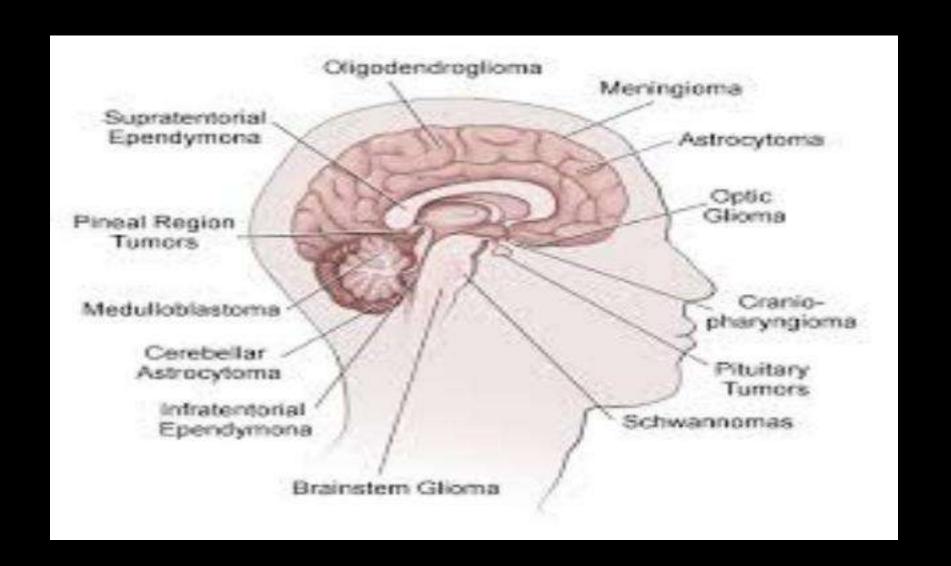
NEUROPSYCHTRIC CESPECTS OF BRAIN TUMORS

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TUMORS IN BROWIN



IMPRODUCTION

- Tumors involving the central nervous system CNES form a diverse group as regards their pathology and clinical course
- In one study the incidence rate for glial tumors was 67 per 100 000 population per year accounting for approximately 51 of all CNS primary neoplasms. Bondy et al 2005
- · Ce study by Veschner et al reported that 78 of 530 patients with brain tumors had psychiatric symptoms
- However 18 of the 530 presented only with these symptoms as the first clinical manifestation of a brain tumor

EPIDEMIQLOGY

- In United States primary brain tumors are reportable diseases
- "primary" refers to a tumor which arises de novo in the brain and is not the result of metastatic spread from a site out with the CNeS
- Pige group Children and adolescents age () to 19 years with an average annual incidence of 54 per 100000
- In adults 279 per 100 000
- · Gender primary brain tumors females 58 vs 42
- Type of tumor females likely benign Males likely malignant

An estimated **688,000+ PEOPLE** in the U.S. are living with a primary brain or central nervous system (CNS) tumor diagnosis:

138,000 WITH MALIGNANT TUMORS 550,000 WITH BENIGN TUMORS

APPROXIMATELY

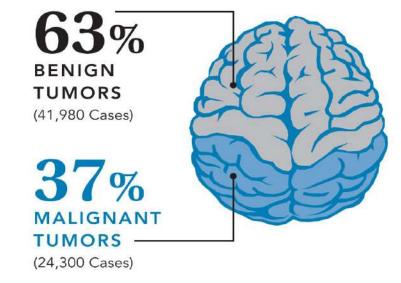
20-40%

OF ALL OTHER CANCERS LATER DEVELOP A BRAIN METASTASES

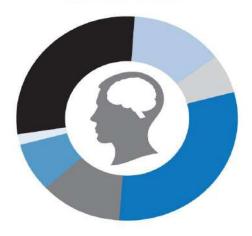


This accounts for 98,000 to 170,000 new metastatic brain tumor cases each year.

IN 2012, NEW PRIMARY BRAIN TUMOR DIAGNOSES INCLUDED:



PRIMARY BRAIN TUMOR TYPES



- 16% Glioblastoma
- 7% Astrocytoma
- 35% Meningioma
- 14% Pituitary
- 9% Nerve Sheath
- 2% Lymphoma
- 33% Other

(Ependymoma, Ogliodendroglimoa, Embryonal, etc.)

