Table 1: Summary of characteristics of the newly recognized CNS tumors in the 2021 WHO classification.

Tumor	Patient demographics	WHO grade	Imaging features	Imaging differential	Histopathology	Molecular and genetic markers	Number of cases in the largest described series
Diffuse astrocytoma, *MYB*- or *MYBL1*-altered	Median age 5 years (range 0-26 years), no sex predilection	1	Cerebral hemisphere cortex, then cerebral white matter/deep gray nuclei, then brainstem; infiltrative; T1 iso- to hypointense, heterogeneously T2 hyperintense, no diffusion restriction or enhancement	Angiocentric glioma; polymorphous low-grade neuroepithelial tumor of the young; diffuse low-grade glioma, MAPK pathway-altered; diffuse midline glioma, H3 K27-altered; diffuse hemispheric glioma, H3 G34-mutant; diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype; infant-type hemispheric glioma; dysembryoplastic neuroepithelial tumor, cortical tuber, cortical dysplasia	Non-specific; astrocytes, oligodendrocytes, or both; infiltrative of CNS parenchyma, no or rare mitotic activity, no microvascular proliferation, no necrosis	Alteration (e.g., fusion, rearrangements, amplifications) of *MYB* or *MYBL1*; IDH wildtype and H3 wildtype	46[17]

Polymorphous low-grade neuroepithelial tumor of the young	Median age 15.5 years (range 5-57 years), slight female predominance (M:F 1:1.7)	1	Supratentorial, usually temporal lobe, cortical/subcortical, calcifications that are often dense, cystic and solid, no or mild enhancement	Oligodendroglioma, IDH-mutant and 1p/19q-codeleted; diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters; other pediatric low-grade tumors; dysembryoplastic neuroepithelial tumor; pleomorphic xanthoastrocytoma; ganglioglioma	Glial tumor often with oligodendroglioma-like components, frequent calcification, diffuse growth	Genetic abnormalities activating the MAPK pathway (*BRAF*, FGFR); CD34 positive	13[91]
Diffuse low-grade glioma, MAPK pathway-altered	Limited data; children, occasionally adults	Histologically like 2*	Limited data; temporal lobe, cortical, T2 FLAIR hyperintense, no enhancement	Other pediatric-type low-grade gliomas; ganglioglioma; cortical tuber; cortical dysplasia	Oligodendroglial, astrocytic, or both with an infiltrative growth pattern, minimal cellular atypia, absent/rare mitotic activity, no microvascular proliferation, no necrosis	Various; *FGFR1/2*, *BRAF*, *NTRK1/2/3*, *MET*, *MAP2K1*; absent *IDH1/2* and *H3F3A* mutations, absent *CDKN2A* homozygous deletions	9[92]

Diffuse hemispheric glioma, H3 G34-mutant	Median age 15.8 years (interquartile range 13-22 years), slight male predominance (M:F 1.5:1)	4	Cerebral hemisphere, usually with leptomeningeal or ependymal contact; T1 hypointense, T2 hyperintense, diffusion restriction, usually enhancement, hemorrhage, necrosis, occasionally calcifications	Other pediatric-type high-grade gliomas; metastatic disease	Malignant hypercellular astrocytic gliomas with high mitotic rate, microvascular proliferation, and necrosis ("glioblastoma-type") or "small blue cells" ("primitive neuroectodermal tumor-type")	*H3F3A* missense mutation causing substitution of the normal glycine 34 of histone H3 by arginine or valine; also *ATRX* loss and *TP53* mutation	81[20]
Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype	Median age 8-11 years (range 2-18 years), no sex predilection overall but slight male predominance for *EGFR* subtype (M:F 1.6:1)	*	Usually supratentorial (temporal lobe most common) but can occur in the brainstem and cerebellum; commonly abuts the meninges; solid, enhancing, diffusion-restricting, well marginated, necrotic, rare hemorrhage, no calcifications	Other pediatric-type high-grade gliomas; AT/RT and other CNS embryonal tumors; medulloblastoma	Hypercellular, spindle and epithelioid cells, high mitotic rate, necrosis, and microvascular proliferation	Variable; most commonly amplifications of *MYCN* then *PDGFRA* then *EFGR*	87[24]
Infant-type hemispheric glioma	Median age 2.8 months (range 0.0-12.0 months), no sex predilection	*	Cerebral hemisphere; large with solid with prominent cystic components, hemorrhage, regions of enhancement	Other pediatric-type high-grade gliomas; desmoplastic infantile ganglioglioma or astrocytoma; ependymoma; ganglioglioma	Hypercellular astrocytic gliomas with necrosis, microvascular proliferation, and nuclear pleomorphism	Gene fusions of *ALK*, *ROS1*, *NTRK1/2/3*, or *MET*	65[28]

