



The seventh London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures



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ABSTRACT

The 7th London-Innsbruck Colloquium on Status Epilepticus was held in London on 7–9 April 2019, with a faculty of 47 clinicians and scientists from 16 countries and a total of 401 delegates from 41 countries. This paper is an introduction to the proceedings of the colloquium, and outlines the recent developments in status epilepticus which formed the core of colloquium program in the areas of 1. basic science; 2. clinical description, etiology, and investigation; and 3. treatment.

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Since 2007, a series of biennial colloquia have been held on the topic of Status Epilepticus and Acute Seizures, alternating between venues in Britain and Austria. University College London, the Universities of Innsbruck, and the Paracelsus Medical University of Salzburg have acted as patrons, latterly with the local branches of the International League Against Epilepsy (ILAE), and with financial support in the form of education grants and exhibitions by industry. The proceedings of each have been published in *Epilepsy and Behavior* and *Epilepsia* ([1–6]) and have provided a summary of the main discussions and presentations. The term ‘colloquia’ was chosen deliberately as a homage to Henri Gastaut’s *Colloques de Marseilles*, in the hope that these meetings would be as productive scientifically and as convivial professionally as Gastaut’s series were, would bring together all those interested in what some would consider the niche topic of status epilepticus, and would like the meetings in Marseilles inspire the younger generation of clinicians and scientists. We hope that these goals have been realized, at least to an extent.

The 7th Colloquium in the series was held at the Francis Crick Institute in London on April 6–8, 2019, with a faculty of 47 clinicians and scientists from the Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Ireland, India, Israel, Italy, Lebanon,

Switzerland, UK, and USA, and a total of 401 delegates from 41 countries. The meeting took place over three full days, and was preceded on April 6th by a teaching course run in collaboration of the British Branch of the ILAE on the topic of *EEG in status epilepticus and on the intensive care unit*.

Other new features of the program included, as well as the teaching course, two parallel workshops a Nobel Laureate lecture (given by Professor James Rothman FRS), a session on controversies, and two data-blast sessions with topics chosen from the poster sessions.

The eleven plenary sessions were on the topics of *Networks and novel targets; biomarkers; physical treatments of status epilepticus; Hullabaloo-controversies; Big data, seizure detection, and prediction; Genes and paediatrics; Nobel Laureate lecture; Paediatrics and research networks; Novel drugs and devices in development; Novel treatment approaches; and Novel drugs in the treatment of status epilepticus*. The two workshops were entitled *Outcome in status epilepticus* and *When backs are against the wall - the clinical management of status epilepticus in specific situation*. The two data-blast sessions were on *epidemiology, outcome, and novel clinical treatments; and EEG, basic aspects, and experimental treatments*. In addition to the scientific program, there was a conference dinner held at the Athenaeum Club in Pall Mall, which itself has had a long tradition in the neurosciences, and a Young Epilepsy Society (YES) evening at a pool club in Kings Cross.

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We were fortunate to be holding the meeting in the Francis Crick Institute (Fig. 1), which was opened in 2016 as an institute funded by UCL and Imperial College in association with the MRC, Cancer Research UK, and Wellcome Trust and philanthropic donations. It acts as a high-level 'incubator' site dedicated to understanding the fundamental biology underlying health and disease and so was a natural venue for our three objectives of scientific productivity, professional development, and inspiring research and innovation. Whether the Colloquium succeeded in these goals is for the audience to decide, but the organizers worked hard to achieve this.

1. Developments in status epilepticus

Over the 12-year period, much has developed in the field of status epilepticus. In the last report, we presented an albeit personal list of the most important advances that had taken place during the 10 years of the Colloquia, between 2007 and 2017, and since then, a further 1500 papers have been published in the field (i.e., where the key term 'status epilepticus' is entered into PubMed) which have including areas covered in the Colloquia. In our view, the most significant developments in the last few years are the following:

1.1. Basic science

There continue to be significant advances in the basic sciences. In particular, advances have been made in understanding the brain networks underlying the progression of focal to generalized status epilepticus with the involvement of corticothalamic circuits and structures critical for memory consolidation (perhaps explaining some of the morbidities associated with status epilepticus). In addition, novel

mathematical approaches such as dynamic causal modeling can give insights into circuit dysfunctions that maintain seizure activity. These advances were discussed in the Colloquium.

We also learned about the mechanisms underlying and novel potential treatment approaches to organophosphate poisoning; the importance of this research was brought home by a talk on Novichok poisoning in Salisbury. We also heard about preclinical work on new treatments for status epilepticus and, in particular, the role for polytherapy which will hopefully inform clinical trial design in the future.

However, perhaps some of the most exciting translational advances were in the understanding of the mechanisms underlying the potentially devastating consequences of status epilepticus (neuronal damage, cognitive decline, and epilepsy) including breakdown of the blood-brain barrier, changes in microRNA (micro-ribonucleic acid) expression, neuroinflammation, release of reactive oxygen species, and activation of the mTOR (Mammalian target of rapamycin) pathway. Preclinical data indicate that many of these pathways/effects can be used as prognostic biomarkers but, perhaps more importantly, targeting these processes can successfully improve the prognosis of status epilepticus. The challenge for the future is to translate these exciting preclinical findings into the clinic.

1.2. Clinical description, etiology, and investigation

There have been important contributions to the epidemiology of status epilepticus, its clinical staging, and definitive studies of a number of different types of status published in recent years, and of etiology including the explosion of genetic information about infantile forms. In parallel to genetic discovery have been advances in knowledge about



Fig. 1. The Francis Crick Institute, London.

the clinical role of inflammation, oxidative stress, and mitochondrial mechanisms. The new ILAE classification of status epilepticus is an important step in clinical description, and emphasizes the temporal issues involved in the twin goals of controlling seizures and preventing cerebral damage. The advances have been particularly in the area of pediatrics and in super-refractory status epilepticus, and many have improved clinical practice. In terms of investigation, the role of EEG (electroencephalogram) monitoring has been the focus of much interest, and the EEG patterns of different types of status. Health service studies have focused on outcome and service provision.

1.3. Treatment

Four randomized controlled trials have recently been completed in the field of status epilepticus. The first was of course the RAMPART study which was a model of how to conduct an RCT and had important findings. Although two others were negative – the trial of hypothermia and the trial of neurosteroids in super-refractory status epilepticus, both threw up a large amount of interesting data, and all three studies were discussed at length at the Colloquia. A third RCT, the ESETT study, has been completed although the results have not yet been published. The trial too was discussed at the Colloquium as well as the plans for a further study, using the same network, this time of ketamine as an anesthetic in refractory status epilepticus. Other trials on the horizon that are recently reported include the CONCEPT and ECLIPSE studies. A key to these developments has been the development of research networks which facilitate collaborative research and make such studies feasible. Such networks are increasing and are themselves, in our view, an important development. A number of new drugs have been licensed or are in late clinical development including cannabidiol, fenfluramine,

perampanel, brivaracetam, and lacosamide. There have been also interesting studies of the early use of polytherapy and ketamine. In all, the importance of treating the person underneath the status epilepticus, and not just the seizures themselves, should always be primary in our mind.

Many of these aspects were subject of discussions at the recent colloquia, and as before in the previous colloquia, the choice of program for the next meeting in April 2021 will pay great attention to those topics where research progress is currently being made.

Declaration of competing interest

The Colloquium received unrestricted educational grants and exhibitions from the following commercial sponsors: AIT, Biomarin, Cerebral Therapeutics, Ceribell, Eisai, Marinus, Neurelis, Nutricia, Engage Therapeutics, Epi-minder, Livanova, UCB, Veriton, Zoginex

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