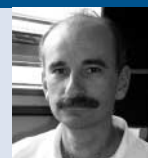


## Editorial

## Convulsive therapy turns 75

Gabor Gazdag, Istvan Bitter, Gabor S. Ungvari and Brigitta Baran



## Summary

The Hungarian psychiatrist Laszlo Meduna was the first who induced epileptic fits to influence the course of mental illness. The following account, based on a review of Meduna's recently unearthed files and

his writings, traces the beginnings of convulsive therapy.

## Declaration of interest

None.

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## Convulsive therapy: the first steps

According to recently recovered case notes,<sup>1,2</sup> at 16.00 h on 2 January 1934, Laszlo Meduna, a 38-year-old Hungarian psychiatrist with a background in neuropathology, administered intramuscular injections of 10 ml of oily solution containing 20% camphor to five patients and 20 ml to one further patient at the Royal Hungarian State Psychiatric Institute in Budapest. Meduna's objective was to attempt to treat schizophrenia through the induction of epileptic seizures. This initiative led to the birth of convulsive therapy and Meduna regarded himself as the originator of this type of treatment, although better techniques of inducing convulsions were later developed.<sup>3</sup> Five of the patients he treated had been diagnosed with catatonic schizophrenia, with four of them being stuporous and requiring tube-feeding for several months; the sixth patient, who received the higher dose of camphor, was an agitated 'oligophrenic'. As all six patients failed to develop seizures after the initial treatment, Meduna doubled the dose of camphor for all the patients the next day. Two patients developed seizures without major adverse effects; however, the patient with oligophrenia had two fits and his treatment was stopped. Encouraged, despite the lack of evidence at this stage of therapeutic benefits, Meduna carried on with convulsive treatment at 2- to 3-day intervals, gradually involving more patients.

Meduna's persistence was admirable as the results of his novel treatment were far from convincing. Only two of the first five patients showed improvement, but even these positive changes may not have been directly related to convulsive therapy. One patient had only one seizure from 13 attempts and suddenly remitted 18 days after this successful seizure. The second patient had four fits after 19 camphor injections and started speaking 6 weeks after the last treatment. Both patients had a history of illness of less than 2 years and both were lost to follow-up shortly after their discharge so the long-term outcome was not known. On the other hand, tube-feeding was no longer necessary after convulsive therapy in any of the patients from the first series, and this may have been regarded as a therapeutic breakthrough given the lack of effective interventions for severe schizophrenia in the early 1930s.

Meduna's insistence on continuing the treatment is all the more remarkable because his mentor, Karoly Schaffer, the leading

authority on neuropsychiatry in contemporary Hungary, adopted an incredulous stance towards the convulsive treatment of schizophrenia believing the reasoning behind this treatment to be quite implausible.<sup>3</sup> Intramuscular camphor was painful, caused abscesses and nausea. Furthermore, the latency between the injection and the seizure ranged from 30 min to 3 h; during the waiting period, patients were overwhelmed with increasing anxiety and horror.

Because of the adverse effects of camphor, Meduna turned to the analeptic agent pentamethylenetetrazol (cardiazol), a water-soluble short-acting cardiac stimulant, as an alternative agent to induce seizures. Cardiazol was not only much more rapid in inducing seizures, which occurred within 30 s after intravenous injection,<sup>4</sup> but was also more reliable in causing fits and less expensive. Nevertheless, use of this drug was not without major hazards. Its serious adverse effects also included overwhelming fear before the seizure, joint dislocations and vertebral fractures.<sup>5</sup>

Meduna persisted in his experiments to induce seizures as a therapeutic measure on the basis of two hypotheses. The first was his belief in a biological antagonism between schizophrenia and epilepsy that he enunciated on neuropathological, clinical and epidemiological grounds.<sup>3,4,6</sup> The pitfalls and controversies of such a biological antagonism have been thoroughly analysed since that time, resolving some of the disagreements surrounding this complex conundrum.<sup>7</sup>

The second hypothesis, which Meduna borrowed from Somogyi and Rath,<sup>6</sup> is now rarely mentioned. These authors posited three basic types of schizophrenia according to aetiology: endogenous or genotypic, exogenous or paratypic, and a combination of the two. Meduna assumed that induced epileptic seizures would only offer therapeutic benefit for the latter two non-genetic types.