Most common tumor as per Pige

Age Range (yr)	Tumor Types		
0-9	Primitive Neuroectodermal tumors medulloblastomas		
10-19	Astrocytomas		
20-34	Pituitary tumors		
35-44	Menigiomas		
45-75	Glioblastomas		
76 and older	Meningiomas		

EPIDEMIQLOGY

- · Site of benign tumors arise in meninges pitutary gland or cranial nerve sheaths
- Site of malignant primary tumors gliomas more common in whites Glioma is cancer arising from neuroepithelial tissue in the brain
- · Malignancy severity
- The CIHO grades glioma on a level from I to II where II is the most malignant type also known as glioblastoma multiforme GBM
- · By convention CHHO grades I and II are called "low grade"
- · CHO grades III and IV are "high grade"

WHO classification of CNS tumors	Grading	Male	Female	Total (%)	0-4 years	>5-9 years	>10-18 years
Embryonal tumors							-
Medulloblastomas		13	5	18 (34.6)	8 1	5	5
Anaplastic	IV	1	1	2 (3.8)	1	1	0
Desmoplastic/nodular		12	4	16 (30.7)	7	4	5
Large cell		0	0	0	0	0	0
Medulloblastoma with extensive nodularity		0	0	0	0	0	5 0 5 0 0
PNET	IV	2	0	2 (3.8)	2	0	0
ATRT	IV	5	0	5 (9.6)	4	1	0
Tumors of the pineal region							
Pineoblastoma	IV	2	0	2 (3.8)	1	1	0
Tumors of the neuroepithelial origin							
Astrocytic tumors							
Pilocytic astrocytoma	I	3	0	3 (5.7)	1	1	1
Glioblastoma	IV	1	1	2 (3.8)	0	2	0
Gliomas	Π	5	4	9 (17.3)	3	6	0
PDLG	III	1	0	1 (1.9)	1	0	0
Ependymal tumors				87 (1 55%)			
Ependymoma	II	2	3	5 (9.6)	5	0	0
Germ cell tumors				REST AND			
Germinoma		2	1	3 (5.7)	1	2	0
NGCT		1	1	2 (3.8)	0	0	2
Total (%)		37	15	52 (100)	26 (50)	18 (34.6)	8 (4.16)

PNET: Primitive neuroectodermal tumor, ATRT: Atypical teratoid/rhabdoid tumor, PDLG: Primary diffuse leptomeningeal gliomatosis, NGCT: Nongerminomatous germ cell tumor

Anatomic location	% of all Brain tumors	% with Psychiatric & Behavioral Symptoms	
Frontal lobes	22	As much as 90	
Temporal lobes	22	50-55	
Parietal lobes	12	As much as 16	
Pituitary	10	As much as 60	
Occipital	4	As much as 25	
Diencephalic Region	2	50 or more	
Posterior fossa, Cerebellum and Brainstem	28	Uncertain, Numerous neuropsychiatric symptoms reported	
		4.0	

PREDISPOSING FOOTORS

- TUMOR LOCATION
- Tumors in left hemisphere cause dysphoria and depression
- · Right hemisphere tumors cause euphoria and symptom denial
- · TUMOR MOLIGNANCY
- Rapidly growing high grade tumors greater severity and faster progression of psychopathology
- Patients with indolent low grade tumors more limited and stable symptoms

Mantespations of primary Brain tumores by Location

Tumor location	Neurologic signs
Frontal lobe	Dementia, personality changes, gait disturbances, generalized or focal seizures, expressive aphasia
Parietal lobe	Receptive aphasia, sensory loss, hemianopia, spatial disorientation
Temporal lobe	Complex partial or generalized seizures, quadrantanopia, behavioral alterations
Occipital lobe	Contralateral hemianopia
Thalamus	Contralateral sensory loss, behavioral changes, language disorder
Cerebellum	Ataxia, dysmetria, nystagmus
Brain stem	Cranial nerve dysfunction, ataxia, papillary abnormalities, nystagmus, hemiparesis, autonomic dysfunction

· PREMORBID AND PSYCHOSOCIAL FACTORS

- Datient's premorbid cognitive capacity
- Coping skills
- · Cidaptive or maladaptive behavioral styles
- · Pedequacy and availability of family support systems
- Dsychosocial support systems play important roles in determining the impact and degree of neuropsychiatric symptoms

