



## Executive function disorder in acute traumatic brain injury in Manado, Indonesia

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### ABSTRACT

Traumatic brain injury (TBI) is known as a major cause of death and chronic disability worldwide. It is one of the leading causes of economic and social problems for patient, family and community. Patients will have serious complication on physics, mental and personality aspect. Executive function disorder is one of the cognitive functions that could be affected by TBI. There is scarcity of data about executive function in acute TBI, especially from developing countries. Our study aimed to investigate the association between acute TBI and executive function disorder. This study was a hospital-based cross-sectional study. Samples consisted of 20 patients and 40 demographically matched controls that meet the inclusion criteria. For executive function measurement we applied TMT-A, TMT-B and Stroop Test. The result showed that mean score of TMT-A for case group was 1.06 minute (95% CI 0.70-1.06) which was longer than control group (0.32 minute). For TMT-B test, the mean score was 2.68 minute (95% CI 2.05-2.8) for case group and 0.77 minute for control group. On Stroop Test 3 we found that the mean score was 17 correct items (95% CI 13.52-20.48) which was lower than control group (52.5). For all of the tests, we detected that acute TBI significantly associate with executive function disorder ( $p > 0.05$ ). Conclusion: There was a significant association between acute TBI and executive function disorder.

**Keywords:** Traumatic Brain Injury, Executive Function, Cognitive, Manado, Indonesia

### INTRODUCTION

Globally, traumatic brain injury (TBI) is a main public health and social problem. It has serious impact not only in hospitalization issues but also in broader socio-economic dimensions. TBI is a giant killer for young adults group of age. The consequences of TBI is severe both in high and low-income countries. Most of the death happen within 48 hour after the injury.<sup>1</sup>

In Indonesia the prevalence of TBI among other trauma were increase from 14.5% in 2007 to 14.9% in 2013.<sup>2</sup> There were increasing number of death from 6 per-100 000 population in 2000 to almost 9 per-100 000 population in 2009.<sup>3</sup> In 2014 the number of death

from road traffic accident (RTA) were 120 cases everyday.<sup>4</sup> In Manado, one of the fastest growing city in eastern part of Indonesia, TBI is the main cause of death among victims of RTA. Most of the death were in 20-40 group of age (43.1%), male (82.4%) and was driving when the RTA happened. Based on clinical forensic findings, most of pathologic finding was found in temporal lobe.<sup>5,6</sup>

In addition to severe disability and death, the long term impact of the TBI patient is also in physic, emotion and personality aspects. Cognitive dysfunction due to TBI deteriorates the problems. Several cognitive dysfunction, such as problem in attention, difficulty in finding words, lower performance of academic ability and disorder of

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executive function, could be detected in TBI patients. Most of these problems were under-estimated in early phase until the patients back to daily and routine work.<sup>7</sup> The development of cognitive dysfunction will affect their safety, productivity and interpersonal relationship. In other word, both the patients and their family will have to face the chronic burden of TBI.<sup>8</sup> According to Teasdale, who reported a population-based study in 2003, severe TBI in children and adolescent were associated with cognitive function disorder in early adult periode.<sup>9</sup>

Roozenbeek<sup>10</sup> highlighted the important of long term cognitive function disorder of TBI. In Roozenbeek's opinion TBI could trigger or accelerate cognitive function disorder. Executive function disorder is one of the cognitive dysfunction that could be discovered after TBI. According to Zimmermann<sup>11</sup> there are several general profiles of executive function disorder after TBI such as impaired of verbal working memory, verbal initiation, inhibition, planning and switching components. While several articles reported long term consequences of TBI on cognitive function, there was lack of data about executive function disorders in acute phase of TBI. Specifically, very few study from low- and middle-income countries in Asia assess executive function disorders in acute setting. The objective of this study was to find out the association between acute TBI and executive function disorders.

## MATERIALS AND METHODOS

### Research design, place and time of study

This was a hospital-based cross-sectional study conducted in Prof. dr. R. D. Kandou Manado General Hospital, North Sulawesi Province, Indonesia. The study was conducted during September – December 2014.

### Source population, sample and sampling methodology

All TBI patients were diagnosed clinically based on history, physical examination and/or neuroimaging study. Sample were recruited through consecutive sampling method. During the study period, 20 sample of patients were eligible to participate in the study.

### Eligibility criteria

Study criteria included:

- a) Age between 16-60 year;
- b) Onset of TBI before admission was less than 24 hour;
- c) Mild to moderate TBI;
- d) Accompanied by their family/caregiver; and
- e) Agreed to participate.

