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Editorial

A summary of data presented at the XIV conference on new antiepileptic drug and devices (EILAT XIV)

ABSTRACT

The Fourteenth Eilat Conference on New Antiepileptic Drugs and Devices (EILAT XIV) took place in Madrid, Spain from May 13th to 16th 2018. Again, presentations on new medical devices and neuromodulation and discussions on device-related regulatory aspects were included in the programme. The virtual special issue on "neuromodulation" summarises the presentations focusing firstly, on the pre-clinical developments and the difficulties of clinical trial designs for neuromodulatory therapies, including vagus nerve stimulation (VNS) and Brain-Responsive Neurostimulation (RNS), and the use of transcutaneous vagus nerve stimulation (tVNS) as a potential screening tool for determining the efficacy of neuromodulatory treatments in individual patients; secondly, on wearable devices for seizure monitoring through indices of peripheral sympathetic nervous activity, the use of such devices in combination with biofeedback for the treatment of epilepsy, and its potential for improving epilepsy specialist services, particularly in remote areas.

Neurostimulation is an emerging treatment for neurological diseases, not only for epilepsy. In many ways, the development of a therapeutic device mirrors the change in indications seen over time for the primary use of anti-seizure drugs, first licensed for the treatment of focal seizures, then subsequently approved and used for pain, anxiety or depression, which are common co-morbidities of epilepsy. Closed loop systems, currently in clinical use, generate large data-sets in individual subjects, which permits an ability to assess the significance of diurnal fluctuations, or the effects of behavioural or environmental factors on seizure frequency. The ability to detect and record seizures objectively has wider repercussions for clinical practice, and enhances our understanding of ictogenesis and factors contibuting to seizure frequency, and facilitates clinical trial designs of AEDs, best illustrated in the study by Cook et al. (2013) showing high type 1 and 2 error rates when relying on self-reported seizures. One of the purposes of the bi-annual Eilat Conference on New Antiepileptic Drugs and Devices (EILAT) is to bring together and allow for cross-talk between clinicians, scientists and industry, to discuss new compounds and treatment strategies, and for the fields of drug and device development to learn from, and influence each other.

This virtual special issue on “neuromodulation” summarises the presentations on new medical devices, and discussions on device-related regulatory aspects. It complements the summaries on drug development (Bialer et al., 2018a,b) arising from EILAT XIV, which took place from May 13th to 16th 2018 in Madrid, Spain.

Here, we focus firstly on the pre-clinical developments and the difficulties of clinical trial designs for neuromodulatory therapies, including vagus nerve stimulation (VNS) and Brain-Responsive Neurostimulation (RNS), and the use of transcutaneous vagus nerve stimulation (tVNS) as a potential screening tool for determining the efficacy of neuromodulatory treatments in individual patients; secondly, on wearable devices for seizure monitoring through indices of peripheral sympathetic nervous activity, the use of such devices in combination with biofeedback for the treatment of epilepsy, and its potential for improving epilepsy specialist services, particularly in remote areas.

Despite their proven clinical benefit in diverse disorders, such as epilepsy, mood disorders and pain, the underlying mechanisms of neuromodulatory techniques are unclear, with very little knowledge on operating aspects, like dose response curves or individual responder identification (Maxine Dibué-Adjei et al., 2019). This is in part due to the difficulties in trial design of an intervention, which claims to be “modulatory”, or disease-modifying, in addition to suppressing or stopping seizures.

Responsive methodologies could theoretically be superior to open-loop random stimulation, but this has not been shown yet in randomised controlled trials. Closed-loop systems rely on the early detection of seizures to trigger stimulation, either indirectly through specific signs of ictal cardiac dysfunction for responsive VNS (rVNS), or ictal electrocorticography (EcoG) for RNS. (Skarpaas et al., 2019) Both systems require surgical device implantation. Based on promising data from a first controlled tVNS study, future research may consider testing this non-invasive method as a screening tool for potential responders to neuromodulatory treatments. (Hamer and Bauer, 2019).

Wearable devices, like the Embrace Smart Watch, allow the unobtrusive collection of large data sets, both for clinical management with individual seizure monitoring, as well as for advancing research (Lai et al., 2019). Measuring indices of peripheral sympathetic nervous activity has also been used for therapeutic approaches, Autonomic Cognitive Rehabituation Training (ACRT), by combining measurements of galvanic skin response (GSR) with specific biofeedback therapy for epilepsy (Nagai, 2019). The “Epilepsy Network Project” illustrates how wearable seizure-detection and monitor devices can improve the provision of specialist care, in particular in remote areas, (Page, 2019).

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