REDITINGSIGNES

- 1 Headache The classical headache of raised intracranial pressure ICD is worse on wakening
- · 2 Nausea or vomiting Projectile vomiting without nausea should raise particular suspicion
- 3 Cognitive impairment Détailed neuropsychological testing careful history
- · Reduction in the speed of information processing

- · 4 Epilepsy Most brain turnor patients will have a seizure at some point
- Epilepsy mc in low grade glioma Petternative explanations in psychiatric patients may include alcohol or benzodiazepine withdrawal lowering of the seizure threshold secondary to antipsychotic use or pseudoseizures
- 5 Weakness or clumsiness classically pyramidal
- If due to brain tumor subacute gradually progressive

- 6 Visual or sensory disturbance Hemisensory or visual neglect may for example asymmetry of personal grooming
- 7 [Inusual "noncanonical" psychiatric symptoms the literature is quite striking in how often odd symptoms which "don't quite fit" with the classical psychiatric syndromes herald an occult brain tumor
- 8 Dapilledema most difficult "high yield" sign of a brain tumor to elicit

- 9 Objective neurological deficit Cobnormalities
- testing pupils and eye movements
- · for pronator drift
- testing muscle tone and spinal reflexes
- assessing gait including a heel to toe test
- · screening for dysmetria with the finger to nose test
- In isolation neurological "soft signs" such as sensory abnormalities and the subtle persistence of developmental reflexes lack specificity in psychiatric patients

- 10 Endocrinological abnormality___
- Systemic physical or blood biochemical signs of acromegaly Eushing disease abnormal lactation or altered menstruation should raise clinical suspicion
- The classical neurological deficit of pitutary tumor is a bitemporal hemianopia These patients may also walk out into traffic

INVERTIGOTIONS

- · Brain CT or MRI scan
- · Clectroencephalography & & G
- · Lumbar puncture with CS + examination
- Lumbar puncture may however be helpful when cytology studies are required in the assessment of tumors such as leukemias lymphomas and meningeal metastasis
- Chest x ray will help inform a basic assessment of the likelihood and source of any metastasis

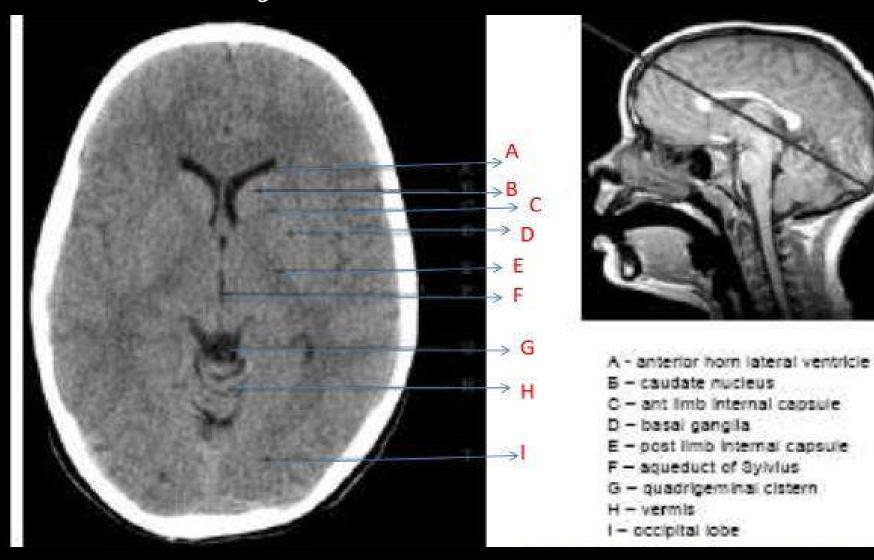
NEUROIMEGING

- Colscans evaluation of tumors which are calcified eroding bony intracranial structures or causing shifts in middle cerebral structures
- Evaluate abnormalities involving the ventricular system obstructive hydrocephalus and gauge the extent of cerebral edema
- MRI better at identifying the architecture of brain tumors whether they are solid or cystic or both
- · More precisely defining the relationship of a tumor to nearby vascular structures
- Lunctional MRI fMRI preoperative localization of specialized cortical function such as motor speech and vision

