# CHAPTER I INTRODUCTION

# **Background and Statement of the Problems**

Among terrifying diseases, tumor or cancer is probably one of them. According to the statistics of non-infectious diseases that caused death in 2011 by The Ministry of Public Health, neoplasm was the first cause. The statistics says that 95.2 people of 100,000 died because of neoplasms. This is one of the biggest public health concerns. Neoplasm or tumor is a result of an abnormal growth of abnormal tissues in an organ. Neoplasms can be either benign or malignant. Despite the part of the body a tumor is formed, it still has a great impact, physically and emotionally, on the patient and the family members.

Moreover, should the tumor or cancer occurs within the brain, the effect is even more fatal since the brain is the organ that controls all of the human functions, including body functions, mentality, and hormone production. A brain tumor within a certain part of the brain certainly affects the functionality of that part of the brain. To give an example, a tumor in temporal lobe, which is the part that involves storing memories, may cause the patient a memory loss. The problems gradually increase the severity. If the patient is undergone the treatment in time, those problems whence can be reduced or prevented. In most cases, patients come to the doctor because of the headache, nausea, or some odd bahaviors noticed by relatives, such as speech deficit or personality changes.

The most important impact to the brain that should be concerned is the incognitive impairment. It worsens the patient's intellect. The ability to learn, analyze, and problem solve is lower. This affects the patient's study, work, or routine life. Furthermore, it also causes a mental impact. Since the discovery of the disease in a patient, the patient may feel nervous, stressed, and insomniac (Sompop Reungtrakul. 2001). A brain tumor also induces psychopathology and personality disorders, for

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example, a patient with a frontal lobe brain tumor may show similar indications of the affective disorder or the mental disorder – a change of personality, easily agitated, unable to control emotions and behaviors, and inappropriate social behaviors, such as using foul words or inproper sexual behaviors (Sompop Reungtrakul. 2011).

Siriraj Hospital is a medical center that is specialized in brain tumor surgery with approximately almost 1,000 patients undergone brain tumor treatments per year (Theerapol Wotthiwej, personal communication, December, 4 2012). Brain tumors can be categorized into benign tumor and malignant tumor. The treatments are varied, including surgery, radiation, and medication. Surgery is the main method to treat most of the brain tumor symptoms.

This study is cross-sectional research that is interested in studying the impacts on patients with benign brain tumor that undergo the first surgery in terms of cognition and neuropsychiatric symptom. It is intended to be useful in nursing the brain tumor patients, and to be fundamental information for the panel study after the treatment of the patients.

#### **Research Ouestions**

How much do brain tumor patients have cognitive impairment and neuropsychiatric symptoms?

## **Research Objectives**

- 1. To study the prevalence of cognitive impairment in brain tumor patients
- 2. To study the prevalence of neuropsychiatric symptoms in brain tumor patients
- 3. To find the relation between each individual's variables that influence the neuropsychiatric symptoms and the cognitive impairment of brain tumor patients

# **Expected Outcome**

- 1. Understand the prevalence of cognitive impairment and neuropsychiatric symptoms in brain tumor patients
- 2. Understand the relation between the variables that influence the neuropsychiatric symptoms and the cognitive impairment of brain tumor patients

#### **Scope of Study**

This study is a research about the cognitive impairment and the neuropsychiatric symptoms in brain tumor patients at the Department of Surgery, Siriraj Hospital. The tools for data collection include five parts: general questionnaire, Glasgow Coma Scale to assess the level of consciousness in a patient, the MMSE-Thai 2002, the Montreal Cognitive Assessment-Thai Version (MoCA Thai Version) to assess cognitive impairment, and the Neuropsychiatric Inventory (NPI) to assess neuropsychiatric symptoms. The data was collected from the sample of 43 benign tumor patients and their relatives.

#### **Definitions**

**Brain tumor** is a mass of tissues that abnormally grow within the brain, including a tumor in cranial nerves, meningiomas, a Pituitary tumor, a skull base tumor that invades into the brain, and a metastatic tumor that spreads to the brain.

**Cognition** is the process by which the brain restores the data. It includes different elements. The Montreal Cognitive Assessment (MoCA) Thai version assesses from the attention, concentration, executive function, visuoconstructional, concept, computation, and orientation.

**Neuropsychiatric symptoms** are symptoms occurred in brain tumor patients. The NPI categorizes the symptoms into Delusions, Hallucination, Agitation/Aggression, Depression/Dysphoria, Anxiety, Elation/Euphoria, Apathy/Indifference, Disinhibition, Irritability/Lability, Aberrant Motor Behavior, Sleep, and Appetite and Eating Disorders.

# CHAPTER II

# LITERATURE REVIEW

The study of cognitive impairment and neuropsychiatric symptoms in brain tumor patients at Siriraj Hospital was conducted by researching the concepts and theories from documents, textbooks, articles, and related research to conjure up the study's methodology. The details are mentioned below.

## **Brain Tumor**

Definition of brain tumors

Diagnosis of brain tumors

Classification of brain tumors

Brain tumor treatments

Impacts of brain tumors on patients

## Cognitive

Definition of cognitive

Assessment of cognitive

Cognitive impairment in brain tumor patients

# **Neuropsychiatric symptoms**

Definition of neuropsychiatric symptoms

Neuropsychiatric manifestations of brain tumors

Assessment neuropsychiatric symptoms

## **Related literature**

## **Brain tumors**

#### **Definition of brain tumors**

Jesada Nimmannitya (1994) says that a brain tumor is an important pathology. It is grouped as an intracranial expanding lesion, in which causes the dysfunction of the part of the brain that a tumor occurs. The patient's neurological symptoms can vary. When a tumor gets big enough, it can increase the intracranial pressure, and eventually causes death. Most brain tumors are primary brain tumors, few are metastatic brain tumors.

Trevor (2012) suggests the locations most often found the brain tumors, respectively, are posterior fossa (30%), frontal and temporal lobe (22%), parietal lobe (12%), pituitary (10%), and occipital lobe (4%).

#### Diagnosis of brain tumors

Jarae Phonprasert (1985) mentions that a brain tumor diagnosis includes

- 1. Asking about the patient's personal and family health history and a physical exam are very important. However, directly asking the petient may not give accurate information as the result. The best means is to combine the information from family that observes the initial symptoms, different behaviors, and result from previous medical treatment together with the physical exam and a thorough neurological exam.
- 2. **X-ray** of the lungs is necessary to look at bronchogenic carcinoma that spreads to the brain. An X-ray of the skull to see the location of the pineal calcification, the skull deterioration, the decay of sellar turcica at lamina dura or posterior clinoid process. It shows increased intracranial pressure.
- 3. **CT** scan (computerized tomogram) helps a lot in dianosing an intracranial tumor since it can tell the location of the tumor, the swelling, the midline shift, the brain's shape, the size of ventricle, and the number of tumor vascularity.

4. **Radioisotope brain scan** by injecting technetium pertechnitate, the location and size of the tumor can be identified, but unlike CT scan, the size of ventricle and the midline shift cannot be identified.

- 5. **Cerebral angiography** helps pinpont the lesions and size of the tumor, and shows the arteries carrying blood into and the veins carrying blood out of the tumor.
- 6. **Pneumoencephalography** and **ventriculography** help locate the tumor that invades or block the ventricle.

#### Classification of brain tumors

The classification of brain tumors have been evolving since 1926. Bailey and Cushing categorized a glioma by using metallic impregnation technique along with a contrast dye to show different types of tumor cells. The combined method classified tumors into 14 types. After that, more approaches to classify the tumors were developed. Eventually, the World Health Organization attempted to develop the new classification of brain tumors so that they would be universal and easier to compare each type's statistics. The World Health Organization's classification of brain tumors (Jarae Phonprasert .2528, Andrew H. Kaye.2005, Andrew H. Kaye. (2012) can be concluded as the following.

