Investigations for the work up of the patient with psychosis or altered mental status

Routine Investigations

Investigation	What it might suggest
CBC	• Low hct/hgb may indicate IDA from malignancy • Low MCV suggests IDA • High MCV could suggest alcoholism – alcoholic hallucinosis, delirium tremens • High MCV could suggest B12/folate deficiency- "megaloblastic madness" • Pancytopenia and other blood dyscrasias could suggest vasculitis/autoimmune disease or malignancy • Leukocytosis could suggest infection, autoimmune process
BUN/Cr	• High urea could suggest dehydration – delirium • High urea – uremic encephalopathy • Renal impairment could suggest vasculitis/autoimmune disease
Na	• Hyper/hypo-natremia causes delirium • Changes in Na cause central pontine myelinolysis – peduncular hallucinosis, also altered mental state • Hyponatremia could suggest VGKC autoimmune limbic encephalitis
Ca	• Hypercalcemia/hypocalcemia can cause delirium, fatigue, depressive psychosis • Hypercalcemia could suggest malignancy (mets) • Hypercalcemia could suggest sarcoidosis
TSH	• Raised TSH suggests hypothyroidism – "myxedema madness"/myxedema coma • Low TSH suggests hyperthyroidism – particularly causes anxiety
AST/ALT	• 2:1 AST/ALT raised ratio suggest alcohol abuse/dependence • could suggest cirrhosis – hepatic encephalopathy • raised LFTs also suggestive of Wilson's disease which can cause depression, mania, psychosis, in addition to various neurological disorders such as tremors, ataxia, chorea
GGT	• raised GGT occurs in alcohol abuse
Bilirubin	• hyperbilirubinemia could suggest cirrhosis – hepatic encephalopathy • could suggest hemolysis such as G6PD deficiency which can present as mania, psychosis, catatonia
Albumin/Total Protein	• TP more than twice albumin suggests hypergammaglobulinemia – can occur in infection e.g. HIV, also plasma cell disorders e.g. multiple myeloma, Wäldenstrom's

ESR/CRP	• Raised ESR >100 suggests chronic severe inflammatory process including TB, myeloma, malignancy, autoimmune disease • Raised CRP suggests acute inflammation – e.g. infection, autoimmune
B12 (and methylmalonic acid)	• B12 deficiency can cause dementia and psychosis
Folate (and homocysteine)	• More rarely, Folate deficiency can cause dementia and psychosis
Ammonia	• Hyperammonemia suggests liver failure, urea cycle disorders such as ornithine transcarbamylase deficiency or drugs (e.g. valproate, cyclophosphamide)
Urinalysis	• Nitrites, wcc, leukocyte esterase suggest UTI – can cause delirium • Hematuria could suggest autoimmune/vasculitis • Cast cells suggest glomerulonephritis – autoimmune/vasculitis
Urine Toxicology (immunoassay or gas chromatography-mass spectrometry)	• Screens for drugs of abuse
CXR	• Bilateral hilar lymphadenopathy suggests sarcoidosis (or TB) • Fibrosis could suggest autoimmune/vasculitis • Lung or bone metastases suggest disseminated carcinomatosis or malignancy w/ lung mets

Special Investigations

Investigation	**What it might suggest**
Syphilis IgG (replaces VDRL and RPR for serum)	• Could suggest tertiary syphilis which causes general paresis of the insane (need check CSF VDRL); neuropsych symptoms can occur in any phase • Neuropsychiatric manifestations of syphilis more common in HIV
HIV antigen	• HIV+ patients with altered mental status has wide differential including cryptococcal meningitis, cerebral lymphoma, toxoplasmosis, PML (jc/bk virus), VZV/HSV encephalitis • HIV can cause dementia and neuropsychiatric manifestations through direct destruction of microglia • HIV common occurrence in severe mental illness
Coagulation screen	• Prolonged PT/INR could suggest impaired synthetic liver function – liver disease • Prolonged PTT that fails to correct w/ 50:50 dilution could suggest antiphospholipid syndrome • Coagulopathy could also suggest malignancy, infection with element of DIC

