Table S1. Clinical approach to chorea

Clinical presentation	Possible aetiologies	Diagnostic investigations
Acute or subacute hemichorea/ hemiballism	Immune-mediated › Sydenham's chorea › Antiphospholipid antibody syndrome › Systemic lupus erythematosus › Other connective tissue diseases (eg Sjogren's syndrome) › Coeliac disease › Paraneoplastic (associated with anti-CRMP5 and anti-Hu antibodies)	First level › Magnetic resonance imaging head (including contrast-enhanced, diffusion-weighted or susceptibility-weighted sequences; plus magnetic resonance angiography or conventional angiography, if required) › Antistreptolysin O and anti-deoxyribonuclease B antibodies › Anti-β_2-glycoprotein I (IgG) antibodies › Anti-double stranded DNA antibodies › Lupus anticoagulant › Acute phase reactants (erythrocyte sedimentation rate, C-reactive protein) › Full blood count › Electrolytes › Thyroid function tests › Throat culture analysis for group A Streptococcus › Glycemic level – plasma osmolality – plasma ketones › Doppler echocardiography › ECG › HIV test Second level › Anti-NMDA receptor antibodies (followed by computed tomography pelvis, if justified by clinical presentation) › Anti-neuronal antibodies (anti-CRMP5/CV2, anti-Hu, anti-Yo antibodies) › Anti-SS-A and anti-SS-B antibodies › Anti-gliadin and anti-transglutaminase antibodies › Genetic screening for *PRRT2*, *MR1*, *SLC2A1*, *GLUT1* gene mutations (if paroxysmal) › Cerebral SPECT (if required) › Carotid/vertebral arterial Doppler studies › Pregnancy test (if justified by clinical presentation) › EEG (if justified by clinical presentation) Third level (if the cause remains undefined) › Cerebrospinal fluid analysis (14-3-3 protein, cells, viral or bacterial antibodies/PCR)
Acute or subacute generalised chorea	Autoimmune encephalitides/encephalopathies (secondary to anti-NMDA receptor, anti-LGI1, anti-GAD65, anti-CASPR2, anti-GABA-B receptor antibodies) Endocrinological › Thyrotoxicosis › Chorea gravidarum › Chorea secondary to oral contraceptives or hormone replacement therapy Drug- and toxin-induced › Drugs (antiepileptics, calcium channel blockers, anticholinergics, digoxin, lithium, tricyclic antidepressants, fluoxetine, cyclosporine, ciprofloxacin, baclofen, theophylline, methotrexate, interferon-alpha, ribavirin, methadone) › Recreational drugs (D-amphetamine and derivatives, pemoline, cocaine, crack) › Carbon monoxide encephalopathy Infectious › Viral encephalitides (HSV-1, VZV, measles, German measles, CMV, West Nile virus, Parvovirus B19, Japanese B encephalitis) › Bacterial infections (Diphtheria, Legionella and Salmonella species, Neuroborreliosis, Neurosyphilis) Other metabolic aetiologies › Posterior reversible encephalopathy syndrome › Hypocalcaemia › Type 2 diabetes and uraemia with T_2 striatal hyperintensities › Central extrapontine myelinolysis Vascular/haemodynamic › Polycythemia vera › Essential thrombocytemia › 'Post-pump' syndrome	
Episodic (paroxysmal) chorea	Genetic › Paroxysmal kinesigenic dyskinesias (*PRRT2* gene mutations, genetically undetermined) › Paroxysmal exercise-induced dyskinesia (*GLUT1* gene mutations) › Paroxysmal non-kinesigenic dyskinesias (*MR1* gene mutations) Acquired › Intracerebral arterial stenosis or Moyamoya (episodic hemichorea)	

(*Continued*)

Table S1. (*Continued*)

Clinical presentation	Possible aetiologies	Diagnostic investigations
Chronic, progressive chorea	Early onset > Friedreich ataxia > Ataxia-teleangiectasia > Ataxia with oculomotor apraxia types 1 and 2 > Pantothenate kinase-associated neurodegeneration > Wilson's disease > Aceruloplasminemia > Lesch-Nyhan syndrome > Leigh syndrome > Infantile bilateral striatal necrosis syndrome > Non-ketotic hyperglycinemia > Recessive hereditary methemoglobinemia type 2 > Beta-ketothiolase deficiency *Adult-onset* > Huntington's disease > *C9orf72* gene expansion-related neurodegeneration > Huntington's disease-like 2 > Neuroacanthocytosis syndromes (chorea-acanthocytosis, McLeod syndrome) > Spinocerebellar ataxia 17 (much less commonly other types, eg 1, 2, 3, 7, 8, 14, dentato-rubro-pallido-luysian atrophy, POLG-1 mutations) > Pallido-nigro-luysian atrophy > Neuroferritinopathy > Basal ganglia calcifications > Hepatocerebral degeneration > Huntington's disease-like 1 and Creutzfeldt-Jakob disease > *RNF216*-associated neurodegeneration (variant of Gordon Holmes syndrome) Mixed age at onset > Niemann-Pick disease type C > Non-ketotic hyperglycinemia > Hereditary methemoglobinaemia type 2 > Beta-ketothiolase deficiency > Neurosyphilis	*First level* > Magnetic resonance imaging head > Thyroid function tests > Copper/coeruloplasmin studies > Uric acid > Liver function tests, calcium and phosphate > Anti-β2-glycoprotein I (IgG) antibodies > Anti-double stranded DNA antibodies > Lupus anticoagulant > Albumin > Cholesterol > Plasma and CSF lactate/pyruvate > Urinary and serum organic and amino acids > Creatine phosphokinase > Ferritin *Second level* > alpha 1-fetoprotein serum > Cerebral SPECT > Somatosensory evoked potentials > Genetic screening for *TITF1/NKX2.1*, *FRDA*, *APTX*, *SETX* gene mutations > Genetic screening for *IT15*, *JPH3*, SCAs, DRPLA, *PRNP* and others > Peripheral blood film for acanthocyte search > Erythrocyte Kx and Kell antigen screening > Skin biopsy for filipin staining on fibroblasts
Chronic, non-progressive chorea	Benign hereditary chorea (*TITF1/NKX2.1* gene mutations) Dyskinetic cerebral palsy spectrum Tardive dyskinesia L-dopa-induced dyskinesia (may worsen over time)	

CSF = cerebrospinal fluid; DRPLA = Dentatorubral-pallidoluysian atrophy; ECG = Electrocardiogram; PCR = polymerase chain reaction; SCA = spinocerebellar ataxia; SPECT = single-photon emission computed tomography;
Martino D, Espay AJ, Fasano A, Morgante F. *Disorders of movement: a guide to diagnosis and treatment*. Heidelberg: Springer-Verlag, 2016.