needstornkoimaging

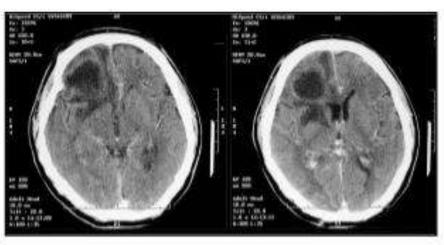
Patient's age	Most common types of brain tumor	MRI vs CT	Indications to image
≥40 years	Metastases High-grade gliomas Meningiomas	Roughly equivalent for imaging common tumor types. Base on cost, availability, and relative patient contraindications	New-onset cognitive or emotional dysfunction. Patient is not responding to appropriate pharmacotherapy for psychiatric diagnosis
<40 years	Low-grade astrocytomas Oligodendrogliomas	MRI preferred	New-onset cognitive or emotional dysfunction with associated somatic symptoms (headache, nausea, vomiting, papilledema, seizures, or focal deficits). Patient is not responding to appropriate pharmacotherapy for the psychiatric diagnosis

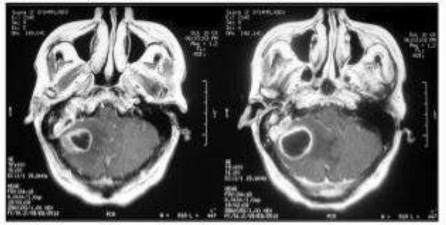
anceromy of BRAIN



CTCONTROLSTUDY

- Improves detection and characterization of intra cranial lesions.
- Opacifies blood vessels and detects areas of abnormal BBB break down.
- Normal renal function is a prerequisite.
- Ionic vs non-ionic contrast.





PROGNOSES

- Depends on the type
- Meningiomas and pituitary tumors can often be cured surgically
- Glioma presents an insurmountable challenge to surgical cure because by the time of clinical presentation tumor cells are dispersed throughout much of the brain
- · Higher grade tumors are more rapidly are fatal
- Ground one quarter of these patients survived to 2 year post diagnosis and only 10 were alive after 5 years
- Large population based epidemiological datasets suggest that among all occult developing cancers the risk for psychiatric hospitalization in the period before cancer diagnosis is highest for brain tumors

TRECTMENT

- Newly diagnosed patients combinations of surgery radiotherapy chemotherapy watchful waiting or supportive
 palliative care
- The most common active primary treatment for the most common glioma GBM is a combination of maximal surgical debulking radiotherapy and chemotherapy
- High dose corticosteroids are often started with the intention of reducing cerebral edema as soon as the radiological diagnosis is suspected
- · Centiepileptic drugs are also very often prescribed at this time
- Childhood brain tumors are often managed with treatments focused on the posterior fossa or brainstem again including surgery radiotherapy and chemotherapy

TRECTMENT

- In general though most psychiatric morbidity in brain tumor patients occurs after surgery during primary treatment and follow up
- The psychiatrist is most likely to be consulted when the patient's behavior or neurocognitive symptoms persist become more severe or arise de novo during follow up
- Monpharmacological support pharmacotherapy when necessary psychoeducation and support of the family