## Tumours of neuroepithelial tissue

- Astrocytic tumors
- Oligodendroglial tumors
- Oligoastrocytic tumors
- Ependymal tumors
- Choroid plexus tumors
- Other neuroepithelial tumors
- Neuronal and mixed neuronal-glial tumors
- Tumors of the pineal region
- Embryonal tumours

# Tumours of cranial and paraspinal nerves

#### **Tumours of the meninges**

- Tumours of meningothelial cells

- Mesenchymal tumors
- Primary melanocytic lesions
- Other neoplasms related to the meninges

# Lymphomas and haematopoietic tumours

#### **Germ cell tumours**

## **Tumours of the sellar region**

#### **Metastatic tumours**

The prevalence of brain tumor incidence according to the World Health Organization is shown in Table 2.1

**Table 2.1:** Incidence of common cerebral tumors

| Incidence of common cerebral tumors             | (%) |
|---|-----|
| Neuroepithelial                                 | 52  |
| Astrocytoma (all grades including glioblastoma) | 44  |
| Ependymoma                                      | 3   |
| Oligodendroglioma                               | 2   |
| Medulloblastoma                                 | 3   |
| Metastatic                                      | 15  |
| Meningioma                                      | 15  |
| Pituitary                                       | 8   |
| Acoustic neuroma                                | 8   |

Source : Table 6.2 Andrew H. Kaye (2005) in Essential Neurosurgery Third edition p. 65

#### **Brain tumor treatments**

Jarae Phonprasert (2528) mentions two types of brain tumor treatments.

- 1. Curative treatment is a surgery to remove the tumor. Patients hence are fully cured from the disease.
- 2. Palliative treatment is operated with an intra-axial tumor that cannot be completely removed because of its hazardous lesions. There are many ways of the operation.

- External decompression is a craniotomy that opens the skull flap and the dura to allow the brain to swell, and then a biopsy is performed.

- *Internal decompression* is an external decompression operation with removing unnecessary part of the brain and some part of the tumor. The aim is to decrease the intracranial pressure and to make room for the swelling brain and tumor that were caused by radiation or medication.

- CSF shunting is a surgery that allows excess cerebrospinal fluid from the ventricle to drain out in order to reduce the intracranial pressure.

- Radiation therapy to cure brain tumors and cancerous tumors uses X-rays and gamma rays. The aim is to use the radiation to kill cancer cells. Normal tumors are more resistant to the radiation than cancerous tumors.

- Chemotherapy

- Steroid therapy reduces the swelling brain areas nearby the tumor. The treatments mentioned above help stop the growth of tumors before they further damage the brain. However, there are also some side-effects to be considered. Murial (2012) says about the effects from brain tumor treatments as the following.

- Radiation therapy: It is found that 25-30% of the patients cured by radiation suffer from the malfunction of the brain, and more than 70% encounter cognitive dysfunction and neuropsychiatric symptoms.

- Chemotherapy: After being treated through all stages, whether with standard dose or high dose, the impairment of cognitive function, including speed of information processing, memory, executive function, spatial abilities, and simple attention span, may occur. Mood disturbance is often found in patients whom are cured by cytokine. Using opioids for pain relief may cause some changes in nervouse system related to behaviors and emotions, and even slow down the movements. Some cases may have hallucination or delirium.

The aforementioned information is relevant to research related to brain tumor patients as Fox SW (2012) mentions that treatments by surgery, radiation, and chemotherapy all affect the cognitive function.

## **Impacts of brain tumors on patients**

Before talking about the impacts of brain tumors on patients, the functions of each division of the brain should be discussed. Jessica Kraker and Jaishri Blakeley (2009) summarize them as in Table 2.2

**Table 2.2**: The divisions of the Central Nervous System and Their Major Roles

| Devision of central nervous Major functions |   |
|---|---|
| system                                      |   |
| Frontal lobes                               | Forethought and planning, executive functions,      |
|   | personality, premotor cortex, motor cortex          |
| Parietal lobes                              | Somatosensory cortex, perception, integrating input |
|   | to construct spatial coordinate system for world    |
|   | around us. Visual pathways.                         |
| Temporal lobes                              | Memory, auditory receptive area, language. Visual   |
|   | pathways.   |
| Occipital lobes                             | Visual reception and interpretation                 |
| Limbic system                               | Including amygdala, hypothalamus, hippocampus:      |
|   | integration of memory, emotions, homeostasis        |
| Cerebellum                                  | Coordination, balance, tone                         |
| Brain stem                                  | Cranial nerves, pathway to spinal cord, cardiac and |
|   | respiratory function                                |
| Spinal cord                                 | Relays motor information to periphery, and sensory  |
|   | information to CNS                                  |

Source : Table 1.2 Jessica Kraker and Jaishri Blakeley (2009) in Brain Metastasis: Multidisciplinary Approach p. 11

Jesada Nimmannitya (1994) talks about the impacts on patients by classifying them into general symptoms and specific symptoms that only happen in case of tumors in different brain areas.

1. **General symptoms** are caused by increased intracranial pressure. There are three significant symptoms: headache, projectile vomitting, and visual defect due to papilledema (chocked disc). When a tumor gets bigger, some other symptoms also show, such as personality changes, lower consciousness,

diplopia, strabismus due to abducens nerve palsy, dizziness, generalized epilepsy, and Cushing's reflex. Yet these symptoms can also happen due to other causes, for example, a blood clot in the brain, brain abscess, swelling brain, etc.

2. **Specific symptoms** are symptoms of losing particular functions of destroyed divisions of the brain caused by tumors. These symptoms are significant in terms of dianosing the location of tumors. Generally, when patients see the doctor, they do not really suffer from the specific symptoms, but also the symptoms casued by the loss functions of the division of the brain near the tumor. Since the brain keeps swelling, the neighboring regions get pressed into, thus the additional destruction gradually increase. Thorough findings of medical interview helps identify the origin of the particular brain's function loss. Aside from the symptoms caused from the brain destruction, there are also symptoms caused from the brain getting stimulated. They show in different types of seizures, such as focal seizure, which are as important since they also help localize the tumors.

The brain has divisions. Each division has particular function and connects to one another. A tumor in a particular location of the brain causes specific fuction loss of that division and the nearby; however, the symptoms may not be distinct due to other factors, such as age, type of the tumor (benign or malignant), the growth rate of the tumor, and herniation. Frequently, patients do not have any shown specific symptoms, only increased intracranial pressure, which the location of the tumor can only be known by the radiation.

The impacts of brain tumors in different areas can be divided into:

#### Frontal lobe

Jesada Nimmannitya (1994)states that the frontal lobe is the biggest part of the brain. The frontal lobe's function loss causes the impacts as listed below.

1. **Monoplegia, Hemiplegia** Patients with tumors in the motor area mostly come to the doctor quickly because it is the area that causes torpidity of organs or spasms. Tumors located in subcortex cause function loss of the areas called monopregia. If the motor area linkaged to arms and hands is suppressed by a tumor, the torpidity of the opposite side of arms and hands occurs. Patients with a tumor at

flax in paracentral lobule, such as flax meningioma, may have the torpidity of both legs, and some patients may even suffer from anuria.

Tumors located in the lower part of the frontal lobe in the dominant hemisphere, the central of facial muscles and Broca's area, result in speech deficit (dysphasia) or inability to articulate at all (aphasia) and the torpidity of facial muscles. If these tumors cause a convulsion, patients will not be able to speak while having a seizure or after the seizure stops for a while.

Tumors in the deep white matter that contains corticospinal fibres cause hemiplegia even though the tumors are small.

Myasthenia starts with little torpidity before getting more sever and spreading to other parts of the body. Knowing medical and physical background has diagnostic significance for brain tumor patients.

