Progressive myoclonus epilepsies (PMEs) are an extremely heterogeneous group of inherited disorders (<1% of all epilepsies) with different patterns of transmission, clinically characterized by the association of myoclonus, seizures and variable degree of cognitive impairment. Other focal neurological deficits may occur. Age at onset varies from infancy to adulthood and the course is progressive [1]. The most common and less severe form of PMEs is Unverricht-Lundborg disease (ULD) [2,3]. Other PMEs include Lafora disease (LD), neuronal ceroid lipofuscinoses (NCL), mitochondrial encephalopathy with ragged red fibres (MERFF) and sialidosis [4]. Tremendous advances in genetic and genomic techniques allowed to discover new PMEs in last decade. In particular, exome sequencing studies have led to a substantial reduction of unsolved cases with description of many ULD-like conditions [5]. The most recently described PMEs (including SCARB2, GOSR2, CERS, PRICKLE1, KCTD7, KCNCl) share some common clinical and neurophysiological features with the classical forms of PMEs (i.e. Unverricht-Lundborg and Lafora disease). In this scenario, physicians are required to play a challenging role, because they should not only face with novelities but also define the boundaries between the classical and the new forms of PMEs. Despite extensive investigations, many PMEs remain undiagnosed [4]. With further advances of genetic and genomic technique, it is reasonable to expect that additional forms of PMEs will be described in a few years. Treatment of PMEs is still predominantly symptomatic (i.e. pharmacological management of seizures and myoclonus) and usually relies on a combination of 2 or more antiepileptic drugs (AEDs). The majority of available data on the efficacy of AEDs in PMEs are primarily anecdotal or observational, mostly based on individual responses in small series. Valproate (VPA) is the drug of choice [6], except for PMEs associated to mitochondrial encephalopathies like MERFF, due to VPA known interaction with mitochondrial respiration and metabolism [7]. Alternatively, levetiracetam is a valid option for all PMEs [6]. Clonazepam is efficacious on myoclonus and seizures, and, therefore, it is frequently administered as add-on treatment [8]. Also zonisamide and topiramate showed promising results [9,10]. Lamotrigine should be used with caution due to its unpredictable effect on myoclonus [11]. Of interest, two recent open label series showed the efficacy of PER in ULD and LD. In the series by Goldsmith and Minassian [12], 10 LD subjects were given PER as add-on treatment, with drastically improvement of myoclonus in 7 patients and reduction of seizure frequency in 4. However, three subjects withdrew PER due to inefficacy or side effects including irritability and cognitive slowing. In the study by Crespel et al. [13], PER was given as add-on treatment to 12 ULD or ULD-like patients. Ten patients had a clear-cut reduction of myoclonus severity, and all patients with seizures experienced disappearance of attacks. Nevertheless, psychological or behavioural side-effects occurred in 50% of subjects, leading to PER withdrawal in 3 patients. Hence, PER seems to be a promising drug in patients with PMEs but close monitoring of psychiatric side effect is necessary. Drugs known to aggravate myoclonus and generalized seizures, such as carbamazepine, phenytoin and gabapentin, should of course be avoided in PMEs [14]. Gene and enzyme-replacement therapies are promising options, especially in pre-symptomatic patients. Indeed, PMEs occur in previously healthy and well-developed brains. Target therapies for the two commonest forms of PMEs (ULD and LD) are not currently available. Antisense oligonucleotides are designed to downregulate messenger RNA and may be a promising therapeutic option for some PMEs [15]. Gene therapy and enzyme-replacement therapy clinical trials for NCL are currently ongoing [16]. Further dissection of the genetic background of the different PMEs might hopefully help in the future with individualised treatment options.

Competing interests

The author declare that no competing interests exist.

References


*Corresponding Author: Dr. Edoardo Ferlazzo, Department of Medical and Surgical Sciences, Magna Graecia University, Viale Europa, 88100 Catanzaro CZ, Italy; Email: ferlazzo@unicz.it


Copyright: © 2016 Ferlazzo. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.