High-grade astrocytoma with piloid features	Pediatrics to the elderly (median age 41.5 years), no sex predilection, associated with neurofibromatosis type 1	Behaves like 3 or 4*	Most posterior fossa, then supratentorial, then spinal; T1 iso- to hypointense, T2 hyperintense, heterogeneous enhancement, no diffusion restriction; well or poorly marginated, with or without adjacent edema/infiltration, usually no necrosis	Glioblastoma; pilocytic astrocytoma; diffuse midline glioma, H3 K27-altered	Variable; moderate cellularity, moderate nuclear pleomorphism, elevated mitotic rate, vascular hypertrophy, and infiltrative growth pattern, lack of necrosis, can have glioblastoma-like foci	Characteristic DNA methylation profile; commonly *CDKN2A/B* deletion, MAPK pathway alteration (*NF1*, *BRAF*, *FGFR1*), *ATRX* mutation or loss of expression	83[32]
Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters (provisional type)	Median age 9 years (range 2-75 years), no sex predilection	*	Limited data; cerebral hemisphere (temporal lobe more common); T1 hypointense, T2 hyperintense, calcifications, minimal to no enhancement, predominantly solid with cystic components	Polymorphous low-grade neuroepithelial tumor of the young; other pediatric-type low-grade gliomas; oligodendroglioma, IDH-mutant and 1p/19q-codeleted; neurocytoma; dysembryoplastic neuroepithelial tumor; glioblastoma	Oligodendroglioma-like perinuclear haloes, clear cells, vascular proliferation, nuclear clusters (“pennies on a plate”), moderate to high cellularity, infiltrative growth pattern, calcifications	Characteristic DNA methylation profile, monosomy 14	31[34]

Myxoid glioneuronal tumor	Median age 23.6 years (range 6-65 years), no sex predilection	1	Often at the septum pellucidum; well circumscribed lobulated mass, T1 hypointense, T2 hyperintense, peripheral rim of T2 FLAIR hyperintensity with partially suppressed signal centrally, facilitated diffusion, no adjacent edema	Third ventricle colloid cyst; central neurocytoma; subependymoma	Low-grade oligodendrocyte-like tumor cells in a mucin-rich stroma, neurocytic rosettes	*PDGFRA* p.K385 mutation; positive for GFAP and Olig2	8[38]
Multinodular and vacuolating neuronal tumor	Median age 41 years (range 8-63 years), slight female predominance (M:F 1:1.4)	1	Variably sized nodular lesions in the subcortical white matter following the gyral contour, most common in the frontal lobe; T1 isointense, T2 hyperintense; no enhancement, diffusion restriction, mass effect, or adjacent edema	Dysembryoplastic neuroepithelial tumor; ganglion cell tumors; low grade gliomas; focal cortical dysplasia; enlarged perivascular space	Discrete nodules with immature neuronal cells, prominent nucleoli, pericellular eccentric vacuolization	*MAP2K1* mutation (most common); *FGFR2-ZMYND11* translocation; alterations of *BRAF*, *DEPDC5*, *SMO*, *TP53*, *PIK3CA*, *CIC*; positive for Olig2, alpha INA, synaptophysin	33[41]

