Table 8. (*continued*)

Psychiatric symptoms	Class/drug or procedure
Catatonia	• Benzodiazepines/lorazepam, first line • ECT, second line • Second-generation antipsychotics/quetiapine 300-800 mg/day, olanzapine 5-20 mg/day, third line • Avoid haloperidol and high-potency antidopaminergic agents • Avoid long-acting antipsychotics

BTX, botulinum toxin A; ECT, electroconvulsive therapy; RBD, REM sleep behaviour disorder; RLS, restless legs syndrome; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

BTX injected into the most affected muscles. Only a few case and series reports have provided data about the effectiveness of oral treatments for dystonia. Anticholinergic drugs show moderate efficacy with well-known side effects to watch for (confusion, urinary retention, blurred vision, etc.) (trihexyphenidyl with a starting dose of 2 mg, slowly increased up to a maximum of 30 mg/day, or biperiden with a starting dose of 6 mg/day in three doses, slowly increased up to 16 mg/day).[292,311] Other pharmacological agents include (a) baclofen (ranging between 60 and 120 mg/day),[292] (b) benzodiazepines[294] (c) levodopa or dopamine agonists,[312–316] (d) tetrabenazine (starting dose 12.5 mg, increased up to 50–75 mg/day),[294] and (e) carbamazepine (up to 900 mg/day) or oxcarbazepine (up to 300 mg/day).[317–319] More anecdotally, a single case report described the efficacy of cannabis in reducing dystonic symptoms.[320] More recently, two trials investigating the efficacy of repetitive transcranial magnetic stimulation over the somatosensory or the motor cortex in limb dystonia found some improvements.[321–323] Results of exceptional surgical procedures such as DBS or thalamotomy in cases of severe generalized dystonia refractory to long-term anti-copper treatment and symptomatic pharmacological treatment are not convincing.[302,303,305,324] Severe structural changes of basal ganglia and thalami should be absent as the efficacy of DBS with electrodes placed in damaged targets is unpredictable and often limited.[292]

Parkinsonism

The majority of reports indicate no significant effect of dopaminergic drugs on Parkinsonian symptoms in WD. Nevertheless, considering the established alteration in dopaminergic neurotransmission among patients with WD[325] and the low prevalence of adverse reactions to dopaminergic treatment, a trial of dopaminergic treatment should be considered for patients with WD to address dystonia and parkinsonism.[297,313,314,326–328]

Chorea and choreoathetosis

Treatment of chorea and choreoathetosis are poorly studied in WD. Only one case reported good efficacy of tetrabenazine in treating chorea in WD.[297] Neuroleptic drugs and dopamine antagonists should not be used in WD due to a high risk of neurological deterioration.[213]

Dysarthria

Speech therapy is the primary treatment for this highly prevalent and debilitating symptom associated with social challenges due to reduced communication. Speech rehabilitation is tailored to the specific type of dysarthria, incorporating targeted training on relaxation techniques for the spastic form, methods to modify speech rate and prosody in cases of ataxic disturbances, and intensive voice treatment, such as the Lee Silverman voice treatment, to enhance loudness and improve articulation in the hypokinetic form.[329] In instances of dystonic dysarthria, the use of zolpidem (2x 10 mg and 5x 5 mg orally) has been reported to yield positive effects without sedative side effects.[330] For spasmodic dysphonia or voice tremor, injections of BTX have been identified as a viable treatment option in isolated cases.[307,331] In cases of severe dysarthria with limited or poor vocalisation, the recommendation is to utilise alternative and augmentative communication devices, such as computer systems, tablets, or smartphone applications.

Dysphagia

Objective methods, such as videofluoroscopy and fibre optic endoscopic evaluation, should be employed to assess swallowing and determine the severity of dysphagia for the purpose of tailoring treatment.[292] Initial interventions should encompass discontinuation of sedatives and drugs that may affect arousal, as well as anticholinergic drugs contributing to mouth dryness, thereby exacerbating swallowing difficulties. In addition to specific behavioural therapies aiming to enhance food bolus preparation and ingestion (including optimising position, maintaining concentration on the task, and swallowing before the next bite), dietary modifications are recommended. These modifications involve avoiding dry and sticky foods and opting for cold liquids or those with gas. Neuromuscular electrical stimulation, explored in dysphagia rehabilitation for improving swallowing, holds significant promise.[332,333] In cases of severe dysphagia accompanied by weight loss, tube feeding with direct delivery of food into the stomach may be contemplated to prevent food aspiration, address malnutrition, and facilitate anti-copper therapy. However, this procedure may exacerbate dystonia, necessitating prompt consideration of percutaneous endoscopic gastrostomy.[334] Both solutions may be implemented temporarily and discontinued upon neurological improvement and recovery from dysphagia.

Drooling/hypersialorrhea

The severity of drooling should be assessed using objective tools such as the drooling severity and frequency scale and objective assessment of saliva secretion.[335,336] Factors contributing to drooling (saliva hypersecretion, salivary stasis, swallowing dysfunction, extrapyramidal postural abnormalities, oro-facial dystonia, sensitive alterations, cognitive, and behavioural impairment) must be considered. Chewing gum or sucking candies, which reduces salivation by triggering automatic swallowing and reduces saliva volume in the mouth, should be tried.[337] As no therapeutic study exists in WD, pharmacological options used for drooling in other neurological conditions should be considered, including anticholinergics (*e.g.* benzatropine, trihexyphenidyl, transdermal scopolamine, sublingual 1% atropine drops), adrenergic alpha-2 receptor agonists (clonidine 0.15 mg/day), or BTX injection in parotid and/or sublingual glands or to treat oro-mandibular dystonia.[336–338]