Name	*Gene symbol*	OCD	Anxiety	Behavioral disorder	Depression	Psychosis	Aggressive behavior	ASD	Hyperactivity	Other	Laboratory investigations	Specific treatment	Representative references PMID
DISORDERS OF NITROGEN-CONTAINING COMPOUNDS													
Disorders of pyrimidine metabolism													
Pyrimidine 5'-nucleotidase superactivity	*NT5C3A*								x		Uric acid (U)	Uridine, possibly ribose	9326656
Disorders of purine metabolism													
Adenosine deaminase deficiency	*ADA*			x					x		Purines (U)	ERT, HSCT, gene therapy	11445793
Adenylosuccinate lyase deficiency	*ADSL*							x			Purines (CSF, U)		6150139
Hypoxanthine guanine phosphoribosyltransferase deficiency	*HPRT1*	x	x	x			x			Self-harm	Uric acid (U, P), Purines (U)	Allopurinol	20176575, 1086851
Disorders of nucleotide and nucleic acid metabolism													
TREX1 deficiency	*TREX1*		x		x	x					ASAT/ALAT (P), pterins (CSF)		27604306, 31536185
Disorders of creatine metabolism													
Arginine:glycine amidinotransferase deficiency	*GATM*			x							Creatinine (P, U), Guanidino compounds (P, U)	Creatine supplementation	20301745
Guanidinoacetate methyltransferase deficiency	*GAMT*			x			x	x	x		Creatinine (P, U), Guanidino compounds (P, U)	Creatine and ornithine supplementation, arginine restriction	24268530
Creatine transporter deficiency	*SLC6A8*	x					x	x	x		Creatinine (P, U), Guanidino compounds (P, U)	Creatine, arginine and glycine supplementation	23644449
Disorders of glutathione metabolism													
Gamma-glutamylcysteine synthetase deficiency	*GCLC*					x					Hemoglobin (B), Reticulocytes (B), Glutathione (RBC)	Avoid drugs that precipitate hemolytic crisis in G6PD deficiency (phenobarbital, acetylsalycicliс acid, sulfonamides)	4852017
Gamma-glutamyl transpeptidase deficiency (glutathionuria)	*GGT1*			x			x				Glutathione (RBC, P, U); Leukotrienes (P)		6118466
Disorders of ammonia detoxification													
Carbamoylphosphate synthetase I deficiency	*CPS1*					x	x	x	x	Agitation	Ammonia (B), ASAT/ALAT (P), Urea (P), Amino acids (P)	Protein restriction, ammonia scavengers, citrulline, liver transplant	28725569, 21642480, 19684305
Ornithine transcarbamylase deficiency	*OTC*	x		x	x	x			x	Agitation, delirium	Ammonia (B), ASAT/ALAT (P), Urea (P), Amino acids (P), Orotic acid (U)	Protein restriction, ammonia scavengers, citrulline, liver transplant	28725569, 19684305
Argininosuccinate synthetase deficiency	*ASS1*					x			x	Delirium	Ammonia (B), ASAT/ALAT (P), Urea (P), Amino acids (P), Orotic acid (U)	Protein restriction, ammonia scavengers, arginine, liver transplant	20005624, 15863597, 19684305
Disorders of amino acid transport													
Hartnup disorder	*SLC6A19*		x		x	x					Amino acids (U)	Dietary niacin, high quality protein diet (tryptophan), oral nicotinamide 50-300 mg/day	13271980, 14401403
Dicarboxylic aminoaciduria	*SLC1A1*	x				x					Amino acids (U)		23341099, 23695234
SLC6A17 deficiency	*SLC6A17*						x				DNA		25704603
Large neutral amino acid transporter light chain deficiency	*SLC7A5*							x			Amino acids (P, CSF)	Branched-chain amino acids?	27912058
Disorders of monoamine metabolism													
Dopamine beta-hydroxylase deficiency	*DBH*			x							Biogenic amines (CSF, U)	L-dihydroxyphenylserine (L-DOPS) 100-500 mg po BID or TID	1677640
Monoamine oxidase A deficiency	*MAOA*				x		x	x	x		Biogenic amines (P, U)	Serotonin reuptake inhibitors?	8613523, 24169519, 25807999, 11700166
Dopamine transporter deficiency	*SLC6A3*							x	x	Lack of impulse control	Biogenic amines (CSF, U)		24911152
Disorders of phenylalanine and tetrahydrobiopterin metabolism													