- 2. **Epilepsy, convulsion, seizure, fit** These are very crucial, especially in adults who have never had a record of having a convulsion. In addition, focal seizure and Jacksonian or marching epilepsy are even more crucial because they can define the cause and locate the disease.
- 3. **Frontal ataxia** is when a tumor damages the fibres in the frontal lobe in the premotor and the motor areas that connect to other important regions of the brain, namely pons and cerebellum.
- 4. **Abnormal conjugate gaze** The frontal premotor area, at the back of middle frontal gyrus, called frontal eye field (Brodman's area 8), controls the movement of both eyeballs to roll to the same direction (conjugate gaze), which is voluntary. When this area gets stimulated, the eyes get conjugate deviation into opposite directions, and may cause the face and the body to turn to the same direction as the eyes go. The eye movement stimulated by sight requires impulse from area 17 at the occipital lobe through inferior occipitofrontal fasciculus to frontal eye field. If this is destroyed, the paresis of conjugate gaze to the opposite side occurs. The eyes thus look to the direction of the damaged side. This is temporary for those who are conscious because they can adjust, but lasts longer in those who are delirious.
- 5. **Personality changes** The prefrontal cortex in human is advance in higher intelligence function, namely memorization, consideration, logical thinking, self-controlling, thoughts, and personality. Tumors in this area, thus, cause changing

personality and thoughts. Generally, tumors in this area do not cause obvious specific symptoms until they get very big. The initial changes are mostly unseen by patients and family. Patients may complain about worse memory and the lack of concentration, resulting in less productive work as a consequence, lower sense of responsibility, and worse cognition. These problems slowly grow stronger to the point of having dementia. Next there will be changing in personality, for instance, having no initiative idea, lack of attention, decrease of personal hygiene, using foul words or bad temper, eating slowlier and messier, urinary and fecal incontinence, drowsiness, and indifference to any stimuli.

- 6. **Tremor** can be found in patients with big, deep frontal lobe brain tumors. Tremor can happen on the opposite side or both. The shaking is similar to Parkinsinism, but less severe, and does not resemble pill rolling movement.
- 7. **Grasping and Groping reflex** Grasping reflex is accounted for a great clinical significance and a pathognomonic sign of the disease in the frontal lobe.

Grasping reflex is a reaction of clasping by fingers when the palm is stimulated by an object, especially on the area between index finger and thumb. This is the action to grasp the object. Patients will not let go. The more you try to pull out the object, the tighter they hold. In some patients, when closed their eyes and softly touched on their palm or finger, they will react by grasping or groping arond. That is called groping reflex.

Grasping and groping reflexes are infant's reactions. The disease in the frontal lobe makes patients have the infant state, thus grasping reflex is found.

The information above is coherent to what Sompop Reungtrakul(2554) explains about the damage to each brain division in the context of psychiatry.

The symptoms of having abnormality in the frontal lobe are listed below.

- 1. Changes in personality in terms of lacking self-constarint, being overly familiar with strangers, acting inappropriately, being overtalkative, being child-like when getting excited, or having a crude humor.
- 2. Lower social relationship and ethical behavior, resulting in no consideration of consequences
  - 3. Unusual sexual behaviors, such as showing off the sexual organ
  - 4. May commit some minor criminal case, such as stealing

- 5. Decision making regarding finance and having relationship are considerably twisted
  - 6. Being inconsiderate or indifferent
  - 7. No anxiety or self-awareness
  - 8. Being joyful without any particular reason
  - 9. Lack of initiative idea for any work
- 10. Thinking and movement become very slow. If getting severe, there will be no response similar to the stupor.
- 11. Impairment in concentration, attention, and competence to work on planned activities, yet normal intellect

#### Parietal lobe

Jesada Nimmannitya (1994) mentions that the superior and the inferior parietal lobes are called psychosensory or sensory association area. The parietal lobe receives and translates the sensations from the thalamus, especially regarding tactile, pressure, and position sensations. Tumors in this area make patient lose joint sense, vibration sense, tactile localization, light touch, two-point discrimination, and stereognosis. Symptoms of losing sensations that are mosty found include:

- 1. **Astereognosis or tactile agnosia** is the loss of cortical sensation that is found the most. The loss occurs on the opposite side of where the tumor is. Patients are not able to tell the names of any objects that they used to know and use by touching, since they can sense neither size, weight, shape, nor component.
- 2. **Abnormal two-point discrimination** Patients cannot discriminate two-point stimulation that happens at the same time. It shows the loss of both touch and pressure. This happens on the opposite side of the tumor.
- 3. **Sensory inattention** is another clinical significance in patients who hvae tumors or other dieseases in the parietal lobe. Patients cannot sense the stimulation on the opposite side of the disease when stimulated both sides, same place, at the same time. To illustrate, a patient who has the sensory inattention on the right side cannot tell that the right palm is being stimulated when stimulated on both palms at the same time. If the patient's palm is stimulated one at a time, he or she can sense it, though.

4. **Sensory epilepsy** The beginning of the symptom is having some feelings that are difficult to explain. For example, patients may have a tingling feeling, like being electrified, or paresthesia in the part of the body that is starting the disease, then spreads to other parts. It is called sensory Jacksonian fit. The sensory epilepsy probably occurs in a particular place, stops, and then disappears. If it spreads to the motor area that makes the patient have a convulsion – only of some part or all over, though, it can make the patient unconscious (generalized convulsion). Sometimes, the symptom of this sensation is thought to be the aura of the motor epilepsy.

- 5. **Pseudo-athetosis** Tumors or other diseases in the postcentral gyrus make muscles hypotonia and atrophic, resulting an ataxia both while moving and staying still. When patients are resting, there might be some movement of their arms and legs called pseudo-athetosis.
- 6. **Contralateral homonymous inferior quadrantanopia** is found in patients who have large tumors in the rear parietal lobe that are deep into the white matter, near the side of lateral ventricle, and press or destroy the upper optic radiation, resulting the visual field defect.
- 7. **Gerstmann's syndrome** is when tumors or other diseases occur in the rear parietal lobe, near the angular gyrus in the dominant hemisphere. Patients have the finger agnosia (unability to tell apart the fingers), dysgraphia (unability to write), dyscalculia (unability to calculate), and left-right disprientation (unability to tell left and right).
- 8. **Sensory aphasia or Dysphasia** happens when there is a tumor in the postero-inferior of the parietal lobe, which is the same place as Wernicke's center in the dominant hemisphere. Patients are not able to understand verbal language (dysphasia) or interpretation. They also have inabilities to read (dyslexia) and calculate (dyscalculia). If the tumor gets bigger, the loss is also greater. It also causes global dysphasia, which is talking nonsense or jibberish. It is not understandable, thus verbal communicating is futile.
- 9. **Agnosia and Apraxia** can be found in the cases that have a tumor in the rear parietal lobe, close to the temporal lobe and the occipital lobe.

Agnosia is a loss of ability to understand or memorize things associated by visuality or touch due to the receptive defect.

Apraxia is a loss of ability to perform a task, despite having a desire to do so, for example, unable to unpin even though the patient knows how to, yet there is no sign of motor paralysis, sensory loss, or ataxia.

Sompop Reungtrakul (2011) talks about the parietal lobe that if there is an abnormality, it will cause a complex cognitive impairment as the following.

- 1. Abnormality in 3D visual perception (visuospatial difficulties) and inability to locate the object in the air, or inability to explain the relation of objects just by looking
- 2. Topographical disorientation : Problem to learn and memorize directions
  - 3. Dysphasia: The difficulties in putting words together to make meaning
  - a. Motor dysphasia or ataxic dysphasia: patients cannot control muscles to work cooperatively
  - b. Sensory dysphasia: patients do not understand meaning of written laguage or speech
  - 4. Motor apraxia: inability to use objects properly
  - 5. Body image perception and external space abnormalities
    - a. Anosognosia: denial of having paralysis or hemiplegia
  - b. Hemisomatognosia: patients feel that some of their limbs are missing or getting twice bigger, which is a hallucination.
  - c. Patients may not recognize or perceive anything on their left visual field. It is shown when having patients mimic a drawing and they leave the details of the left side.
    - d. Dressing apraxia: difficulty in getting dressed
- 6. Prosopagnosia: patients severly have an impairment in recognizing their own face, especially when the abnomality is at the back and related to the occipital lobe.

