**Table 2. ASD and SCHZ genes implicated in synaptic activity**

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| --- | --- | --- | --- | --- |
| **Gene** | **Name** | **Function** | **Risk / other** | **References** |
| **Neurotransmission** | | | | |
| *GRIN2B* | Glutamate receptor, ionotropic, NMDA 2B | Glutamate neurotransmission | ASD, high de novo mutations | (73) |
| *GRIN2A* | Glutamate receptor, ionotropic, NMDA 2A | Glutamate neurotransmission | SCHZ variants | (40) |
| *GRM3* | Metabotropic Glu receptor 3 | Glutamate neurotransmission | SCHZ variants | (67) |
| *GRIA1* | Glutamate receptor 1 | Glutamate neurotransmission | SCHZ variants | (67) |
| *SRR* | Serine racemase | Glutamate neurotransmission | SCHZ variants | (67) |
| *GABRA3* | GABA receptor subunit alpha-3 | GABA neurotransmission | ASD, high de novo mutations | (97) |
| *GABRB3* | GABA receptor subunit beta-3 | GABA neurotransmission | ASD, de novo mutations | (98) |
| *GABRA4,5* | GABA receptor subunits alpha-4 and 5 | GABA neurotransmission | ASD, de novo mutations | (99, 100) |
| *GABRG3* | GABA acid receptor subunit gamma-3 | GABA neurotransmission | ASD, de novo mutations | (99, 100) |
| *GABRB1* | GABA receptor beta-1 | GABA neurotransmission | ASD, de novo mutations | (99, 100) |
| *GABRQ* | GABA receptor theta | GABA neurotransmission | ASD, de novo mutations | (97) |
| *GLYRA2* | Glycine receptor subunit α2 | Glycine neurotransmission | ASD, de novo mutations | (101) |
| *DRD2* | Dopamine receptor D2 | Main target of anti-psychotic drugs | SCHZ, several mutations | (56) |
| *STXBP5* | Syntaxin –binding protein 5 | docking / fusion of synaptic vesicles with presynaptic membrane | ASD, de novo mutations | (102) |
| *SYTL4* | Synaptotagmin-like 4 | Regulates exocytosis of dense-core granules | ASD, de novo mutations | (97) |
| ***Ion Channels*** | | | | |
| *CACNA1C* | voltage-dependent calcium channel subunit α1 | Activity-dependent transcriptional regulation | ASD + SCHZ + Timothy syndrome | (35) |
| *CACNAD3* | voltage-dependent calcium channel subunit δ 3 | Activity-dependent transcriptional regulation regulatory subunit | ASD, de novo mutations | (35) |
| *CACNB2* | Voltage-dependent L-type Ca channel subunit beta-2 | Activity-dependent transcriptional regulation | SCHZ mutations | (35) |
| *CACNA1I* | Voltage-dependent T-type Ca channel subunit alpha-1I | Activity-dependent transcriptional regulation Pacemaker, modulation of firing patterns of neurons | SCHZ mutations | (67) |
| *CACNA1S* | Voltage-dependent L-type Ca channel alpha-1S | Activity-dependent transcriptional regulation | ASD + SCHZ de novo mutations | (35) |
| *SCN1A, SCN2A* | Sodium channel protein types α 1 and 2 | voltage-dependent sodium ion permeability, sensory perception of mechanical pain | ASD, de novo mutations | (72, 73) |
| *CLCN6* | Chloride channel, voltage sensitive 6 | Voltage-gated Cl channel | ASD + lysosome storage disorder | (103) |
| *KCNMA1* | Potassium large conductance calcium-activated channel, subfamily M, alpha 1 | Potassium channel activated by membrane depolarization and increase in cytosolic Ca2+ | ASD + epilepsy | (57) |
| *KCND2* | Potassium voltage-gated channel, Shal-related 2 | Regulates circadian rhythm in suprachiasmatic nucleus, which regulates circadian rhythm of locomotor activity | ASD + cardiovascular disease | (104) |
| *KCNV1* | Potassium channel V 1 | Modulates KCNB1 and KCNB2 channel activity | ASD, de novo mutations | (105) |
| **Scaffold/cytoskeleton** | | | | |
| *SHANK3* | SH3 and multiple ankyrin repeat domain protein 3 | Postsynaptic density adapter between NMDA and metabotropic Glut receptors and actin-based cytoskeleton | ↑ ASD + Phelan-McDermid Syndrome | (106) |
| *SHANK1, 2* | SH3 and multiple ankyrin repeat domain proteins 1, 2 | Postsynaptic density adapter between NMDA and metabotropic Glut receptors and actin-based cytoskeleton | ASD + SCHZ, de novo mutations | (72) (40) |
| *ACTN1* | Alpha actinin 1 | F-actin cross-linking protein | SCHZ de novo mutations | (40) |
| *ANK2, 3* | Ankyrin-2 and 3 | Attachment of membrane proteins to cytoskeleton | ASD, de novo mutations | (89, 96) |