Phenylketonuria	*PAH*		x		x			x			Amino acids (P)	Phe-restricted diet, large neutral amino acids, glycomacropeptide, sapropterin, pegvaliase	21274394, 20123472, 10682302, 28285739, 31551819
Autosomal dominant GTP cyclohydrolase I deficiency	*GCH1*	x	x		x					Panic attacks	Pterins (DBS, U), Biogenic amines (CSF)	L-dopa/carbidopa	19332422, 16361586, 11346370
6-Pyruvoyl-tetrahydropterin synthase deficiency	*PTS*	x		x			x	x		Panic attacks	Amino acids (P), Pterins (DBS, U), Biogenic amines (CSF)	BH4, L-dopa/carbidopa, 5 hydroxytryptophan	30746422, 16601879, 16161143, 21777827
Sepiapterin reductase deficiency	*SPR*	x	x		x	x	x		x	Irritability	Pterins (DBS, U), Biogenic amines (CSF)	BH4, L-dopa/carbidopa, 5 hydroxytryptophan +/- SSRI, dopa-agonist, MOAI, melatonin, dopa-, noradrenaline reuptake inhibitor	11443547, 22522443
Dihydropteridine reductase deficiency	*QDPR*						x		x		Amino acids (P), Pterins (DBS, U), Biogenic amines (CSF), 5-methyl-THF (CSF)	Low Phe, L-dopa, 5-hydroxytryptophan, folinic acid	29594939
DNAJC12-deficient hyperphenylalaninemia	*DNAJC12*							x			Amino acids (P), Biogenic amines (CSF); DNA	BH4, L-dopa/carbidopa, 5 hydroxytryptophan	28132689
Disorders of sulfur amino acid and sulfide metabolism													
Cystathionine beta-synthase deficiency	*CBS*	x	x	x	x	x					Amino acids (P); Homocysteine (P)	Methionine restricted diet, pyridoxine 10 mg/day (max 500 mg/day), betaine 100 mg/kg in children, 6 g in adults divided BID	25939413, 12585732, 3965612, 3591841, 30643218
S-adenosylhomocysteine hydrolase deficiency	*AHCY*	x		x			x		x		Amino acids (P); Homocysteine (P); S-Adenosylcysteine (P)	Methionine or protein restricted diet, phosphatidylcholine and creatine supplements, liver transplant	26095522, 16736098
Disorders of branched-chain amino acid metabolism													
Maple syrup urine disease	*BCKDHA, BCKDHB, DBT*	x	x		x			x	x		Amino acids (P); Organic acids (U)	Low BCAA diet; isoleucine/valine supplementation	30023285, 23478409
HSD10 disease	*HSD17B10*			x		x	x				Organic acids (U)		10521307
Branched-chain ketoacid dehydrogenase kinase deficiency	*BCKDK*							x			Amino acids (P)	Branched-chain amino acids?	22956686
Propionic acidemia	*PCCA, PCCB*					x		x			Amino acids (P), Organic acids (U), Acylcarnitines (DBS, P)	Low protein diet, carnitine	28856627, 24334345, 27825584, 22156789
Disorders of β- and γ-amino acids													
Dihydropyrimidine dehydrogenase deficiency (Thymine-uraciluria)	*DPYD*							x	x		Purines and pyrimidines (U, P)	No treatment in pediatrics, in adults discontinue fluorouracil treatment	10071185, 19296131, 6488556
Succinic semialdehyde dehydrogenase deficiency	*ALDH5A1*	x	x			x	x	x	x		Organic acids (U)	Benzodiazepines, vigabatrin, ongoing trial with GABAB receptor antagonist SGS-742 (NCT02019667)	26806207, 14512218, 19172412, 18622364
Disorders of glycine metabolism													
Glycine encephalopathy due to glycine decarboxylase deficiency	*GLDC*			x			x	x	x	Delirium, agitation	Amino acids (P, CSF)	Na benzoate 250-750 mg/kg/day, divided in 3-6 doses, dextrometorphan 3-15 mg/kg/day, avoid high dietary gelatin, high protein	22002442, 26749113, 8636821, doi:10.1093/med/9780199972135.003.0030
Glycine encephalopathy due to aminomethyltransferase deficiency	*AMT*							x	x		Amino acids (P, CSF)	Na benzoate 250-750 mg/kg/day, divided in 3-6 doses, dextrometorphan 3-15 mg/kg/day, avoid high dietary gelatin, high protein	22002442
DISORDERS OF VITAMINS, COFACTORS, METALS AND MINERALS													
Disorders of cobalamin metabolism													
Amnionless deficiency	*AMN*						x				Homocysteine (P); Organic acids (U); Vitamin B12 (S)	Hydroxycobalamin IM	18181028