Exclusion criteria were: Attention disturbances, decrease of consciousness, anterograde amnesia, any history of psychiatric disorders, diabetes mellitus, dementia, depression, recreational drug user, epilepsy, severe metabolic disorders, mental retardation, neurologic disease and chronic alcoholic. Demographically match control (n=40) was employed to detect any difference of executive function tests.

### Operational definition

TBI was defined as history of "insult or trauma to the brain from the an external mechanical force, possibly leading to temporary or permanent impairment of physical, cognitive and psychosocial functions with an associated diminished or altered state of consciousness".<sup>12</sup> Mild TBI was based on Glasgow Coma Scale (GCS) score 13-15 and/or history of unconsciousness less than 10 minutes and/or post-traumatic amnesia (PTA) less than 1 hour and Moderate TBI was defined when GCS score 9-12 and/or history of unconsciousness less than 6 hours and/or PTA less than 24 hour.

### Technical procedure information

Data were collected in emergency room after finishing primary resuscitation and secondary survey. Data collector explained concisely the objective and method of the study to patients and their family members or caregivers. Patients agreed to participate were asked to answer relevant questions and procedures. Demographic data were obtained from medical record. History and physical examination to collect clinical data and to detect eligibility criteria. Attention was assessed with digit span examination. Overall cognitive function were assessed with Mini Mental Status Examination (MMSE). Executive function was assessed by using Trail Making Test A (TMT-A) ( $\leq 1.00$  minute was normal), TMT-B ( $\leq 3.00$  minute was normal) and



Stroop Test 3 (color word > 40 items correct in 45 second was normal).

### Statistical analysis

Categorical data were presented in number and percentage. Numerical data were expressed with mean value (if the distribution was normal) or median value (if the distribution was not normal). To find out the association between acute TBI and executive function disorders we employed independent t-test (if the distribution was normal) or Mann-Whitney test (if the distribution was not normal). A p-value less than 0.05 level was determined as statistically significant association. We For this analysis, SPSS version 21 was implemented.

### Ethical consideration

Ethical consideration and approval was obtained from local Research Ethical Committee of Faculty of Medicine, Sam Ratulangi University. All TBI patients were informed about the objective of the study. They had full right to decide whether they would or would not like to participate in the study.

### RESULTS

Among all patients with TBI cases, mostly were male (70%). Majority of the patients were in 25-34 group of age (40%). Most of the TBI patient passed high secondary school (45%), were Minahasan (80%) and Christian (75%) (Table 1).

**Table 1 Demographic Characteristics**

Demographic Characteristics	N=20	%
Male	14	70%
Age group (25-34)	8	40%
High secondary school	9	45%
Minahasan ethnic	16	80%
Christian	15	75%

On table 2, we found that based on clinical characteristics of TBI patients, almost half of them were admitted to hospital 6 hour after trauma/injury (45%). Most of them were admitted due to head trauma after road traffic injury (55%). We also found that the GCS score group was mostly were in the

range of 13-15 when admitted to hospital. Duration of unconsciousness of 75% of case were less than 10 minute.

**Table 2 Clinical Characteristics**

Clinical characteristics	N=20	%
Onset time before admission (> 6 hour)	9	45%
Mechanism of injury (road traffic accident)	11	55%
GCS (13-15)	15	75%
Duration of unconsciousness (< 10 minute)	15	75%

Table 3 showed that for case group the mean score of TMT-A was 1.06 minute (95% CI 0.70-1.06) which was longer than control group. For TMT-B test, the mean score was 2.68 minute (95% CI 2.05-2.8) for case

group. On Stroop Test 3 we found that the mean score was 17.00 (95% CI 13.52-20.48) which was lower than control group.

**Table 3 Mean and SDs by sample group for executive function measures**

Variable	Group	N	Mean	SD	Min - Max	95% CI
TMT-A	Case	20	1.06	0.66	0.32-3.20	0.70-1.06
	Control	40	0.32	0.06	0.18-0.56	0.24-0.55
TMT-B	Case	20	2.68	1.08	1.14-5.20	2.05-2.78
	Control	40	0.77	0.62	0.33-3.00	0.55-1.17
Stroop test 3 (color word)	Case	20	17.00	6.80	2-25	13.52-20.48
	Control	40	52.50	7.83	17-74	49.28-55.72



Based on distribution of mean among several executive function tests, it is shown in table 4 that on TMT-A test for case group was 0.88 (SD  $\pm$  0.51) minute and control was 0.39 (SD  $\pm$  0.46) minute. On statistic analysis we found p-value  $<$  0.05 which means that there was significantly difference of TMT-A score between case and control group. The same result was calculated for mean score of TMT-B. For case group mean score of TMT-B was 2.41 (SD  $\pm$  1.21)

minute, and for control group it was 0.86 (SD  $\pm$  0.93) minute. Finally, for Stroop Test 3 (color-word test), we found that mean score of Stroop test 3 for case group was 16.65 (SD  $\pm$  6.80) and 53.83 (SD  $\pm$  7.83) for the opposite group. In statistic analysis we detected a significantly difference of mean between the two group (p $<$ 0.05).