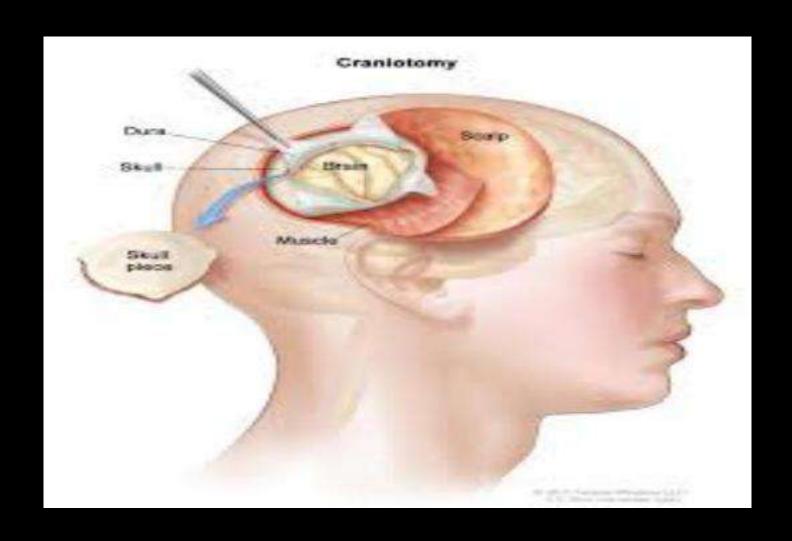
Managementostrumores

- Surgical excision
- Brain mapping with steriotatic approach
- Brachytherapy
- Gamma knife for radiosurgery
- Radiation
- Chemotherapy
- Mannitol to allow more chemotherapy across blood brain barrier
- Thalidomide- decrease vascular supply
- Growth Factor inhibitor tx- shrink tumor size
- Decrease ICP
- Assess for seizure activity and early signs of motor function impairment

SKRGKOLL MONOUGEMENT

- Craniotomy: surgically creating an opening in to the skull
- Burr Hole: Opening the cranium with a drill
- Craniectomy: Excision in to the cranium to cut away a bone flap
- Cranioplasty: Repair of cranial defect, using artificial materials to replace lost bone
- Stereotaxis: It uses computer guided apparatus to precisely target an area of the brain
- Shunt procedures: redirecting CSF from one area to another

CRONTOTOMY



Dsychiatric and behavioral complications of treatment

- Therapeutic interventions causing abnormalities
- Intraoperative injury to normal brain tissue in resection/debulking.
 - e.g. Nonverbal learning disabilities & psychotic symptoms in children, in frontal lobe –executive dysfunction.
- Radiation induced damage transient & reversible vs Permanent
- · Chemotherapy causing Delirium
- Treatment of ↑ ICT / Cerebral oedema, Corticosteroid result in Psychotic and affective symptoms

DEPRESSIVE DISORDER

- Epidemiology MDD is considerably more common in glioma patients than in the general population
- Longitudinal studies of depression are rare most likely a clinical diagnosis of depression persists in about half of patients for at least 3 months
- Etiology unknown though Genetic influences can be inferred when there is a family history of depression
- Ct Mood disorder due to brain tumor requires clinical interview evidence of a prominent persistent and socially disruptive change of mood

- Labs Cin endocrine screen is particularly indicated in patients with a remote history of radiotherapy to the brain if the radiation field included the pituitary gland
- Ddx The main competing psychiatric diagnoses are delirium neurocognitive disorder due to a brain tumor and probably most commonly adjustment disorder with depressed mood
- Course and Prognosis MDD is most likely in functionally impaired patients who generally have a poor prognosis
- Quailable evidence suggests that of those patients who can be followed up the disorder persists for at least 3
 months in around one half
- Brain tumor patients have one of the highest risk ratios for completed suicide in the year following diagnosis of tumor

· Treatment

· SERTICA MAD IN HECT Refractory cases and stimulants Methylphenidate

· SERT sertraline first line treatment most studies done

• Cen ECG should be checked before prescribing to confirm that the GTc interval has not been prolonged by chemotherapy

Cidapted from Trends in Brain Cancer Research New York Nova Science Dublishers Inc 2006 Depression and brain tumors

Ref	Dsychiatric symptoms	Tumor location	Tumor type	Remarks
Zúkoú Ć et al 2014	Depression impairment in numery <u>nativation</u> concentration insomnia increased appetite hadaches	Danistal lobe	Epidermoid tumor	Subsequent neurological symptoms led to CIT scan and diagnosis of the brain tumor
Assefa et al 2012	Depression anxiet <u>y insor</u> min headache nausea vomiting unilatural abducens palsy	Darasellar and retresellar areas of the petrous aper temporal lobe	Mentegiora	Neurologic deficit with psychiatric symptoms
Ozdílsk et al 2011	Depression auxiet <u>y head</u> ache	Left tengaral lobe	Glial tumor	Persistent headache led to neurologic consult and CT and diagnosis
Cheema et al 2010	Depression anhedonia low energy <u>insor</u> mia suicidal ideations	Left frontal and temporal lobe	Glioblastema multiforme	Duration of psychiatric symptoms of 10 yr make the association of glioblastoma questionable and possibly unrelated

CINXIETY

- · Epidemiology Trequency 30 and 50
- · Etiology Rarely anxiety can be caused directly by the brain tumor
- Cot adjustment disorder 3no GMD duration (months
- Classical panic attacks have a characteristically <u>sudden</u> onset stereotyped repeating pattern of features and relatively <u>short</u> duration
- Unfortunately in brain tumor patients much the same things can be said about epileptic seizures