cblC disease	*MMACHC*				x	x					Homocysteine, total (P), B12 (S), Blood count, Organic acids (U), Acylcarnitines (DBS, P), Amino acids (P)	Hydroxycobalamin, betaine	25367534, 28218226, 14568819
Disorders of folate metabolism													
Methylenetetrahydrofolate reductase deficiency	*MTHFR*				x	x					Amino acids (P); Homocysteine (P); 5-Methyltetrahydrofolate (CSF), Folate (S)	Betaine 2-3 g/day divided in BID, to 6-9 g/day in adults, +/- folic acid, methionine, pyridoxine, cobalamin, carnitine	29391032, 18356252, 28241805, 1117892, 8006671, 18854913, 24797679, 26025547
Folate receptor alpha deficiency	*FOLR1*						x	x			5-Methyltetrahydrofolate (CSF), Folate (S)	Folinic acid 5-15 mg/day	22586289

Name	*Gene symbol*	OCD	Anxiety	Behavioral disorder	Depression	Psychosis	Aggressive behavior	ASD	Hyperactivity	Other	Laboratory investigations	Specific treatment	Representative references PMID
Disorders of copper metabolism													
Wilson's disease	*ATP7B*			x	x	x	x			Disinhibition, apathy, bipolar	Copper (S, U); Ceruloplasmin (S); DNA	Penicillamine 750-1500 mg/day in adults, (10 mg/kg/day in children) divided in 2-3 doses together with 25 mg pyridoxine ; trientine 900-2500 mg/day in adults divided in 2-3 doses; zinc sulphate 600 mg/day divided in 3 doses in adults	29977520, 7872138, 28681670, 19559640, 18305288, 24120023
Disorders of pantothenate metabolism													
Pantothenate kinase-associated neurodegeneration (PKAN)	*PANK2*	x			x	x				Violent outbursts, impulsivity, Tourette's	Iron (brain), DNA	Possible iron chelation, possible panthotenate	21769749, 2914882, 14531762, 15834858, 15911822, 18981035
Coenzyme A synthase deficiency (CoPAN)	*COASY*	x			x						Acylcarnitines (DBS); Iron (brain)		24360804
Disorders of iron metabolism													
Neuroferritinopathy	*FTL*		x		x	x					DNA		18854324, 16116125, 15390032, 27022507
Disorders of zinc metabolism													
Acrodermatitis enteropathica	*SLC39A4*				x					Irritability	Zinc (S); ALP (P)	Zinc po 150-400 Zn sulfate/day (35-90 mg elemental Zn)	6413773
Disorders of manganese metabolism													
ATP1A1 deficiency	*ATP1A1*							x			Magnesium (P, U)	Magnesium supplementation	30388404
DISORDERS OF CARBOHYDRATES													
Disorders of carbohydrate transport and absorption													
Brain glucose transporter SLC45A1 deficiency	*SLC45A1*	x	x	x				x		Echolalia	Glucose (P, CSF)	Ketogenic diet	28434495
Disorders of the pentose phosphate pathway and polyol metabolism													
Ribose-5-phosphate isomerase deficiency	*RPIA*			x			x				Polyols (U, P, CSF)		28801340
Transketolase deficiency	*TKT*	x							x		Polyols (U, P, CSF); Sugar phosphates (U)	Investigational: thiamine, benfotiamine	27259054
MITOCHONDRIAL DISORDERS OF ENERGY METABOLISM													
Disorders of complex III assembly													
TTC19 deficiency	*TTC19*	x	x		x	x					DNA		23532514
Disorders of mitochondrial DNA depletion, multiple DNA deletion, or intergenomic communication													
Mitochondrial DNA polymerase γ catalytic subunit deficiency	*POLG*		x		x	x	x				Lactate (P), ASAT/ALAT (P)		21654874, 16080118, 22579150
Disorders of mitochondrial tRNA													
Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like epi	*MT-TL1 (and others)*		x	x	x	x				Phobias	Lactate (P)		22579150, 22403016, 9598702, 9285090, 2333139, 25639022
Disorders of mitochondrial fission													
MSTO1 deficiency	*MSTO1*		x		x	x		x		Impulsivity	Lactate (P)		28554942
Disorders of mitochondrial phospholipid metabolism													
MEGDEL Syndrome	*SERAC1*			x						Self-harm	Lactate (P); Organic acids (U); Filipin staining		25345337