Supratentorial ependymoma, *YAP1* fusion-positive	Median age 1.4 years (range 0-51 years), female predominance (M:F 1:3)	2 or 3	Within or adjacent to the lateral ventricles; heterogenously T1 iso- to hypointense, T2 iso- to hyperintense; calcification common, enhances, restricts diffusion, can have hemorrhage	High-grade glioma; oligodendroglioma, IDH-mutant and 1p/19q-codeleted	Bipolar spindle cells with elongated processes, prominent hyalinization, scattered calcification, perivascular pseudorosettes	*YAP1:MAMLD1* fusion, *YAP1:FAM118B* fusion; positive for GFAP, S-100, vimentin	13[45]
Posterior fossa ependymoma, group PFA	Median age 3 years (range 0-51 years), slight male predominance (M:F 1.8:1)	2 or 3	Arises from fourth ventricular roof or cerebellopontine angle, extends through foramen of Luschka/Magendie; T1 iso- to hypointense, T2 hyperintense; heterogenous enhancement, usually restricts diffusion	Medulloblastoma; subependymoma; choroid plexus papilloma/carcinoma; choroid plexus metastasis	Well-differentiated cells with ependymal rosettes; perivascular pseudorosettes and dystrophic calcifications can be present	Loss of H3 K27 trimethylation due to *EZHIP* overexpression	240[45]
Posterior fossa ependymoma, group PFB	Median age 27.5 years (range 1-72 years), no sex predilection	2 or 3	Similar to group PFA except: more commonly arise from the floor of the fourth ventricle, more cystic, less calcified, less enhancing	Medulloblastoma; subependymoma; choroid plexus papilloma/carcinoma; choroid plexus metastasis	Similar to group PFA	Increased H3 K27 trimethylation; positive for GFAP, S100, vimentin	212[55]

Spinal ependymoma, *MYCN*-amplified	Median age 32 years (range 12-56 years), no sex predilection	Histologically like 3, can be like 2*	Spinal cord; iso- to hyperdense; T1 iso- to hypointense, T2 iso- to hyperintense; enhances; usually has cystic components, hemorrhage, necrosis, calcification	Spinal astrocytoma; spinal cavernous malformation	Anaplastic features; hypercellular, marked cellular atypia, nuclear hyperchromasia, prominent nucleoli, necrosis, glomeruloid vascular proliferation	*MYCN* amplification; positive for GFAP and EMA	13[58]
Cribriform neuroepithelial tumor (provisional type)	Median age 1.7 years (range 0.8-10.8 years), no definite sex predilection	*	Within or adjacent to the lateral, third, or fourth ventricles; T1 hypointense, T2 hyperintense, enhances, restricts diffusion	Choroid plexus papilloma/carcinoma	Cribriform strands and ribbons, nuclei with dense chromatin and ill-defined cytoplasm	*SMARCB1* deletion; positive for tyrosinase, EMA, vimentin, MAP2C, synaptophysin	10[65]
CNS neuroblastoma, *FOXR2*-activated	Median age 4.5 years (range 1.4-16 years), no sex predilection	*	Supratentorial, deep white matter; cortical and ependymal involvement common; often multiple regions with frontal the most common; multilobulated solid/cystic; internal hemorrhage/calcification (40%); little/no peritumoral edema; remodeling/signal changes of overlying bone (50%)	CNS tumor with *BCOR* internal tandem duplication; AT/RT; embryonal tumor with multilayered rosettes	Small cell tumor with embryonal architecture, high mitotic count; neuropil, neurocytic cell, or ganglion cell differentiation; vascular pseudorosettes, nuclear palisades; positive Olig2 and synaptophysin	Inter-/intra-chromosomal rearrangements converging on *FOXR2* causing expression; mitochondrial DNA insertion within *USP51* as a novel *FOXR2* promoter	25[69]

CNS tumor with *BCOR* internal tandem duplication	Median age 1.8 years (range 1.2-7.6 years), female predominance (M:F 1:2.3)	*	Supra- or infratentorial, typically peripheral with dural abutment; large, solid, central necrosis, with or without blood products/calcification; T2 hyperintense, diffusion restriction, variable mild heterogenous enhancement, little to no peritumoral edema, large intratumoral macroscopic vessels	CNS neuroblastoma, *FOXR2*-activated; AT/RT; embryonal tumor with multilayered rosettes	Perivascular pseudorosettes, fibrillary processes (glial differentiation feature); peripheral palisading necrosis; rich branching capillary network; positive for Olig2, NeuN; diffuse strong nuclear staining for BCOR protein; negative for GFAP, synaptophysin, S-100	In-frame internal tandem duplications in exon 15 of *BCL6 corepressor* (*BCOR*)	10[70]