- Ddx psychosis depressive disorder complex partial epileptic seizures pituitary related endocrinological abnormalities
- Prognosis Cipart from the terminal phase when palliative services should be consulted patients and their families can usually be reassured that it is normal and will pass
- Treatment & SKIs buspirone and low dose long acting benzodiazepines in conjunction with supportive or structured psychotherapy Dregabalin some reports
- Datients with fear or panic disorder symptoms occurring as a part of a temporal lobe tumor induced complex partial seizure may respond to treatment with PLGDs

STEROID INDUCED PSYCHOTIC DESORDER

- Epidemiology Corticosteroids typically high doses 8 mg dexamethasone orally twice per day and often urgent necessity mean that newly diagnosed brain tumor patients are at risk of developing a steroid induced psychotic disorder
- Treg less than 5
- Et psychotic symptoms delusions and or hallucinations occurring in association with the use of corticosteroids
- The risk is highest soon after starting treatment
- High dose 40 mg prednisolone equivalent day makes the syndrome more likely but is not essential

- Ddx delirium psychosis secondary to complex partial epilepsy MDD with psychotic features and a stress induced relapse of a pre existing functional affective psychosis
- Course and Prognosis Psychotic symptoms should resolve with the combination of antipsychotic and a lowering or reduction of steroid dose
- The literature is sparse on prognostic guidance
- Treatment If possible the offending corticosteroid should be reduced or stopped
- Nursing by familiar faces adequate ambient lighting regular reassurance and reorientation and de escalation and gentle distraction when necessary
- · Pentipsychotic medication is also indicated careful as it increases likelihood of seizures
- · El also reported some use in such patients

Dsychosis and brain tumors

Ref	Dsychiatric symptoms	Tumor location	Tumor type	Remarks
Lrayem et al 2014	Dsychosis auditory hallucinations self injurious behavior	Right temporal lobe	Astrocytoma	Psychosis developed either from tumor recurrence or right temperal brain tissue loss post surgery
Kaloshí et al 2013	Visual and auditory <u>hallucinations</u> spasmodic laughter minimal spontaneous speech	Cerebellum	Glioneuronal	Dartial improvement of symptoms with surgery
Gnazappa et al 2013	Lethargy anhedonia persecutory delusions and third person auditory hallucinations	Lowth ventricle	Choroid plexus papilloma	Inspresement with surgery

PERSONCITTY DISORDERS COND BEHOW TORCIL CHONGES

- · Epidemiology frequent troublesome behavioral changes are reported
- Studies conducted in various primary brain tumor populations report a point prevalence ranging from 16 in patients with low grade oligodendroglisma during follow up to over 70 in patients with primary CNES lymphoma
- · Behavioral symptoms are highly prevalent in the palliative stage of glioma No gender diff noted
- Etiology Lesion location especially when the tumor is in the frontal lobe is often assumed to be the "cause" of personality or behavioral change
- · Multifactorial encompassing biological psychological social and introgenic causes attributed

- Et establish the patient's premorbid personality and behavioral characteristics and confirm that the onset of the troublesome behavior was at the earliest in the months leading up to initial presentation of the brain tumor
- the severity of impact on the patient or his immediate environment including carers should at least be moderate
- In the long term clear pattern of new harmful behavior
- Cin assessment of exacerbating and alleviating factors is helpful therapeutically
- Ddx MDD and generalized anxiety disorder delirium and the possible role of any medication changes contemporaneous with onset of the troublesome behavior

·Labs

- standard hematological and biochemical screens for causes of delirium
- pulse eximeter reading to rule out frank hypoxia DIPDE is very common in these patients
- blood glucose measurement to exclude steroid associated diabetes and consequent hypoglycemic episodes
- chest x ray to exclude chest infection or DIPE
- · repeat head CT or MRI to exclude tumor progression or intratumoral bleed
- Course and Prognosis tend to persist and are difficult to treat perhaps unsurprisingly in a progressive disease