Disorders of mitochondrial protein import													
TIMM50 deficiency	*TIMM50*						x		x		Lactate (P); Organic acids (U)		27573165, 27573165
Disorders of mitochondrial protein quality control													
Pitrilysin metallopeptidase 1 deficiency	*PITRM1*	x				x					Lactate (P); Pyruvate (P); CK (P), LDH (P)		26697887, 29764912
USP9X deficiency	*USP9X*	x		x			x	x			DNA		24607389
Other disorders of mitochondrial homeostasis													
MICU2 deficiency	*MICU2*								x		DNA		29053821
DISORDERS OF LIPIDS													
Disorders of carnitine metabolism													
ε-N-trimethyllysine hydroxylase deficiency	*TMLHE*							x			γ-Butyrobetaine (U, P, CSF)	L-Carnitine	22566635, 25943046
γ-Butyrobetaine hydroxylase deficiency	*BBOX1*								x		γ-Butyrobetaine (U, P, CSF)	L-Carnitine	24986124
Disorders of non-mitochondrial phospholipid metabolism													
Phospholipase A2 group 6 deficiency	*PLA2G6*			x	x	x		x	x	Impulsivity	DNA		18799783, 30619057, 28549837
Fatty acid 2-hydroxylase deficiency	*FA2H*		x		x						DNA		28017243
Fatty acid amide hydrolase 2 deficiency	*FAAH2*		x		x			x			DNA		25885783
Disorders of cholesterol biosynthesis													
CK syndrome (NSDHL deficiency)	*NSDHL*			x			x		x	Irritability	Sterols (P)		19842190
7-dehydrocholesterol reductase deficiency (SLO)	*DHCR7*						x	x	x	Irritability, self-injury	Cholesterol (P); Sterols (P)	Dietary supplementation of cholesterol 25-300 mg/kg/day, +/- bile acids	23538569, 10899806, 17974928, 16761297, 8259166, 11223857
Disorders of steroid metabolism													
Steroid sulfatase deficiency	*STS*					x		x			Maternal unconjugated estriol (S)		18413370, 28934990, 30768640
Disorders of bile acid synthesis													
Cerebrotendinous xanthomatosis	*CYP27A1*		x	x	x	x	x		x	Irritability	Cholesterol (P); Sterols (P)	Chenodeoxycholic acid 750 mg/day (adults), HMG-CoA reductase inhibitors, low density lipoprotein apheresis	3344851, 6886686, 12141707, 20414172, 24002088
DISORDERS OF TETRAPYRROLES													
Disorders of heme metabolism													
Aute Intermittent porphyria	*HMBS*		x		x	x	x				Porphyrins (U); Porphobilinogen (U), Delta-ALA (U); DNA	Intravenous hemin (haem arginate or haematin) 3-4 mg/kg OD x 4days; carbohydrate infusion Dextrose 10%; liver transplantation	27407502, 4073306, 8657842, 16910386, 20844651, 24763782, 9120442
Coproporphyrinogen oxidase deficiency	*CPOX*				x	x					Porphyrins (U); Porphobilinogen (U), Delta-ALA (U); DNA	Intravenous hemin (haem arginate or haematin) 3-4 mg/kg OD x 4days; carbohydrate infusion Dextrose 10%; liver transplantation	22454794, 24687017, doi.org/10.14740/jh315w
Protoporphyrinogen oxidase deficiency	*PPOX*					x					Porphyrins (U); Porphobilinogen (U), Delta-ALA (U); DNA	Intravenous hemin (haem arginate or haematin) 3-4 mg/kg OD x 4days; carbohydrate infusion Dextrose 10%; liver transplantation	doi.org/10.1016/S0957-5847(98)80041-3
STORAGE DISORDERS													
Neuronal ceroid lipofuscinosis													
CLN3 disease	*CLN3*		x		x	x	x				DNA	In trial gene therapy (NCT03770572)	15634309, 16542512, doi: 10.1055/s-0031-1274053
CLN4 disease	*DNAJC5*	x	x	x	x						DNA		21820099, 22235333
CLN6 disease	*CLN6*	x		x	x						DNA		28587997
ATP13A2 deficiency	*ATP13A2*			x		x				Hypersexuality	DNA		20683840, 30713959
Sphingolipidoses													
GM1 gangliosidosis	*GLB1*	x	x		x		x	x	x		Enzyme (DBS, L, F), Oligosaccharide (U)	In trial gene therapy (NCT03952637)	31497487
Beta-hexosaminidase alpha subunit deficiency (Tay-Sachs disease)	*HEXA*	x		x		x					Enzyme (DBS, L, F), Oligosaccharide (U)		9547461, 15714079, 7635850, 17015493
