Channelopathies associated with ion channels localized in **brain**

- Voltage-gated Ca^{++} channels

Disorder	Clinical characteristics	Type of mutation	Notes
Familial Hemiplegic Migraine (FHM)	• **Migraine attacks** - typicallylast one to three days. - Duringsuch episodes, patients experience severeheadaches and vomiting.	• Several mutationsin a human Ca2+ channel have been identified in families with FHM, each having different clinical symptoms. • A mutation in the **pore-forming region** of the channel produces hemiplegic migraine with progressive cerebellar ataxia. • Other mutations cause only the usual FHM symptoms.	How these altered Ca2+ channel properties lead to migraine attacks is not known.
Episodic **Ataxia type 2** (EA2)	• Recurrent attacks of abnormal **limb movements** and severe **ataxia**. - sometimes accompanied by vertigo, nausea, and headache - usually attacks are precipitated by emotional stress, exercise, or alcohol - last for a few hours.	• Truncation of Ca2+ channels at various sites, which prevents the normal assembly of Ca2+ channels in the membrane.	
X-Linked Congenital Stationary Night Blindness (CSNB)	• Nightblindness, decreased visual acuity, myopia, nystagmus, and strabismus.	• **Incomplete type** of CSNB is caused by mutations producing **truncated Ca2+ channels**. **Abnormal retinal function** may arise from decreased Ca2+ currents and neurotransmitter release from photoreceptors.	• recessive retinaldisorder • **Complete CSNB**causes retinal rod photoreceptors to be **nonfunctional**. • **Incomplete** CSNB causes **subnormal** (but measurable) functioning of both rod and cone photoreceptors

- Voltage-gated K^+channels

Disorder	Clinical characteristics	Type of mutation	notes
benign familial neonatal convulsion (BFNC),	• frequent **brief seizures** • commencing within the first week of life • disappearingspontaneously withina few months.	• The mutation has been mapped to at least two voltage-gated K+ channel genes.	Areduction in K+ currentflow through the mutated channels probablyaccounts for the **hyperexcitability**associated with this defect.
episodic ataxia **type 1** (EA1),	• brief episodes of **ataxia**		Mutantchannels inhibit the function ofother, non-mutant K+ channels and mayproduce clinical symptoms by impairingaction potential repolarization.

- Voltage-gated Na^+channels

Disorder	Clinical characteristics	Type of mutation	notes
generalized epilepsy with febrile seizures(GEFS)	- begins in infancy - usually continues through early puberty	mapped to two mutations: • one on chromosome 2 that encodes an α-subunit for a voltage-gated Na+ channel • the other on chromosome 19 that encodes a Na+ channel β-subunit.	These mutations cause a slowing of Na+ channel inactivation which may explain the neuronal**hyperexcitability** underlying GEFS.

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