatment of the first 11 patients were followed by generalized seizures in only 28 instances. The ratios of camphor injections per seizure in the 11 patients were as follows: 2/1+1, 13/1, 20/4, 32/2+1, 23/3, 23/4, 19/1, 25/3, 2/0, 9/6 and 10/1.

The number of seizures induced by a course of treatment ranged between 1 and 6. There was no clear correlation between the amount of camphor doses (at a level of 4-5 g) and the induced GTCS. In the abovementioned case, 8 g of camphor provoked two subsequent seizures; however, it turned out that the same effect could be induced by just 4.5 g of camphor. In one of the three patients who eventually improved due to convulsive therapy, 13 camphor injections provoked only one seizure, in the second patient 5 seizures occurred from 23 injections, and in the third patient the ratio was 9 injections from 7 seizures. Why, then, was Meduna not successful in determining a correlation between the number of seizures and the improvement in his first series? This can be partly explained by the fact that Meduna – who was a brilliant researcher, but who had never really become an experienced clinician – considered as epileptic seizures only typical GTCSs. He did not register, and maybe even did not recognise, the simple and complex partial seizures that were later pointed out and differentiated as ‘psychic’ and ‘abortive motor seizures’ by his colleague Lajos Angyal. A close scrutiny of the case notes certainly reveals symptoms that could suggest the presence of simple and complex partial seizures.

The effectiveness of convulsive treatment

Of the first eleven patients who received convulsive therapy, only three improved considerably. Two of them were soon discharged from hospital (one 3 months after the first treatment and the other 8 months after), and were possibly able to continue their work. There is no documentation available to indicate that these two patients were treated again in the institution before the end of 1945. The third patient who improved was the only ‘chronic
case’. After the first course of convulsive therapy he was symptom-free for 3 months and able to participate in occupational therapy in the institution, although he was never discharged. However, in contrast to Meduna’s recollection, there was no symptom-free period longer than one month documented in this patient’s case notes.

The length of illness was longer than two years for most of the patients in Meduna’s first batch; it was shorter than two years in only three cases: two of these patients fully and presumably persistently remitted, but the third patient did not improve at all. The remission rate of 27.3% in the first 11 patients treated with convulsion therapy is below the rates reported by any of the studies in the classical or modern literature.

The safety of convulsive therapy and the dropout rate

Meduna had to stop the treatments of four patients in the first group of eleven. In two cases this was necessary because of side effects: a gluteal abscess developed after the 18\textsuperscript{th} camphor injection in one patient, and another experienced superficial skin damage around his eyebrow caused by the seizure. A third patient did not receive more than a single session of convulsive therapy because his diagnosis was oligophrenia. A fourth patient was discharged against medical advice; he was taken home by his mother who claimed responsibility for arranging tube feeding.

Meduna administered a total of 178 camphor injections to the first 11 patients, causing one (0.56%) gluteal abscess. Altogether, 28 (3.57%) GTCSs were induced by 178 camphor injections resulting in only two adverse reactions. Considering the total number of sessions and the number of seizures, adverse effects cannot be regarded too highly. However, from the treated patients’ perspective the picture is less favourable: two (18.2%) of the eleven patients suffered adverse effects that were not negligible in the light of the modern practice, and in all likelihood Meduna was not satisfied with the side effect profile of convulsive therapy either. As documented in the case notes, Meduna changed camphor to cardiazol to induce seizures on the 10\textsuperscript{th} of August 1934, mentioning problems with gluteal administration as one of the reasons for this change in his later publications.

CONCLUSIONS

The new findings of this thesis are summarised in the following points.
A) **The inspiring scientific-intellectual background of the Schaffer school.** Schaffer’s school was at the forefront of international brain research in the 1930s, and Meduna’s exceptional qualities as a researcher (creative fantasy, courage and flexibility in putting his ideas into practice) led to the discovery of camphor-induced convulsive therapy that was firmly grounded in contemporary scientific concepts.

B) **The practice of the first sessions of convulsive therapy.** Meduna conducted convulsive therapy by following a well-designed ‘protocol’ (i.e. defined frequency, appointment, observation criteria, dose titration etc.). On the first day, he started convulsive treatment for six patients (11 patients in total in the first month). Hence, the therapeutic success was not a anomaly created by a spectacularly improved patient who was selected accidentally (from an historical perspective, it is largely irrelevant who this first patient was). Twenty years after his first attempts at convulsive therapy, not having the original documents at his disposal, Meduna mistakenly recalled the most spectacular case as the first one. Despite the low effectiveness of convulsive therapy in treating the first 11 patients, he persisted with great enthusiasm and enlarged his cohort to 110 patients, with the results of their treatment reported in a monograph.

C) **Conclusions derived from the first convulsive treatments that are still valid.** Seizures are most effective in stupor, catatonia and in the early phase of schizophrenia. Remission and patients’ propensity for seizures are correlated; i.e. the improvement is due to the occurrence of a seizure, regardless of the seizure-inducing agent.

   Retrospective analysis of case notes reveals that Meduna judged the effectiveness of the first courses of convulsive treatment with premature optimism. Yet in those days no other method could achieve even temporary symptom-free periods in severe schizophrenia. If the treatment worked, its effect was dramatic, although transient. The interpretation of the transient improvement could not be explained by Meduna’s working hypothesis that epilepsy and schizophrenia were antagonistic diseases.

   In terms of the indications, Meduna did not at first recognise that convulsive therapy affects the symptoms and not the putative disease process. However, for practical reasons, Meduna chanced upon the primary indication, namely stupor occurring in catatonic schizophrenia. ECT is considered the most effective treatment method in catatonia and stupor of diverse aetiology.
D) From the perspective of safety, at first it seemed that camphor-induced convulsive therapy would be a viable option in the repertoire of biological treatments. Other treatment modalities used at the time were eliminated because of their poor effectiveness and serious side effects: i.e. Klaesi’s ‘Dauerschlaf’ treatment caused frequent pneumonia and Sakel’s insulin coma caused life threatening hypoglycaemia. However, Meduna had to stop the use of camphor for seizure induction after six months, and changed the substance to the much safer and more reliable cardiazol. Then, in 1938, Cerletti and Bini developed a method of inducing seizures with electricity that was far superior to Meduna’s chemical methods from the perspective of reliability and safety.

E) The significance of Meduna’s discovery is not restricted to the creation of a new method of treatment. Even more important was its impact on the medical community’s attitude towards schizophrenia. Convulsive therapy also spawned the biological approach to psychiatric conditions. His method has been overtaken only in terms of the way seizures are induced, and its basic concept is still relevant today. Convulsive therapy, in the form of electroconvulsive therapy (ECT), has an important place in current psychiatric treatment methods. Meduna’s contribution to psychiatry is very significant in exerting a major influence on the psychiatric profession; his discovery significantly contributed to the development of biological psychiatry and initiated a revolutionary change in the approach to the so-called endogenous psychoses.
PUBLICATIONS DIRECTLY RELATED TO THE THESIS


GazdagG., Bitter I., Ungvari GS., Baran B. Convulsive therapy turns 75
BJP (in press)

OTHER PUBLICATIONS


Baran B. Szorongás és depresszió idős korban [Anxiety and depression in late life]. Családorvosi Fórum October, 2000, pp. 32-43.


Chapters in books