## **Occipital lobe**

Jesada Nimmannitya (1994) states that the occipital lobe is a division that is least likely to be found a tumor in. It is said to be the silent area, which means it normally does not show any sign or symptoms in the beginning, not until the tumor

grows large. Patients suffer from increased intracranial pressure, and the symptoms are headache, papillaedema, and vomitting. Impacts from the tumor may result from both the damage and the epilepsy. They are explained as followed.

- 1. Contralateral homonymous hemianopia is the loss of either left or right visual field of both eyes due to the damage at the optic radiation or the calcarine fissure. The loss can be either complete or incomplete homonymous hemianopia depending on the tumor's lesions and size. Should there be any compression on the upper or lower calcarine fissure, homonymous inferior or superior quadrantanopia may occur, respectively. Homonymous hemianopia is accounted to be the most significant symptom of tumors in the occipital lobe. However, some patients are not aware that they have lost half of their visual field, and some show the background record that indicates having hemianopia, for example, telling the doctor that they used to accidentally hit the door often. Some patients can see only half of the word or sentence while reading, or while writing, they usually write to the utmost right margin. These are the symptoms of right hemiamopia.
- 2. **Cortical blindness** is the loss of vision because a tumor has damaged the occipital lobe in the calcarind fissure both sides. It is found in the patients who have large flax meningioma that expands to both sides. But the pupils still react to the light. The convergence and the movement of eyeball are also still normal.
- 3. **Epilepsy** of patients who have tumors in the occipital lobe comes in the form of seeing unstructured visions. It is like having a sudden visual hallucination, such as seeing flickering lights. This is different from temporal lobe epilepsy that patients normally see shape and form. Visual hallucination symptoms may include involuntary eye movement to the other side, and it is a clinical significance for diagnosing occipital lobe tumors.
- 4. **Visual agnosia, alexia, agraphia** In some patients who have large occipital lobe tumors that spread to the peristriate area (area 9) or the parieto-temporal lobes in the dominant hemisphere, they are unable to understand meaning or key of written words, despite having normal vision. In addition, they also have agraphia (inability to express ideas by written words). These symptoms are found in patients with tumors in the parietal or temporal lobes as well. Therefore, it is difficult to

distinguish occipital lobe tumors from parieto-temporal lobe tumors by relying on only this symptom.

Sompop Reungtrakul (2011) mentions about abnormality of the occipital lobe that does not limited to only vision, but also agnosia – not knowing what it is despite seeing it.

- Color agnosia: inability to name colors
- Visual object agnosia: inability to identify seen objects
- Prosopagnosia: inability to recognize own face in the mirror
- Simultanagnosia: inability to tell sophisticated meaning of pictures Apart from agnosia, patients can also have complex hallucinations.

## **Temporal lobe**

Jesada Nimmannitya (1994) states that patients with temporal lobe tumors mostly come to see the doctor when the tumors have already gotten big because the changes in the beginning are not obvious, especially tumors in the frontal temporal lobe. If they occur in the dominant hemisphere, though, the patients may go to the doctor sooner because the abnormality of speech often shows first. Specific symptoms of tumors in the temporal lobe include:

- 1. **Visual field defect** is a significant symptom of tumors in the temporal lobe. A frontal temporal lobe tumor damages Mayer's loop, thus causes the homonymous superior quadrantanopia type of visual field defect. It is the symptom shown only in the case of temporal lobe tumor. When the tumor gets larger and expands to the rear, it destroys the upper fibres of the retina, resulting the homonymous hemianopia type of visual loss. That is found less often than the homonymous superior quadrantanopia, for most patients often see the doctor when the tumors are already big.
- 2. **Dysphasia, aphasia** Tumors at the rear temporal lobe in the dominant hemisphere, near or at the Wernicke's center, cause sensory dysphasia or aphasia. Patients do not understand verbal language. If tumors are frontal, near the Broca's area, they cause motor dysphasia. Global aphasia occurs if tumors are very big.
- 3. **Unicinate fits and temporal lobe epilepsy** Tumors near the center of the temporal lobe, which is the location of uncus and para-hippocampal gyrus that play

important roles of smelling and tasting, cause uncinate fits. Patients initially think that they can smell or taste something weird, then they have actions of tasting or liplicking. In the meantime, they only stare or space out. Finally, they say that it is like they were in a dream.

Temporal lobe epilepsy or psychomotor seizure is a symptom that occurs when the disease takes place in the center of the temporal lobe, namely, uncus, parahippocampal gyrus, amygdale, and subcortical connection. Patients have an automatism. They have strange movements and half-conscious behaviors. Some suddenly stop what they are doing, stare still, look puzzled, but there is no seizure or getting unconscious. Some may wander a long distance, but cannot remember where they have gone to or done (amnesia). Some may have illusions, hallucinations that involve hearing, smelling, or tasting, and may perform an act of chewing and swallowing. Some patients say that it is like they are in a dream that they used to see or have ever been in those situations before. That is called déjà vu. After the psychomotor seizure, patients may feel confused for a while, whereas some may sleep.

- 4. **Amnesia** Tumors deep in the medial of the temporal lobe damage hippocampus, or the channel of transfer, cause loss of recent memory. If more severe, the symptom resembles dementia.
- 5. **Hallucination** can be both seeing and hearing. As for visual hallucinations, patients think they see clearer pictures, which differs from the symptom of occipital lobe tumor that is rather an unstructured image. For auditory hallucinations, patients often say that they can hear noises, such as bell rings or whistles, in their ears.
- 6. **Hemiparesis** A large temporal lobe tumor in the medial presses the corticospinal tact that goes to facial muscles (fibres are on the sides) on the opposite side. Thus it causes weakness of the body on the side opposite the tumor. Or in some cases, if a tumor presses the internal capsule, there can be hemiparesis on the opposite side of the body. This big tumor may press the brain stem and moves it to the opposite side, thus the cerebral peduncle is pressed by the rim of tentorial cerebella. Hence, hemisparesis can be found on the same side of the tumor. Finding homonymous menianopia along with hemiparesis is very significant for localizing a temporal lobe tumor.

- 7. **Trigeminal & oculomotor nerve palsy** Since Gasserian ganglion of the trigeminal nerve is located near the center of middle cranial fossa, it may be pressed by a tumor, and cause face numbness and corneal reflex loss on the same side of the tumor. In some patients, a tumor can grow and expand over the tentorium rim, and press on the oculomotor curve, which is close to uncus. In that case, patients will have ptosis, mydriasis, and no reaction to the light also happens on the same side of the tumor.
- 8. **Unilateral exophthalmos** is found in the patients who have a frontal temporal lobe tumor, such as meningioma of the lesse wing of the sphenoid. It causes a bad blood reverse circulation of the eyes, thickens the sclera, resulting narrower sclera, or the tumor expands into the sclera. These all can case exophthalmos. In some patients, meningioma may thicken the temoral bone, thus makes the patients's temper bigger than the other one.
- 9. **Ataxia** is not found very often. It has the same symptoms as the frontal ataxia, that is tottering or falling to the side opposite the tumor. It is found in patients who have a tumor in the rear of middle and inferior temporal gyrus, in which the emporoponto-cerebellar pathway is destroyed.

Sompop Reungtrakul (2011) says that abnormalities in the temporal lobe may or may not cause any symptoms as the following.

- If there is an abnormality in the dominant lobe, there will be an impairment in intellectual function. Or it may only cause speech deficit with a severe sensory aphasia. Sometimes, it is shown by talikn nonsense. If the disease is located at the backside, there can be alexia (word blindness), resulting inability to read, and causes agraphia (inability to express ideas by writing).
- If there is abnormality in the non-dominant lobem the symptoms may show insignificantly. Sometimes there can be high visuospatial difficulties.
- If it happens in the medial temporal lobe structure (hippocampus), it will cause amnestic syndromes.
- If it happens in the dominant lobe, there will be the ability to learn and memory about language loss. However, if it happens in the non-dominant lobe, there will be learning and memory loss, but excluding speech ability.

- Patients with the chronic disease in the temporal lobe often suffer from severe personality changes, especially being extremely emotional and aggressive. They have a high risk of having a psychiatric disorder, depersonalization, and sexual abnormality.