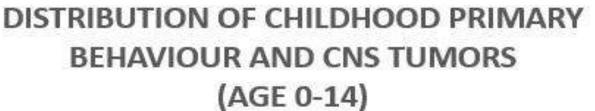
- Treatment Gr home based psychosocial intervention the Making Sense of Brain Tumor" program combines neuropsychological assessment psychological therapy and a person centered approach to treatment
- · Carer education and support is essential
- · Some benefit from treatment trials for psychomotor retardation abulia and apathy which case studies suggest bromocriptine or stimulants methylphenidate or modafinil
- Mood stabilizers for overtly risky settings of severe uncontrolled disinhibition and explosive anger
- · Cognitive rehabilitation techniques treating personality or behavioral change in these patients

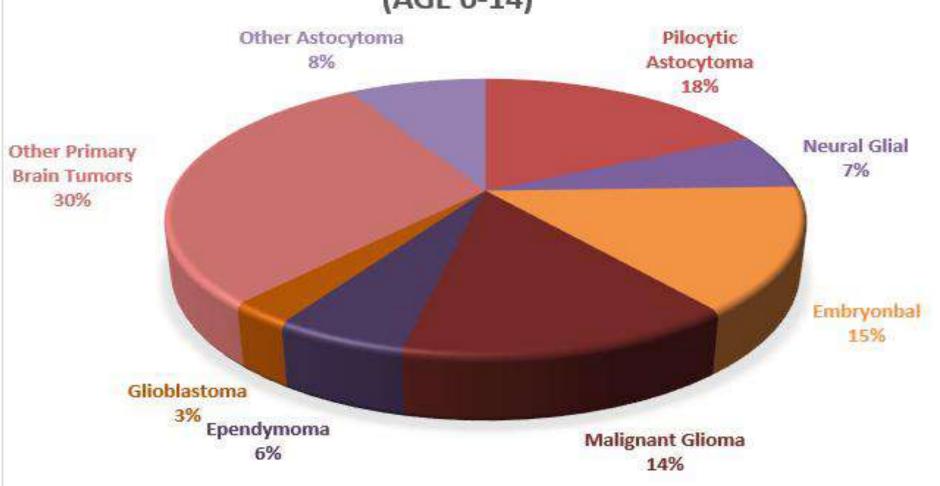
PERSONALITY CHANGES AND BRAIN TUMORS

Ref	Dsychiatric symptoms	Tumor location	Tumor type	Remarks
Lajara Nanson 2000	Dersonality changes and hypersexual behavior	Jentrícular	Ventricular cyst	Ingerovement with surgery
Paul et al 2000	Dersonality <u>changes</u> memory <u>impairment</u> poor concentration	Extramedullary with infiltration of the cerebral dura	Dlazmacy <u>toma</u>	
Lahy et al 1995	Lrontal lobe <u>symptoms</u> in absence of neurological signs	L'iontal	Meningioma	
Jones 1993	Dersonality changes aggressive behavior and emotional lability	(Jentricular	Ventricular cysts	Ingrovement with surgery
Lulton et al 1992	Dersonalit <u>y change</u> s walking difficulties incontinence neurologic signs	Irontal lobe	Multiple metastases	Door response to steroid treatment

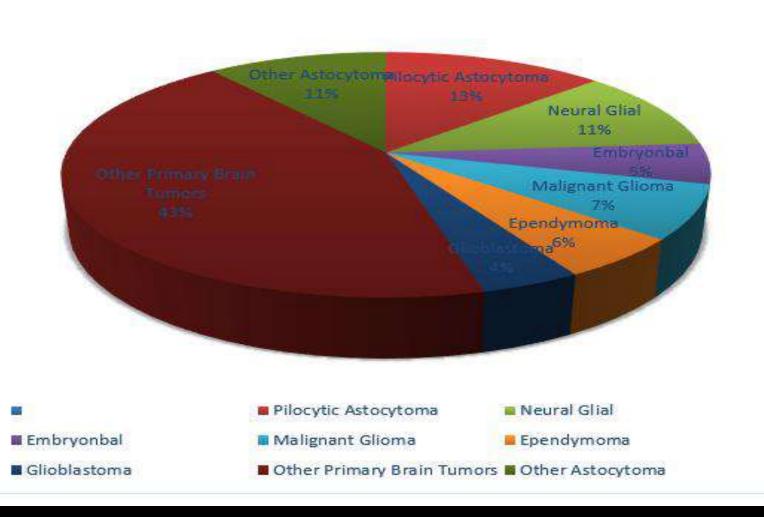
CHILDHOOD BROWN TUMORS

- · Childhood tumors are different diseases from the common adult tumors
- Uniquely challenging constellation of symptoms and disabilities at the crux of which is the long term cognitive effects of radiotherapy and or chemotherapy on the vulnerable developing brain
- · Epidemiology Most childhood brain tumors are infratentorial
- Etiology radiotherapy to the brain adversely affects neural stem cell proliferation and neurogenesis in the rodent hippocampal sub granular zone





