Supplementary material

Single genes: Although variants in some single genes are reported to cause some of GGE/IGE syndromes, they are not likely to be a common cause. Some variants in GABA receptors, such as *GABRG2* and *GABRA1* genes are associated with childhood absence epilepsy and IGE. (Wallace *et al*., 2001; Lachance-Touchette *et al*., 2011) Mutations in *SLC2A1* encoding the sole transporter of glucose into brain GLUT1 is associated with epileptic syndromes, and milder forms of GLUT1 deficiency may lead to otherwise typical GGE/IGE syndromes (Arsov *et al*., 2012). Other mutations mainly causing channelopathies have been described in case series or small family studies (*see table 1 for a comprehensive list*). It is also important to keep in mind that some single gene disorders may mimic GGE/IGE syndromes. Progressive myoclonic epilepsies, such as Unverricht-Lundborg disease, may mimic JME until additional clinical features such as ataxia set in (Amrom *et al*., 2014)

Complex genetics: Copy number variants are defined as deletions and duplications of chromosomal segments and believed to play an important role in diseases with complex inheritance. Deletions on the long arm of chromosome 15 (15q13.3, 15q11.2) and short arm of chromosome 16 (16p13.11) have been associated with IGE/GGE syndromes, however, these variants can also be detected in healthy individuals (Helbig *et al.*, 2009; de Kovel *et al.*, 2010). Therefore, they are likely to be risk factors more than causative agents in GGE/IGE syndromes. Genome-wide associations and linkage analysis is a more sophisticated method to try to understand a disease with complex genetics. This requires a huge number of cases and a similar control group in order to determine single nucleotide polymorphisms (SNPs). Many SNPs have been associated with IGE/GGE syndromes, but relatively low replicability of the results connote an important limitation to generalizability of the findings.

Gene/locus	Inheritance	Associated clinical syndrome	References
2q33-q36	AD	Susceptibility to JME	(Ratnapriya *et al*., 2010)
5q12-q14	AD	JME	(Kapoor *et al*., 2007)
6p21	?	JME	(Greenberg *et al*., 1988)
8q24	AD	Susceptibility to GGE, CAE	(Zara *et al*., 1995)
9q32-33	AR	Susceptibility to GGE	(Baykan *et al*., 2004)
10p11.22	?	Susceptibility to GGE	(Kinirons *et al*., 2008)
10q25-q26	?	Susceptibility to GGE	(Puranam *et al*., 2005)
14q23	?	Susceptibility to GGE	(Sander *et al*., 2000)
15q14	AR	JME, Susceptibility to GGE	(Helbig *et al*., 2009; Dibbens *et al*., 2009)
BRD2	?	SNPs associated with susceptibility to JME	(Pal *et al*., 2003)
CACNA1A	?	SNPs associated with susceptibility to GGE	(Lee *et al*., 2018; Chioza *et al*., 2001)
CACNA1H	?	Susceptibility to CAE, GGE	(Chen *et al*., 2003; Vitko *et al*., 2005; Heron *et al*., 2004)
CACNB4	AD	Susceptibility to JME, GGE	(Escayg *et al*., 2000)
CACNG3	?	Susceptibility to CAE	(Everett *et al*., 2007)
CASR	?	Susceptibility to JME	(Kapoor *et al*., 2008)
CHRFAM7A	?	Lowers risk for IGE	(Rozycka *et al*., 2013)
CHRNA7	?	JME, susceptibility to GGE	(Elmslie *et al*., 1997)
CLCN2	AD	Susceptibility to JME, JAE, GTCS, GGE	(Haug *et al*., 2009) (Retracted in 2009)
CPA6	AD, AR, ?	Susceptibility to JME, GGE	(Sapio *et al*., 2015)
del15q11.2	?	Susceptibility to GGE	(de Kovel *et al*., 2010)
del16p13.11	?	Susceptibility to GGE	(de Kovel *et al*., 2010)
EFHC1	AD	Susceptibility to JME, JAE	(Suzuki *et al*., 2004; Stogmann *et al*., 2006)

EFHC2	?	Associated with JME	(Gu *et al*., 2005)
GABRA1	?	Susceptibility to JME, CAE	(Cossette *et al*., 2002; Johannesen *et al*., 2016; Maljevic *et al*., 2006; Lachance-Touchette *et al*., 2011)
GABRA6	?	Risk factor for IGE, CAE	(Prasad *et al*., 2014; Hernandez *et al*., 2011)
GABRB3	?	Susceptibility to CAE	(Urak *et al*., 2006; Tanaka *et al*., 2008)
GABRD	AD	GGE, JME susceptibility	(Dibbens *et al*., 2004)
GABRG2	AD	Associated with CAE	(Tian and Macdonald, 2012)
GJD2	?	SNPs associated with susceptibility to JME	(Mas *et al*., 2004)
ADGRV1	?	Susceptibility to GGE	(Lee *et al*., 2018)
GRM4	?	SNPs associated with susceptibility to JME	(PARIHAR *et al*., 2014)
ICK	AD	Susceptibility to JME	(Bailey *et al*., 2018)
JH8 (JRK)	?	Associated with CAE	(Moore *et al*., 2001)
KCNJ10	?	Susceptibility to GGE	(Dai *et al*., 2015; Phani *et al*., 2014)
KCNMA1	AD	Susceptibility to GGE	(Lee *et al*., 2018; Li *et al*., 2018)
KCNMB3	?	GGE, especially with absences	(Lorenz *et al*., 2007)
LGI4	?	Susceptibility to GGE	(Gu *et al*., 2004)
ME2	?	SNPs associated with susceptibility to JME, GGE	(Greenberg *et al*., 2005)
NEDD4L	?	Associated with JME with PS	(Dibbens *et al*., 2007)
NIPA2	?	Haploinsufficiency may cause CAE	(Jiang *et al*., 2012)
RORB	AD	Susceptibility to GGE	(Rudolf *et al*., 2016)
SCN1A	?	Associated with JME	(Binini *et al*., 2017; Chan *et al*., 2019)
SLC12A5	AD	Susceptibility to GGE	(Kahle *et al*., 2014)
SLC2A1	AD	Susceptibility to GGE	(Striano *et al*., 2012)
SYN2	?	Risk factor for IGE	(Prasad *et al*., 2014; Lakhan *et al*., 2010)
SYT11	?	Possible association with GGE	(Yilmaz *et al*., 2014)
TOP3B	?	SNPs associated with susceptibility to JME	(Daghsni *et al*., 2018)
TRPC4	?	SNPs associated with GGE+PS	(Von Spiczak *et al*., 2010)
VAMP2	?	Possible association with GGE	(Yilmaz *et al*., 2014)

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