## Thalamus and basal ganglia

Jesada Nimmannitya (1994) says that thalamus and basal ganglia are located very close to each other. Symptoms of the disease in these two divisions, thus, are not much different. Hence, he sums them up as one. This area of the brain is very least likely to have tumors. Yet, the symptoms are normally quick to show since they involve movement (corticospinal tract) and numbness (sensory pathway). The symptoms are listed below.

- 1. **Hemihypesthesia or Hemianesthesia** is being numb on the side opposite the tumor. It is a loss of all kinds of sensation. As for a tumor that originally occurs in the thalamus, this symptom comes before the body's weakness. In patients who have a tumor in the basal ganglia, the hemiplegia generally comes before the numbness, though.
  - 2. **Hemiplegia** is often found and mostly occurs during the first stage.
  - 3. Homonymous hemianopia
- 4. **Upward conjugate gaze palsy and anisocoria** Patients cannot look upward, the pupils are not the same size, and they barely react to the light.
- 5. **Ataxia** Patients may have incoordination of the body opposite side to the tumor. Nevertheless, this is rarely found, but when found, it is normally found during the latter stage of the disease.
- 6. **Mental symptoms** may not be a specific symptom of tumors in this area, but it can be found in patients with thalamus tumors. When the thalamus and subthalamus are damaged, patients will be weary and groggy. They sleep a lot, become dull, and lose memory.

Impacts on brain tumor patients, especially cognitive problem and neurobiological behavior, vary depending on certain factors, that is, ethnicity, location and size of the tumor, growth of the tumor, and treatment process (S.W. Anderson, H. Damasis, and /tranel, 1990; S.W. Anderson, Ryken, 2008; Correa, 2010 cited in

Mutriel Deutsch lezak, 2012). Changes in tumor patients can include cognitive deficit, mood disturbance, behavioral alteration, and diminish adaptive capacities.

# Cognitive

## **Definition of cognitive**

**Bloom (1956) describes that cognitive domain** is a brain's functioning that involves intellect, learning, and problem solving. It is divided into six levels, from lowest to highest.

#### 1. Knowledge

# 1.1 Knowledge of specifics

• Knowledge of terminology regarding definition, term, sign, alphabet, and symbol.

• Knowledge of specific facts regarding formula, law, theory, assumption, size, quantity, place, time, property, objective, cause and effect, advantage and disadvantage, and right and duty.

1.2 Knowledge of ways and means of dealing with

#### specifics

• Knowledge of conventions, customs, traditions,

and cultures

• Knowledge of repetitive trends and sequences,

and continuous processes

• Knowledge of classifications and categories by

using criteria or methods

• Knowledge of criteria to judge of verify things

whether they are good or bad, true or false, and appropriate or inappropriate

• Knowledge of methodology to achieve work

target

1.3 Knowledge of universals and abstractions in

#### the field

• Knowledge of principles and generalization of things that used to happen

• Knowledge of theories and structures from various things that are coherent to one another

## 2. Comprehension

- 1. Translation is the ability to translate one language into another. It includes translating words and messages, pictures and symbols, poetries, and proverbs.
- 2. Interpretation is the act of conceptualization of more than one thing to create another meaning that is different from the original.
- 3. Extrapolation is to infer by extending known information based on enough information. There are four types: imagination, forecast, assumption, and inference.

## 3. Application

Application is the act of using know how, memory, and understanding of a particular matter to solve a new problem. That new problem is unsolvable with only formulas or rules, but requires different tactics to slove it.

#### 4. Analysis

- 1. Analysis of element is to search for the elements of stories in different aspects by specified criteria, for example, distinction of a message, main idea of an article, implication of a speech or an action, analysis of categories, analysis of element, and analysis of hidden motive.
- 2. Analysis of relationships is to relationally search for the relationships between a story's properties and other things.
- 3. Analysis of organizational principles is to find the structure and system of an object, a story, or an action in order to find out how it all is structured, by which criteria, or what the links are.

## 5. Synthesis

1. Production of unique communication is combining knowledge and experience to create messages, outcomes, or new actions in order to communicate ideas and feelings to other people, for example, explaining, writing poetries, drawing, and acting.

- 2. Production of plan or proposed set of operation is to set the direction and procedure beforehand in order to achieve the objectives
- 3. Derivation of set of abstract relation is to integrate key elements and principles into a new issue that has a different relation from before, such as to explain the true problem of corruption in Thailand.

#### 6. Evaluation

- 1. Judgment in terms of internal evidence means to evaluate by using fatcs visible in that matter.
- **2.** Judgment in terms of external criteria means to evaluate by using external criteria that have relationships with that matter. They can be something like social norms, for instance.
- Abigarl B. Sivan and Arthur L. Benton (1999 cited in Muriel. 2012) mention that cognitive function has got four functions.
- 1. Receptive function comprises ability to select, categorize, and integrate data.
  - 2. **Memory and learning** means storing and retrieving data.
  - 3. **Thinking** means organizing and managing data in mind.
  - 4. Expressive function means communicating and other activities.

Solaphat Hemrungrojn (2010) says that cognition is human's information process. It includes attention, pattern recognition, memory, learning, language processing, problem solving, abstract thinking, higher-order intellectual functioning, and psychomotor skills. Each one requires several parts of the brain to function.

In conclusion, cognition is human's brain process to manage information, which comprises different components: attention, pattern recognition, memory, learning, language processing, problem solving, abstract thinking, higher-order intellectual functioning, and psychomotor skills.

# **Cognitive evaluation**

Sompop Reungtrakul (2011) says about the measures of how to evaluate cognitive impairment as mentioned below.

- 1. Neuropsychology test
- 2. Cognitive evaluation techniques

There are several types of measures used to evaluate cognitive functions. They are summarized and shown in table 2.3 and table 2.4.

Table 2.3 Neuropsychiatric measures for cognitive disorders

| Name of measure                       | Disorder or construct assessed             |
|---------------------------------------|--|
| Mini – Mental State Exam(MMSE)        | Brief general survey of broad range of     |
|                                       | cognitive function                         |
| Dementia Rating Scale(DRS)            | Broad, differentiated survey of cognitive  |
|                                       | function in moderate depth                 |
| Cognistat                             | Broad, differentiated survey of cognitive  |
|                                       | function                                   |
| Clock drawing Test                    | Brief assessment of cognitive function,    |
|                                       | with focus on visuospatial skills and      |
|                                       | constructional praxis                      |
| National Institute on Aging (NIA)     | Battery of cognitive tests to assess early |
| Alzheimer's Disease Center Uniform    | dementia                                   |
| Data Set (UDS) cognitive test battery |  |
| Alzheimer's Disease Assessment        | Major cognitive and behavioral             |
| Scale                                 | symptoms of Alzheimer's disease            |
| Cognitive subscale: ADAS-Cog          |  |
| Galveston Orientation and Amnesia     | Disorientation and amnesia caused by       |
| Test (GOAT)                           | head injury                                |
| Cogstate                              | Cognitive dysfunction associated with      |
|                                       | early dementia or concussion               |
| Clinical Dementia Rating (CDR)        | Global rating of dementia severity with    |
| Scale                                 | focus on functional decline                |
| The GDS staging System:               | Systematic rating system for overall       |
| Global Deterioration Scale (GDS)      | (GDS), cognitive (BCRS), and functional    |
| Brief Cognitive Rating Scale          | (FAST) impairment in patients with         |
| (BCRS)                                | dementia                                   |
| Functional Assessment Staging         |  |
| (FAST)                                |  |

