CHANNEL DISORDERS OF NERVE AND MUSCLE

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Ion channels are integral trans-membrane proteins which regulate ion flows through the nerve and muscle membrane. They play such a key-role in the generation and propagation of action potentials that it was long thought that mutations in their genes would be lethal. We now know that mutations in ion channel genes cause nerve and muscle diseases which have in common to manifest as episodes often provoked by environmental factors. Mutations in genes encoding ion channels modify the subtle equilibrium of muscle excitability. The link between abnormal channels' functioning and membrane excitability is well understood for chloride and sodium channel mutations. It however remains mysterious for some of the sodium channel- and calcium channel mutations. Modifications in the membrane state of excitability cause symptoms: stiffness (myotonia), weakness (periodic paralysis) or ataxia (episodic ataxia). Ion channels are not the only proteins which, when mutated, give rise to an abnormal membrane excitability. Attention has been recently attracted to components of the extra-cellular matrix, such as perlecan, which, when mutated, causes Schwartz-Jampel syndrome, a severe form of myotonia. Improvements have been recently achieved in the diagnosis. Exercise tests coupled to electromyography increase the sensitivity of the diagnostic procedure and enable to predict groups of mutations which can be subsequently detected by molecular diagnosis. Clinical and paraclinical investigations of these rare disorders have improved through collaborative networks and reference centers for rare disease which are appropriate structures both for the care and research on these rare disorders.