After the near failure of the first six patients, what made Meduna continue, other than his strong conviction about these two hypotheses? First, he appeared initially unaware of the high rate of side-effects. The first patients were too severely ill to complain of the intense anxiety and fear that preceded the fit. Second, the severity of catatonic stupor, but not the schizophrenic process, was mitigated, although temporarily on the whole. We assume that Meduna probably chose patients in a stuporous catatonic state for two reasons. Two patients with catatonic schizophrenia had already been reported to have improved following spontaneous epileptic fits.<sup>8</sup> Also, patients in a stuporous state who required tube feeding were in grave physical condition and fatal outcome was frequent despite the intensive efforts of medical and nursing staff, so any treatment that might help was worth trying.

The initial unimpressive results did not seem to sap Meduna's enthusiasm. He continued administering convulsive therapy and

published his results on 26 schizophrenia patients, 10 of whom improved significantly in the short term.<sup>6</sup> In a later monograph<sup>4</sup> he reported 54 of 110 patients having 'remitted'. Shorter illness duration and a high propensity to convulse immediately after induction appeared to predict good treatment response.

Meduna eventually came to the conclusion that cardiazol did not cure schizophrenia but only accelerated remission in acute, good-prognosis cases. By then it had also become clear that the main indication for convulsive therapy was not schizophrenia, for which the results were short-lived, but affective disorder.<sup>9</sup>

As a safer, more consistent, less anxiety-provoking and less expensive form of convulsive therapy that provided better seizure control, electroconvulsive therapy (ECT) rapidly became the dominant method of convulsive treatment over the next few years. Although still tainted with misunderstanding and misrepresentation by the public and a measurable part of the psychiatric profession, ECT has saved and significantly improved the lives of tens of thousands of patients since the 1930s.

### Ethical considerations

In accordance with the contemporary ethical standards of psychiatric practice and research, Meduna neither had a study design nor asked consent from patients or relatives; at least there appears to be no trace of any form of consent in the files. Also, there is no reference in the notes to how patients felt about the treatment, and Meduna mentioned patients' subjective experiences only in passing in his papers published in the 1930s.

The discrepancy between clinicians' and patients' (consumers), perceptions of the therapeutic and side-effect profile of ECT is a growing concern in modern psychiatry,<sup>10,11</sup> which illustrates how far the psychiatric profession has come in the past 75 years. However, there is some evidence that patients' concerns may not have been adequately addressed by the psychiatric community. Covering the period 1980–2004 in their review, Rose *et al*<sup>10</sup> concluded that nearly half of the patients who underwent ECT felt that the information provided was inadequate and a third perceived subtle coercion to give consent. The ethical aspects of ECT are becoming particularly timely in low- and middle-income countries where it is widely used – often in its unmodified form – for schizophrenia and affective disorders,<sup>12</sup> and the ethical dilemmas (e.g. with perceived coercion<sup>10</sup>) appear to be the same as in the Western world.

### Meduna's contribution to psychiatry

Meduna's first report<sup>6</sup> created so much interest within the psychiatric community that by 1941 more than 1000 scientific papers had been published on the subject.<sup>3</sup> The acceptance of convulsive therapy was facilitated by the relative success of Wagner-Jauregg's malaria treatment and the early, favorable reports of Sakel's insulin coma treatment. All three of these treatments were based on the therapeutic paradigm of inducing a serious but transient and potentially curable medical condition to treat a neuropsychiatric disorder. Although malaria treatment, insulin coma and earlier, prolonged sleep therapy were introduced on the basis of clinical experience and speculative hypotheses, these treatments provided the 'social and moral warrants' for convulsive therapy.<sup>13</sup> This was understandable given the

desperation in finding a cure for schizophrenia, which by then took up a sizeable proportion of the asylum population in the Western world, contributing to the prevailing atmosphere of widespread therapeutic pessimism.

With the full advantage of hindsight, the importance of Meduna's contribution extends beyond the discovery of a highly effective and frequently life-saving mode of somatic therapy. Cardiazol brought hope amidst the generally pessimistic zeitgeist surrounding schizophrenia. At the same time, it powerfully reinforced the belief in somatic treatment in psychiatry against the purely psychological, mainly psychoanalytic approaches. Research into convulsive therapy's mode of action also stimulated the development of biological psychiatry and further underscored the significance of the organic hypotheses concerning the origin of schizophrenia. Ultimately, this treatment and others of its ilk fostered the development of standardised, scientific methods of assessment of psychiatric conditions by underlining the need for a more reliable diagnostic practice.

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