Source: Handbook of Psychiatric Measure – Second edition p. 399

Table 2.4 Cognitive domain and neuropsychological test

| Cognitive domain      | Tests   |
|-----------------------|---|
| Intelligence          | Wechsler Adult Intelligence Scale, 3 <sup>rd</sup> Edition (WAIS- |
|                       | III)  |
|                       | Wechsler Intelligence Scale for Children, 3 <sup>rd</sup> Edition |
|                       | (WISC-III)  |
|                       | Standford-Binet Intelligence Scale, 4 <sup>th</sup> Edition       |
| Memory                | Wechsler Memory Scale, 3 <sup>rd</sup> Edition (WMS-III)          |
|                       | California Verbal Learning Test                                   |
|                       | Ray-Osterrieth Complex Figure                                     |
|                       | Benton Visual Retention Test (BVRT)                               |
|                       | Hopkins Verbal Learning Test                                      |
|                       | Ray Auditory-Verbal Learning Test                                 |
| Attention             | Digit Span (WAIS-III)   |
|                       | Visual Memory Span (WMS-III)                                      |
|                       | Continuous Performance Test                                       |
|                       | Stroop Test   |
|                       | Trail Making Test   |
|                       | N-Back test   |
|                       | Category Test   |
| Executive functioning | Category test   |
|                       | Wisconsin Card Sorting Test (WCST)                                |
|                       | Tower of London Test  |
|                       | Porteus Maze Test   |
|                       | Stroop Test   |
|                       | Trail Making Test   |
| Language              | Boston Diagnotic Aphasia Examination                              |
|                       | Multilingual Aphasia Examination                                  |
|                       | Reitan-Indiana Aphasia Screening                                  |
|                       | Wepman Auditory Discrimination Test                               |

**Table 2.4** Cognitive domain and neuropsychological test (cont.)

| <b>Cognitive domain</b> | Tests                                  |
|-------------------------|--|
| Motor functioning       | Finger Oscillation/ Tapping Test       |
|                         | Grooved Pegboard Test                  |
|                         | Purdue Pegboard Test                   |
|                         | Grip Strength Test                     |
| Visuospatial and        | Judgment of Line Orientation           |
| visuomotor              | Visual Form Discrimination Test        |
|                         | Facial Recognition Test                |
|                         | Block Design (WAIS-III)                |
|                         | BVRT and Ray-Osterrieth Complex Figure |

Source: Neuropsychiatric assessment (2004) p. 48-50

This research uses the Montreal Cognitive Assessment (MoCA) because it takes less time, has good reliability with Cronbach's alpha coefficient = 0.914, and acceptable validity. MoCA-T score also had significantly positive correlation with TMSE(r = 0.862, p < 0.001) (Tangwongshai S et al., 2011). In addition, it has been translated and used widely in many countries.

## Cognitive impairment in brain tumor patients

Sompop Reungtrakul (2011) explains about cognitive impairment that it is caused by physical illnesses. In that case, patients have at least two types of cognitive disorders. They can be:

- 1. Memory (learning or recalling new information)
- 2. Executive function (for example, planning or rationalization)
- 3. Attention or speed in collecting information (for example, concentration, speed in collecting and analyzing information)
- 4. Perception and movement (for example, integrating perceived information, whether by vision, touch, or hearing, with movement)
- 5. Communication (for example, difficulty in choosing words, less fluency)

Martin JB Taphoorn and Martin Klein (2008) talk about cognitive deficit in brain tumor patients that it can be an effect from a brain tumor; tumor-related epilepsy; treatments, such as surgery, radiotherapy, antiepileptic drugs, chemotherapy, or corticosteroid; and psychological distress. Mostly those factors together cause cognitive dysfunctions.

#### **Causes from brain Tumor**

Apart from epilepsy, physical and sensational impairments, and increased intracranial pressure; brain tumor patients also have to encounter cognitive impairment. Tucha et al. (cited in Martin JB Taphoorn. 2004) studied the changes of brain tumor patients' cognition before and after surgery. The result from studying low graded tumor patients and high graded tumor patients indicates that tumors affect cognitive impairment.

#### Causes from treatments

#### - Surgery

Brain surgery is used to diagnose and relieve neurological symptoms by reducing the size of tumors. Even though a surgery is good for cognitive function, the surgery and the damage cause by it in the surroundings may cause the impairment of nervous system. However, the impairment can recover within three months after the surgery. The brain may get back to normal. There is a study in patients with low grade glimo tumors that have undergone a surgery for one year, it is concluded that surgery does not cause cognitive impairment.

#### - Radiotherapy

The affect of radiotherapy was first reported found in children that were being treated for leukemia of brain tumors. This method of treatment improves patients' cognitive function, but during 1-6 months after the treatment, patients may have cognitive impairment, short memory and attention loss. However, they may fully recover within 12 months.

## - Medical therapy

## **Antiepileptic drugs**

Epilepsy occurs in 30-90% of brain tumor patients. But old types of antiepileptic drugs (phynytonin, calbamazepine, and valproic acid) worsen cognitive function. They cause attention problems, and slow down cognition process. They also affect encoding and retrieving memory. On the other hand, the information regarding effects of using new drugs, such as lamotrigine, levetiracetam, and topiramate, is still not available. There is some research studying in patients who take old antiepileptic drugs or suffer from severe epilepsies that there will be worsened perception speed, psychomotor function, executive function, and working memory.

## Chemotherapy

Affects to cognition of patients who undergo PCV chemotherapy are only reported in those who are treated with high dose.

#### **Steroids**

Using corticosteroids to treat brain tumors cause emotional changes and psychosis.

# **Neuropsychiatric symptoms**

## **Definition of Neuropsychiatric Symptoms**

Stuart C. Yudofsky (2004) defines neuropsychiatric as "the integration and co-performance that affects the brain functions and the behavior," which regards neurology and psychiatry. The aim is to evaluate neurological disorder patients' cognition, behavioral symptoms and emotions. The Neuropsychiatric Inventory (NPI) classifies neuropsychiatric symptoms into 12 types.

- **Delusions** are strong convictions about something despite them being untrue. Patients tend to strongly believe what they want to, and cannot be made to change their minds, for example, believing they are being assassinated (Sompop Reungtrakul. 2005)
  - **Hallucinations** can be manifested in 5 forms:

- Auditory: patients hear sounds from the surroundings. They can be many types of sounds, such as voices.
- Visual: patients see things that are not there, which may be human, animals, or other things.
  - Olfactory: patients smell unpleasant odors, such as smoke.
  - Gustatory: patients perceive unpleasant tastes, such as toxic-like food.
- Tactile: patients sense insects crawling on the body or strange sensations on skins (Sompop Reungtrakul. 2005).
- **Agitation/Aggression** Agitation is an emotion state of being restlessness, upset, and anxious. Anxiety makes patients unable to sit still, but have an urge to rise up and sit down repeatedly many times (Sompop Reungtrakul. 2005). On the other hand, aggression means hostile behavior.
- **Depression/Dysphoria** Patients seem depressed or feel sad, and may say that they are sad.
- **Anxiety** is excessive turmoil that comes with physical symptoms, such as fidget, tiredness, upset, and muscle aches (Sompop Reungtrakul. 2005).
- **Elation/Euphoria** *Euphoria* is a mental state that a patient feels abnormally happy, while *elation* is a mental state that is even beyond euphoria, for example, feeling happy and joyful almost all the time (Sompop Reungtrakul. 2005).
- **Apathy/Indifference** patients have indifferent expressions and are ignorant to everything (Sompop Reungtrakul. 2005).
- **Disinhibition** patients seem to do things harshly and unthoughtfully, or do something that they normally would not do in public.
- Irritability/Lability patients are easily irritated or provoked. They are labile or patientless.
- **Aberrant Motor Behavior** patients may keep walking around or repeatedly do something, such as open and close a closet repeatedly.
- **Sleep disorders** patients have sleeping problems, waking up in the middle of the night to walk around, get dressed, or bother other people's sleep.
- **Appetite and Eating disorders** patients have different appetite, weight, eating habits, or types of food from before.

# Neuropsychiatric manifestations of brain tumors

Sompop Reungtrakul (2011) and Trevor (2012) have the same deduction about the relation of neuropsychiatric symptoms and brain tumor locations that psychopathology and behavior symptoms can be found in patients up to 47-94%. The psychopathology disorders found depend on the locations of tumors. The locations that are often found the psychopathology disorders are frontal, temporal, and diencephalic areas.

**1. Frontal lobe tumors** it is reported that this area of the brain causes psychopathology and behavior disorders up to 90%. They resemble bipolar disorder and psychosis. They include mania, hypomania, catatonia, and delusional disorder and hallucination.