Beta-hexosaminidase beta subunit deficiency (Sandhoff disease)	*HEXB*			x				x			Enzyme (DBS, L, F), Oligosaccharide (U)		17015493, 15159655
Arylsulfatase A deficiency (metachromatic leukodystrophy)	*ARSA*			x		x					Enzyme (DBS, L, F), Protein (CSF), Sulfatides (U)	Hematopoietic stem cell transplantation (HSCT)	12445909, 1532712, 15644995
Metachromatic leukodystrophy-like disorder due to saposin B deficiency	*PSAP*			x	x		x				Sulfatides (U); Protein (CSF)		31289144

Name	*Gene symbol*	OCD	Anxiety	Behavioral disorder	Depression	Psychosis	Aggressive behavior	ASD	Hyperactivity	Other	Laboratory investigations	Specific treatment	Representative references PMID
Oligosaccharidoses													
Alpha-mannosidase deficiency (alpha-mannosidosis)	*MAN2B1*		x		x	x					Oligosaccharides (U); Enzyme assay (DBS, L, F)	Recombinant enzyme replacement therapy (velmanase alfa); HCT	23786919, 16207285
Beta-mannosidase deficiency (beta-mannosidosis)	*MANBA*			x			x		x	Impulsivity, self-biting	Oligosaccharides (U); Enzyme assay (DBS, L, F)		30886116
Alpha-N-acetylgalactosaminidase deficiency (Schindler disease)	*NAGA*							x			Oligosaccharides (U); Enzyme assay (DBS, P, F)		DOI: 10.1036/ommbid.169
Disorders of glycosaminoglycan degradation													
Alpha-iduronidase deficiency	*IDUA*			x	x	x		x			Mucopolysaccharides (U); Enzyme assay (DBS, L, F)	Hematopoietic cell transplantation (HCT), enzyme replacement therapy (laronidase)	24368159, 31304092
Iduronate 2-sulfatase deficiency (Hunter disease)	*IDS*			x					x		Mucopolysaccharides (U); Enzyme assay (DBS, L, F)	Enzyme replacement therapy (idursulfase)	18580692, 28464912
Heparan - N - sulfatase deficiency (Sanfilippo A disease)	*SGSH*			x			x		x		Mucopolysaccharides (U); Enzyme assay (DBS, L, F)	Clinical trial with intracerebroventricular infusion of chimeric fusion of recombinant enzyme +IGF2	24314109, 18392742
N-acetyl-alpha-D-glucosaminidase deficiency (Sanfilippo B disease)	*NAGLU*			x			x		x		Mucopolysaccharides (U); Enzyme assay (DBS, S, F)	Clinical trial with intracerebral adenovirus associated viral vector containing human NAGLU cDNA	20852935
Acetyl-CoA alpha-glucosaminide acetyltransferase deficiency (Sanfilippo C d	*HGSNAT*			x			x		x		Mucopolysaccharides (U); Enzyme assay (DBS, L, F)		18024218
N-acetylglucosamine-6-sulfatase deficiency (Sanfilippo D disease)	*GNS*			x			x		x		Mucopolysaccharides (U); Enzyme assay (DBS, L, F)		17998446, 20232353
Disorders of lysosomal cholesterol metabolism													
Niemann-Pick disease type C	*NPC1*	x	x	x	x	x		x	x		Oxysterols (P); Filipin staining (F)	Miglustat; experimental intrathecal or intravenous 2-hydroxypropyl-beta-cyclodextrin; oral Arimoclomol	30632019, 28914127, 29457916
DISORDERS OF PEROXISOMES													
Disorders of peroxisomal β-oxidation													
X-linked adrenoleukodystrophy	*ABCD1*		x	x	x	x	x		x		VLCFA (P)	HCT at early stages of cerebral X-ALD; HSC gene therapy with lentiviral vector	29201369, 10453801, 3311181, 10440007, 17342190
CONGENITAL DISORDERS OF GLYCOSYLATION													
Disorders of N-glycosylation													
PMM2-CDG	*PMM2*		x		x		x	x			Sialotransferins (S), ASAT/ALAT (P), coagulation factors (P)		25497157, 28425223
ALG6-CDG	*ALG6*				x		x	x			Sialotransferins (S), ASAT/ALAT (P), coagulation factors (P)		27287710
Disorders of O-xylosylation and glycosaminoglycan synthesis													
Heparan sulfate N-deacetylase/N-sulfotransferase 1 deficiency	*NDST1*						x				DNA		25125150
Disorders of glycosylphosphatidylinositol biosynthesis													
PIGH-CDG	*PIGH*						x	x			Triglycerides (S); ALP (P); DNA		29603516, 29573052
Disorders of Golgi transport													
SLC35A3-CDG	*SLC35A3*							x			DNA		24031089