Head CT (MRI usually preferred)	• Bleeds, tumors, strokes, cysts, abscesses, hydrocephaus • Generalized and focal atrophy • Calcifications (e.g. basal ganglia in Fahr's disease)
MRI Brain	• Order "dementia protocol" (including FLAIR and DWI) • May show evidence of stroke, infection, malignancy, vasculitis, atrophy • T2/FLAIR hyperintensities in mesial temporal lobe occur in toxic/metabolic/degenerative/autoimmune/infectious causes of altered mental status, catatonia, psychosis • Lesions of frontal lobes, basal ganglia, thalami, brainstem or cerebellum may also present with neuropsychiatric symptoms
EEG	• Mostly looking for epileptiform activity- non-convulsive status epilepticus in differential for catatonia, temporal lobe and frontal lobe epilepsies in differential for psychosis • Diffuse background slowing occurs in delirium or dementia (global cerebral dysfunction) • Extreme delta brush pathognomic of NMDA-R encephalitis • Triphasic waves found in encephalopathy • Periodic sharp wave complexes found in late stage CJD
CT Chest/Abdomen/Pelvis	• Look for malignancy
Whole Body PET-CT	• Look for occult malignancy
ANA/dsDNA	• Suggests SLE or other autoimmune disease
Anti-SSA/SSB	• Suggest Sjögren's which can have neuropsychiatric presentations in 15% cases
P-ANCA and C-ANCA	• Suggests vasculitic disease
C3/C4	• Low levels suggest connective tissue disease
ACE	• Suggests sarcoidosis
Anticardiolipin Abs/Lupus anticoagulant/beta-2 glycoprotein	• Indicate antiphospholipid syndrome
Antigliadian/anti-endomysial/tissue transglutaminase antibodies	• Indicates Celiac disease – can present with psychosis, depression, cognitive sxs
Trophyrema Whipelli PCR	• Indicates Whipple's disease
Lyme Enzyme Immunoassay (EIA) or Immunofluorescence Assay (IFA)	• If positive with sx for <30 days then IgM and IgG, if >30 days then IgG only

CSF studies Opening Pressure Protein Glucose WCC Oligoclonal bands IgG index	• High WCC, low glucose high protein suggest infection • May be normal in autoimmune disease but CSF pleocytosis commonly seen • Oligoclonal bands may suggest MS, also found in autoimmune disease, syphilis, CNS lymphoma etc • Elevated IgG index indicates inflammatory, infectious or autoimmune process
Serum and CSF thyroid peroxidase and thyroglobulin antibodies	• May suggest Hashimoto's encephalopathy (diagnosis is controversial)
CSF autoimmune encephalopathy panel (NMDAR, VGCC, VGKC [anti-CASPR2, anti-LGI-1], GAD-65, AMPA, GABA-B antibodies etc)	• Suggest autoimmune encephalitis (check CSF and serum)
Paraneoplastic antibodies (e.g. anti-ma2, anti-hu, anti-mGluR5)	• Suggest paraneoplastic cause (e.g. cerebellitis, limbic encephalitis)
14-3-3 Protein	• Found in CJD
RT-QuIC (real-time quaking-induced conversion)	• Highly sensitive and specific for CJD
Aβ42 Tau Phosphorylated tau	• CSF Tau is elevated in Alzheimer's disease and other tauopathies; significantly elevated in CJD • Aβ42 (amyloid β42) is low in Alzheimer's • Phospho-tau is significantly elevated in Alzheimer's
CSF cryptococcal antigen, HSV, VZV, CMV, JC virus, Lyme, West nile virus, Western Equine Encephalitis, Eastern Equine encephalitis	• Suggests infectious meningoencephalitis
CSF Cytology and Flow Cytometry	• Looks for malignant cells in CNS
Porphobilinogen (urine)	• When positive along with negative fecal porphyrins, suggests acute intermittent porphyria
Aminolevulinic Acid (ALA), urine	• Suggests ADP (aminolevulinic acid dehydratase-deficiency porphyria)
Ceruloplasmin and serum copper	• High copper and low ceruloplasmin suggest Wilson's disease
White cell enzymes (arylsulfatase A)	• Deficiency found in metachromatic leukodystrophy which presents with parkinsonism, cognitive impairment and neuropsychiatric symptoms
Alzheimer's Genes (APP, PSEN1, PSEN2)	• Deterministic genes for early onset Alzheimer's disease
bvFTD genes (C9ORF72, MAPT, GRN)	• Most common deterministic genes associated with neuropsychiatric symptoms of bvFTD. Several other genes can also be tested (e.g. FUS, VCP, TARDBP)

Muscle biopsy	• Needed for diagnosis of mitochondrial encephalopathies such as MELAS (mitchondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episode), MERFF (mitochondrial epilepsy, with ragged red fibers)
FISH (fluorescent in situ sterile hybridization) CMA (chromosomal microarray analysis)	• Needed for diagnosis of chromosomal microdeletions such as 22q.11 microdeletion which is associated with velocardiofacial syndrome/DiGeorge syndrome which is associated with psychosis
24 hour urinary heavy metals	• Look for mercury, arsenic, lead, manganese and cadmium toxicity which can present with dementia, psychosis, apathy, tics, movement disorders depending on exposure history