**Orbitofrontal tumors** make patients' personality change. They tend to be easily upset, emotional, cannot control their behaviors, lack inhibition and self-awareness, make bad decisions, and have inappropriate social behaviors.

**Dorsolateral prefrontal convexities tumors** cause apathy, lack of motivation, lack of reactions or simultaneous actions, slow thinking process and slow movement, lack of ability to plan ahead, tiredness of muscles, and deficit concentration and attention. These symptoms are usually diagnosed as major depressive disorder.

**Anterior cingulated tumors** may cause akinetic mutism, where as tumors in the flax may cause complex attention function disorders.

**Ventral right frontal tumors** mostly relate to euphoria and secondary mania or hypomania, especially in those whose have bipolar disorders in the family.

**Left frontal lobe tumors** usually cause deficit in speech. Patients talk less, have a problem in choosing words, and talk ambiguously.

Tumors in the frontal lobes cause confabulation and Capgra's syndrome. Generally, tumors in this area may severely ruin the concentration and attention functions, and disrupt executive function, which lead to loss of abilities, such as abstract thinking, planning for complex activities, collecting and synthesis information, problem solving, initiative thinking, and achieving work targets. These impairments may occur altogether with expressive aphasia and dysprosodic speech.

**2. Temporal lobe tumors** 50-55% of patients with these tumors have psychopathological symptoms and behavioral and personality changes. The psychopathology can be either ictal or interictal (related to/unrelated to seizure).

Patients with temporal lobe seizures often have seizures that are similar to some psychological symptoms in schizophrenia patients, such as auditory hallucination, depersonalization, unconsciousness, and confusion. But they can be differentiated from schizophrenia patients in some ways, that is, having emotional responses and changes during interictal; having normal emotions and being able to normally communicate with other people, but hallucinations, such as olfactory, gustatory, visual, and tactile – smelling unpleasant odors, which are parts of precital auram also occur; and having depression, avolition, upset, and hypomania or mania.

Symptoms resembling schizophrenia are often found in patients with left temporal lobe tumors, and emotional symptoms are often found in patients with right temporal lobe tumors.

The first indicator of tumors in this area is personality changes that have specific chracteristics, called interictal personality. Those characteritics are listed below.

- Less social interaction
- Emotional instability depression, joy, irritability, or altogether
- Unfriendliness and hostility
- No humor
- Being extremely religious
- Philosophical obsession
- Loss of libido
- Eating excessively
- **3. Diencephalic, third ventricar, and hypothalamic tumors** are very least likely to be found, only around 1-2%. Most are found in children, teenagers, and young adults. However, since these tumors are very close to the limbic system, including efferent and afferent tracts, patients often have psychopathological and behavioral symptoms up to 50% or more. The symptoms are psychosis, some that are similar to schizophrenia symptoms, depression, being sentimental, euphoric

sensations, hyperactivity, personality changes, akinetic mutism, eating disorders – eating too much or too little like anorexia, and too much sleep.

The significant neurocognitive function is memory loss. There can be subcortical dementia, that is, lack of initiate abilities and attention, slowness of movement, depression, and apathy.

Tumors in the periventricular region and the ventricular system may block the circulation of cerebrospinal fluid, which will cause psychopathological symptoms and neurocognitive symptoms.

**4. Pituitary tumors** are found around 10% of all brain tumors. Yet, they are substantial related to dysfunctional behaviors, and can be found at 60% of the patients. The symptoms can be varied, and may be similar to some psychopathological symptoms, such as anxiety, depression, and psychosis, which are directly caused from pituitary tumors.

Some neurocognition problems that are found very often are attention problem and delirium.

**5. Parietal lobe tumors** are less likely to cause mental disorders, they are found approximately at 16%. The symptoms are emotion abnormality, depression that is found more often than hypomania, and sometimes there can be psychosis, such as delusional disorder – persecutory type.

Patients will have various neurocognitive disorders with the charateristics of lateralizing. There may be impairments of cortralateral two point discrimation, joint position sense, stereognosis, and graphesthesia.

The dominant parietal lobe tumors may cause difficulties in reading and spelling, and tumors in the nondominant parietal lobe cause visual spatial disorders and anosognosia, in other words, patients lack carefulness, and deny or abandon their attention about their neurological impairment regarding contralateral and apraxia.

**6. Occipital lobe tumors** do not cause psychopathological and behavioral symptoms much, except for emotional changes and hallucinations that can be found around 25% of the patients.

Visual hallucinations caused by tumors in this area are normal lights, not pictures or something complex like what is found in psychopathology or delirium.

Some neurocognitive disorders that are found often include homonymous hemianopsia (visual field loss on the left or right side of both eyes) and visual agnosia, which is an impairment in recognition of visually seen objects.

**7. Corpus callosum tumors** in the frontal area, especially, often cause psychopathological and behavioral symptoms, including depression, psychosis, and personality disorders.

Trevor (2012) describes neuropsychiatric symptoms that they are varied depending on the location of tumors. For instance, depression mostly occurs in frontal lobe tumor patients, whereas mental disorders mostly occur in temporal lobe tumor patients. This conforms to what David A. Tomb (2008) says that neurological diseases can cause mental disorders. 50% of patients with intracranial tumors have mental disorders. Tumors in the temporal and the ventral frontal lobes cause emotional and mental impairments. In addition, occipital tumors mostly cause visual impairment.

# **Assessment of neuropsychiatric symptoms**

Sompop Reungtrakul (2011) talks about neuropsychiatric assessment that it is for **mental status examination**, which is the means to test performance of neurology and psychiatry. The result that can tell the lesions in nervous system comes from the answer of the mental test. There are 8 important tests as followed.

- a. Attention and concentration
- b. Mental control
- c. Speech
- d. Memory
- e. Calculation
- f. Abstract thinking
- g. Insight and judgement
- h. Executive function

Neuropsychological assessment can indicate characteristics and severity of behavior and emotional problems; evaluate evidence, characteristics, and severity of brain dysfunction; and neurological signs and symptoms that can indicate brain diseases.

Table 2.5 Neuropsychological sign and symptom that can indicate brain diseases

| <b>Functional class</b> | Symptoms and sign  |  |
|-------------------------|--|--|
| Speech and language     | Dysarthria   |  |
|                         | Dysfluency   |  |
|                         | Marked change in amount of speech output                 |  |
|                         | Paraphasias  |  |
|                         | Word-finding problems                                    |  |
| Academic skills         | Alterations in reading, writing, calculating, and number |  |
|                         | abilities  |  |
|                         | Frequent letter or number reversals                      |  |
| Thinking                | Perseveration of speech                                  |  |
|                         | Simplified or confused mental tracking, reasoning, and   |  |
|                         | concept formation  |  |
| Motor                   | Weakness or clumsiness, particularly if lateralized      |  |
|                         | Impaired fine motor coordination (e.g., change in        |  |
|                         | handwriting)   |  |
|                         | Apraxias   |  |
|                         | Perseveration of action components                       |  |

**Table 2.5** Neuropsychological sign and symptom that can indicate brain diseases (cont.)

| <b>Functional class</b> | Symptoms and sign  |
|-------------------------|--|
| Memory                  | Impaired recent memory for verbal or visuospatial material |
|                         | or both  |
|                         | Disorientation   |
| Perception              | Doplopia or visual field alterations                       |
|                         | Inattention (usually left-sided)                           |
|                         | Somatosensory alterations (particularly if lateralized)    |
|                         | Inability to recognize familiar stimuli (agnosia)          |
| Visuospatial abilities  | Diminished ability to perform manual skills                |

|             | (e.g., mechanical repairs and sewing)                      |
|-------------|--|
|             | Spatial disorientation                                     |
|             | Left-right disorientation                                  |
|             | Impaired spatial judgement (e.g., angulation of distances) |
| Emotion     | Diminished emotional control with temper outburst and      |
|             | antisocial behavior  |
|             | Diminished empathy or interest in interpersonal            |
|             | relationships  |
|             | Affective changes  |
|             | Irritability without evident precipitating factors         |
|             | Personality change   |
| Comportment | Altered appetites and appetitive activities                |
|             | Altered grooming habits (excessive fastidiousness or       |
|             | carelessness)  |
|             | Hyperactivity or hypoactivity                              |
|             | Social inappropriateness                                   |

Source: table 1-1 Clinical manual of neuropsychiatry -1<sup>st</sup> ed. p. 3-4

## Related literature

Cognitive deficits before treatment among patients with brain tumors of Tucha O et al. (2000) study about the incidence of frontal lobe and temporal lobe brain tumor patients' cognitive impairment. The study was conducted after the patients were diagnosed, but before the treatment. The data was collected by standardized psychometric test to test memory, attention, language, and executive function. The result shows that more than 90% of the patients have cognitive problems at least one area, 78% have executive function problems, and more than 60% have memory and attention problems.