Distribution of Childhood Primary Behaviour and CNS Tumors (Age 15-19)



- Et working memory attention and processing speed are commonly lower than normal levels for the patient's age and developmental stage
- · pediatric patients with an acute postsurgical posterior fossa syndrome
- Ddx MDD anxiety and alcohol or drug use or dependence
- Torms of chemotherapy can cause deafness which may contribute to psychosocial or emotional difficulties
- Children presenting acutely with an apparent DFS MRI brain rule out postoperative bleeding or cerebral edema

- Course and prognosis childhood brain tumor survivors tend to have considerable impairments of cognitive and emotional functioning manifest as social educational and vocational disability
- · Educational achievement compromised Reading spelling and arithmetic may all be affected
- Impaired emotional functioning with increased anxiety with some evidence of defective cognitive processing of emotions
- Behavioral problems may manifest at school including aggression and possibly a higher level of somatization
- Deer relationships suffer accordingly and adaptive and developmentally important behaviors communication and socialization adversely affected

- Lemales may be at greater risk
- Themes of impaired identity formation social isolation difficulty securing financial independence and limited career options young adult survivors
- · Completion of higher education is relatively rare
- Unemployment is often the norm yet most adult patients will be functionally independent in daily
 life

- Treatment Pe person centered problem focused holístic and realistic approach is recommended
- Cognitive rehabilitation structured exercises to boost cognitive skills has some evidence for efficacy in childhood survivors
- Improved executive and memory skills are seen particularly in the domains of attention processing speed cognitive flexibility and declarative memory____
- Evidence of psychostimulant methylphenidate improves attention and may improve behavior in the short term in childhood survivors of brain tumor
- For DFS its supportive management Zolpidem reports some effectiveness

NEUROIMEGING OF CHILDHOOD BREVINTUMORS

A	В		Signs and Symptoms	Diagnosis
		Α	Headache, seizures, hyperpigmented macules	Meningioma, neurofibromatosis 2
	0 3 2 6 3 1	В	Vomiting, facial weakness, ataxia, double vision	Glioblastoma multiforme
C		С	Nystagmus, facial weakness, ataxia, dysphagia	Diffuse intrinsic pontine glioma
		D	Recurrent vomiting	Medulloblastoma
		E	Nocturnal enuresis	CNS germinoma
3-6		F	Failure to thrive, visual abnormalities	Suprasellar juvenile pilocytic astrocytoma
G	H	G	Visual loss, hyperpigmented macules	Optic glioma, neurofibromatosis type 1
		Н	Facial weakness, ataxia, early morning vomiting	Ependymoma

ROLE OF PSYCHIOTREST

- DSYCHTCOTRISTS The mindset technical abilities and time required to conduct comprehensive and holistic person centered assessments
- · Inowledge of how to manage chronic and complex illnesses affecting vulnerable individuals
- Have direct expertise in the assessment and management of the many cognitive and psychiatric problems which very commonly affect these patients

CONCLUSION

- · Diagnosis and treatment of psychiatric symptoms of brain tumors are challenging
- · Dsychiatric symptoms may be the only presenting feature of brain tumors
- Thorough history and medical examination with a high index of suspicion are important for early diagnosis
- Neuroimaging should be considered in patients presenting with new onset psychosis or mood memory symptoms occurrence of new or atypical symptoms personality changes and anorexia without body dysmorphic symptoms

- Treatment is geared towards the tumor its complications and the psychiatric symptoms
- Management of persistent psychiatric symptoms is based on extrapolation of limited evidence assessment of risk is benefits and understanding of potential complications related to the disease and concomitant therapy
- Luther investigation is needed to improve our understanding of the mechanisms by which tumors produce psychiatric symptoms

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THOUR YOU