| *ANK1* | Ankyrin-1 | Attachment of membrane proteins to cytoskeleton | SCHZ de novo mutations | (40) |
| *GPHN* | gephyrin | Microtubule-associated protein, anchors glycine receptor to subsynaptic microtubules | ASD in exonic deletions | (107) |
| *CLTCL1* | Clathrin, heavy chain-like 1 | Intracellular endosome trafficking, distribution of glucose receptor | ASD, de novo mutations | (108) |
| *DCTN5* | Dynactin 5 | Axona transport | ASD, de novo mutations | (73) |
| *KIF1A* | Kinesin-like protein 1A | Motor for anterograde axonal transport of synaptic vesicle precursors | SCHZ de novo mutations | (40) |
| *KIF18A* | Kinesin-like protein KIF18A | Motor for anterograde axonal transport of synaptic vesicle precursors | SCHZ de novo mutations | (40) |
| *BAIAP2* | Brain-specific angiogenesis inhibitor 1-associated protein 2 | Adaptor protein, reorganization of cytoskeleton | SCHZ de novo mutations | (40) |
| *BRSK1* | Serine threonine kinase | localizes to synaptic vesicles and regulates neurotransmitter release by phosphorylating RIMS1, phosphorylates Tau | SCHZ de novo mutations | (40) |
| *DLG1, 2* | Disk-large homologue 1, 2 | Membrane scaffolding, key component of post-synaptic density complex (PSD) | SCHZ de novo mutations | (35) |
| *EPB41, EPB41L1* | Protein 4.1 and Band 4.1-like protein | PSD complex | SCHZ de novo mutations | (40) |
| *GIT1* | ARF GTPase-activating protein | scaffold for signaling modules controlling vesicle trafficking, adhesion and cytoskeletal organization, PSD | SCHZ de novo mutations | (40) |
| *ITSN1* | Intersectin 1 | guanine nucleotide exchange factor (GEF), adapter protein, PSD complex | SCHZ de novo mutations | (40) |
| *MYH11, MYH9* | Myosin 9 and 11 | Cytoskeleton, PSD complex | SCHZ de novo mutations | (40) |
| *MYO18A* | Unconventional myosin 18A | Cytoskeleton, PSD complex | SCHZ de novo mutations | (40) |
| *NCKIPSD* | NCK-interacting protein with SH3 domain | regulation of actin polymerization and cell adhesion, PSD complex | SCHZ de novo mutations | (40) |
| *PTK2B* | Protein tyrosine kinase 2 beta | Non-receptor regulates reorganization of the actin cytoskeleton | SCHZ de novo mutations | (40) (35) |
| *RIMS1* | Regulating synaptic membrane exocytosis protein 1 | scaffold protein that regulates neurotransmitter release at the active zone, PSD complex | SCHZ de novo mutations | (40) |
| *SORBS2* | Sorbin and SH3 domain-containing protein 2 | Adapter protein, assembly of signaling complexes, link between ABL kinases and actin cytoskeleton | SCHZ de novo mutations | (40) |
| *SRCIN1* | SRC kinase signaling inhibitor 1 | negative regulator of SRR, regulates dendritic spine morphology. Involved in calcium-dependent exocytosis | SCHZ de novo mutations | (40) |
| *UNC13A* | Protein UNC-13 homologue A | Synaptic vesicle maturation in most excitatory/glutamatergic synapses | SCHZ de novo mutations | (40) |
| *YWHAZ* | 14-3-3 protein zeta/delta | Adapter protein, PSD complex | SCHZ de novo mutations | (40) |
| ***Cell adhesion/signaling*** | | | | |
| *CNTN6* | Contactin -6 | Cell surface interactions, regulates Notch signaling | ASD, de novo mutations | (109) |
| *NLGN3, 4* | Neuroligin 3, 4 | Cell surface interactions, regulates synapse function and synaptic transmission | ASD, de novo mutations | (110) |
| *NRXN1* | Neurexin 1 | Cell surface interactions, regulation of Ca+ signaling | ASD + SCHZ de novo mutations | (40) (35) |
| *CNTNAP2* | Contactin-associated protein-like 2 | Neuron-glia interaction, K+ channel clustering | ASD + Gilles de la Tourette syndrome | (111) |
| *EPHB2, -6* | Ephrin receptor B6 | Receptor tyrosine kinase binds transmembrane ephrin-B on adjacent cells. regulates axon guidance, dendritic spines and formation of excitatory synapses | ASD, de novo mutations | (18, 73) |
| *LPHN2* | Adhesion G protein-coupled receptor L2 | Calcium-independent Receptor implicated in the regulation of exocytosis. | SCHZ de novo mutations | (40) |
| *NFASC* | Neurofascin | Cell adhesion, ankyrin-binding protein | SCHZ de novo mutations | (40) |
| *PLXNA1* | Plexin-1A | Semaphorin receptor and actin remodeling | SCHZ de novo mutations | (40) |

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