Desmoplastic myxoid tumor of the pineal region, *SMARCB1*-mutant	Median age 40 years (range 15-61 years), no definite sex predilection	*	Limited data; variable T1 signal, T2 isointense, enhances, can compress the cerebral aqueduct	AT/RT; pineal parenchymal tumors; germ cell tumors; metastasis	Variable myxoid morphology combined with spindled and epithelioid cells embedded in a densely collagenized stroma; occasional intranuclear inclusions; no brisk mitotic activity or tumor necrosis as seen in AT/RT; positive for CD34, negative for INI1	Mutation in *SMARCB1*/*INI1* causing loss of SMARCB1 function; characteristic DNA methylation profile in the vicinity of AT/RT	7[72]

Intracranial mesenchymal tumor, FET-CREB fusion positive (provisional type)	Median age 17 years (range 4-70 years), female predominance (M:F 1:2.2)	*	Extra-axial over the cerebral convexities most common; can be intraventricular; circumscribed, lobulated, solid and cystic, enhances, intratumoral blood products, extensive peritumoral edema, variable T2 signal; dural tail and involvement of the overlying bone sometimes observed	Meningioma; solitary fibrous tumor; lymphoma	Variable; pseudo-encapsulation, nodular epithelioid cellular proliferations, prominent subcapsular lymphoplasmacytic aggregates with hemosiderin deposition; positive for desmin, CD99 and EMA; negative for myogenin, MyoD1, actin, caldesmon, calponin, S100, HMB45, GFAP, Olig2	In-frame fusions of FET family RNA-binding proteins (*EWSR1* or *FUS*) to the CREB family transcription factors (*ATF1*, *CREB1*, *CREM*)	20[93]
CIC-rearranged sarcoma	Limited data; children and adults	4	Limited data; anywhere along the neuroaxis; solid, multilobulated, T2 iso- to hyperintense, heterogenous enhancement, peritumoral edema	Ewing's sarcoma family, rhabdomyosarcoma, glioblastoma, metastatic disease	Round cell sarcoma with myxoid features and high mitotic count; histologically resembles Ewing's sarcoma; positive for CD99; extensive ETV4 and WT1 nuclear expression	Rearrangements of *capicua transcriptional repressor* (*CIC*); multiple *CIC* fusion partners: *DUX4* (most common), *FOXO4*, *LEUTX*, *NUTM1*, *NUTM2A*; lacks *ESWR1* fusion	7[94]

Primary intracranial sarcoma, *DICER1*-mutant	Median age 6.0 years (range 2.0-17.5 years), no sex predilection, associated with familial *DICER1* syndrome and neurofibromatosis type 1	*	Limited data; intra-axial (usually peripheral in a cerebral hemisphere) or extra-axial; T2 iso- to hypointense, diffusion restriction, avid enhancement; intratumoral hemorrhage and peritumoral edema typically present; sometimes enhancement of the meninges/leptomeninges	Glioblastoma, metastatic disease, lymphoma, solitary fibrous tumor, meningioma	Variable; contains some areas of fascicular spindle cells; focal regions of differentiation resembling embryonic-type tissues, such as rhabdomyoblastic differentiation; cellular coalescence into “organoid” formations; brightly eosinophilic cytoplasmic globules positive for PAS and alpha-1-antitrypsin; patchy desmin staining; complete loss of H3K27me12	Germline inactivation of the *DICER1* through truncations or deletions	28[84]

Pituitary blastoma	Median age 11 months (range 2-24 months) plus a case report of a 19-year-old, slight female predilection (M:F 1:1.4)	4	Variable; ranges from small solid mass to large heterogenous solid/cystic tumor, can contain calcification	Pituitary adenoma	Hypophyseal tumors resembling embryonic stage pituitary gland; primitive blastemal cells, large secretory epithelial cells expressing neuroendocrine markers such as ACTH (rarely GH); primitive Rathke-type epithelial glandular tissue	Germline or somatic mutations in *DICER1*	17[90]

* = not yet assigned an official WHO grade, IDH = isocitrate dehydrogenase, AT/RT = atypical teratoid/rhabdoid tumor

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See main article for references 1. to 90.

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