Prevalence and clinical correlates of neuropsychiatric symptoms in dementia of Steffens DC et al. (2005) studies about the frequency of the incidence and the severity of neuropsychiatric symptoms in dementia patients by using the

Neuropsychiatric Inventory (NPI). The result suggests that 39.3% have apathy, 31.1% have aberrant motor behavior. Moreover, those symptoms are as well related to alcohol abuse, head injury, and stroke.

#### CHAPTER III

## **METHODOLOGY**

This research is under the topic of "The study of cognitive impairment and neuropsychiatric symptoms in brain tumor patients at Siriraj Hospital" which is a survey research. In order to conduct the research systematically and achieve the research objectives, the researcher hence conduct the research by each step illustrated as the following.

# Population and sample

# **Population**

The population for this study is patients diagnosed to have brain tumors by the doctors at the Department of Surgery, Faculty of Medicine, Siriraj Hospital.

## Sampling

The sample group comprises 43 first-time-diagnosed brain tumor patients during September 2013 to February 2014. Since the population size is unknown, the sample size formula chosen to use belongs to W.G. Cochran (1963).

$$n = \frac{p(1-p)z^2}{d^2}$$

where n is the sample size

Z is the confident interval at 0.05, equals to 1.96 (95% confidence)

*P* is the proportion of an attribute in the population that can be represented by the past value

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d is the acceptable error value, equals to  $\pm 9\%$  or  $\pm 0.09$ 

This research aims to study two issues: the cognitive impairment and the neuropsychological symptoms of brain tumor patients. Since cognitive impairment is likely to be found before neuropsychological symptoms, the incidence of cognitive impairment from previous research is used for the sample size calculation.

According to the literature search, since the incidence of cognitive impairment in Thailand is not found, the incidence from research form other countries is used for the calculation. According to the research of Tucha O (2000), he studied both primary and secondary intracranial cognitive impairment before treatment. The psychological measure was used to evaluate memory, attention, language, and executive function. The result suggests that more than 90% of the patients have at least one issue of cognitive impairment. Therefore, it can be deduced that Thai brain tumor patients have approximately the same incidence rate of cognitive impairment.

The calculation of sample size is calculated as shown.

$$N = \frac{P(1-P)Z^{2}}{d^{2}}$$

$$= \frac{0.9(1-0.9)(1.96)^{2}}{(0.09)^{2}}$$

$$= \frac{0.3457}{0.0081}$$

$$= 42.68$$

The sample size derived form the formula is 43 people. The sampling method is purposive sampling. They are patients who undergo the treatment for the first time from the Common Ward, the Department of Surgery (male-female), the Faculty of Medicine, Siriraj Hospital during September 2013 and February 2014.

## Criteria of the sample

- 1. Male or female patients that are diagnosed to have brain tumors, aged between 18-80 years old
  - 2. Patients that have never undergone any surgery
  - 3. Patients that have good level of consciousness (Glasgow Coma Scale >

4. Patients that are willing to be part of the sample of the research and sign the consent form

#### **Exclusive criteria**

- 1. Patients who refuse to continue the evaluation or are assessed to not be able to continue
  - 2. Patients who are diagnosed to not have a brain tumor after a surgery

## **Data collection**

- 1. The research was examined and accredited by the Siriraj Institutional Review Board.
- 2. Permission to use the Montreal Cognitive Assessment (MoCA) and the Neuropsychiatric Inventory (NPI) from the owners was processed.
- 3. Letter of cooperation to the President of Siriraj Hospital to declare the research objectives and to ask for permission to conduct the research was processed.
- 4. The data collection was conducted by the researcher. Nevertheless, the participants can, anytime, refuse to cooperate during the data collection period.
- 5. The entirety of the data was examined. Then the data was verified for further statistical analysis.

#### **Tools**

The tools used in this research comprise five parts: general questionnaire, the Glasgow Coma Scale, the MMSE-Thai 2002, the Montreal Cognitive Assessment (MoCA), and the Neuropsychiatric Inventory (NPI). The characteristics of each tool are explained below.

- **Part 1 general questionnaire** regards personal information, symptoms and treatments received of brain tumor patients. They are close-ended questions checklist; and there are also some open-ended questions.
- Part 2 consciousness measure using the Glasgow Coma Scale to evaluate eye response, motor movement, and verbal response.

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Part 3 the primarily mental state examination the Thai version (MMSE-Thai 2002) to evaluate the patients. Those who make the score lower than 23 will not go through the Montreal Cognitive Assessment (MoCA) Thai version.

Part 4 the Montreal Cognitive Assessment (MoCA) the Thai version developed by Solaphat Hemrungrojn (2007), which is a tool to quickly screen the first stage cognitive impairment. It takes approximately 10 minutes. It is to evaluate attention, concentration, executive function, memory, visuoconstructional, concept, calculation, and orientation. It is composed of eight components, namely visuospatial/executive (5 marks), naming (3 marks), memory and delayed recall (5 marks), attention (6 marks), language (3 marks), abstraction (2 marks) and orientation (6 marks). The total mark is 30 marks. If a participant accumulates the score more than or equal to 26, that is normal. And if the participant's academic years are less than 12 years, one more mark is added up automatically.

Solaphat Hemrungrojn (2009) points out some advantages of this test that it has been transalated into 17 languages (Thai included), contains good sensitivity value for MCI and dementia, can be well used to evaluate executive and visuospatial function, and was recommended by the NIH to use in vascular cognitive impairment.

Part 5 the Neuropsychiatric Inventory is the comprehensive assessment of psychopathology in brain tumor patients. It was developed to used with Alzheimer's disease or other dementia, and can be used to evaluate personality changes from other diseases as well. This assessment takes less time, and scores only prominent personalities that seem to be problematic and the information received from close relatives. The Neuropsychiatric Inventory categorizes neuropsychiatric symptoms into 12 types.

- Delusions
- Hallucination
- Agitation/Aggression
- Depression/Dysphoria
- Anxiety
- Elation/Euphoria
- Apathy/Indifference
- Disinhibition

- Irritability/Lability
- Aberrant Motor Behavior
- Sleep
- Appetite and Eating disorders

Some advantages of the Neuropsychiatric Inventory are having acceptable reliability and validity, being translated and used in many countries, being able to used to assess various types of neuropathy, and the result from treatment can be tested.

## Data analysis

This research uses SPSS to process and analyse the data as explained below.

Analyze the primary data by descriptive statistics to describe the sample and the characteristics of the variables in the research.

- 1. Use basic statistics for quantitative data, such as age, educational level, and the analysis is based on means and standard deviation. As for qualitative data, such as gender, locations of tumors, types of tumors, complication comorbidity, treatment undergone, and psychopathy background, the analysis is based on frequency and percentage.
- 2. The study of the relation between individual's variables and incidence of cognitive impairment and neuropsychiatric symptoms is divided into two parts.
- In the case that the independent variables are qualitative data gender, locations of tumors, types of tumors, complication comorbidity, treatment undergone, psychopathology background, and the medicine used in treatment the Chi-square statistics is used.
- In the case that the independent variables are quantitative age and educational level MannWhitney U-test statistics is used.