**Table 4 Distribution of Mean of Executive Function Test Score between Case and Control Group**

Variable	Group	N	Mean	SD	p-value*
TMT-A	Case	20	0.88	0.51	0.005
	Control	40	0.39	0.46	
TMT-B	Case	20	2.41	1.21	0.005
	Control	40	0.86	0.93	
Stroop test 3 (color word)	Case	20	16.65	6.80	0.005
	Control	40	53.83	7.83	

\*Independent t-test

## DISCUSSION

The present study revealed that most of TBI patients were male and in young group of age. This is similar with many studies which reported that male preponderance was commonly found in TBI study. The ratio between male and female were 1.2:1 to 2.7:1 in Europe and North America. The ratio is greater in developing countries with 4.8:1 for male domination. Several studies reported that 72-81% of TBI patient were male. Younger group of age, commonly in 13-19 year, is repeatedly found in most TBI studies. The median age were commonly found in 38 year old.<sup>12</sup>

In Roozenbeek's opinion it is common in developing countries that younger people suffer for TBI due to lack of traffic education and low of traffic safety regulation. However, the pattern is different for developed countries. In countries with better income, prevention program for road traffic accident is consistently implemented and thoroughly supervised. Professional measures of RTA incidence in developed countries has led to lower group of young people with TBI. But, in the other hand, due to improvement of life expectancy the older group of people are now more vulnerable to TBI. People in this group of age tend to fall and suffer for TBI.<sup>10</sup>

In this study, we found that the most common cause of TBI were RTA. This data was similar with results of TBI studies conducted by several researchers. According to Critchley,<sup>11</sup> the most common cause are road traffic accident, falls, being struck, assault/violence and related to sport activities. However, several contribution factors such as demographic characteristics could influence the cause of injury. In Langlois' overview, falls are now more commonly found in older people. Sport and recreational injuries are among the major cause of TBI recently.<sup>13</sup>

Most of the patients in the present study were admitted to hospital more than 6 hour after injury. This is mostly due to distance from the location of injury to hospital or because of transportation facilities problems. For low income countries, slow implementation of traffic facilities as a part of low traffic safety regulation will cause a different epidemiology of TBI.<sup>10</sup> It common for people in low income countries to reach the hospital in longer time due to several transportation issues.

Most of the patient in this study were in GCS of 13-15 which was categorised as mild TBI. Glasgow Coma Scale (GCS) is important as a first step in examining



TBI patients. Neurologic examination start with an assessment of level of consciousness with the help of GCS. GCS is worldwide used as a tool to classify the severity of injury. GCS can be conducted to predict the outcome of TBI. The motor component has stronger accuracy in predicting the outcome after TBI.<sup>14</sup>

Based on executive function assessment test, we found that most of the patients have lower score compared to control group. This study revealed that for the patient group the mean score of TMT-A was 1.06 minute (95% CI 0.70-1.06). For TMT-B test, the mean score was 2.68 minute (95% CI 2.05-2.8) for case group. On Stroop Test 3 we found that the mean score was 17.00 (95% CI 13.52-20.48). The lower score of executive function test after TBI mostly related to several mechanism that lead to cognitive dysfunction. Dikmen<sup>15</sup> who conducted a systematic review in 2009 reported that there is a linear correlation between closed TBI and cognitive function disorder. The more severe TBI will contribute to the more severe cognitive dysfunction. Several aspect of cognitive function disorders were attention disorder, episodic memory, speed of thinking, language, visuospatial skill and executive function disorder. When compared to the control group, the same cognitive problems were also detected in open head injury. Intellectual ability was significantly decreased in open head injury patients compared to the intellectual status before trauma. In long term, the decrease of intellectual ability will be getting worse.

Sundman<sup>16</sup> reported that there is association between TBI and several neurodegenerative disorders. In the review, Sundman found that Alzheimer disease, Parkinson disease, Amyotrophic Lateral Sclerosis (ALS) and Chronic Encephalopathy Traumatic have relationship with history of TBI. Although multifactorial causes contributed to these disorders, but history of TBI is one of the primary contributors. The strong relationship was found between TBI and Alzheimer disease. Sixty-percent individual with history of TBI will develop Alzheimer disease. The risk will be greater 10-folds if the individual have Apolipoprotein-E (APOE) type of allele. Histopathologic findings in acute TBI revealed

that deposit plaq of Amyloid- $\beta$  in the brain. This data was detected in 30% of acute TBI patients who died after the trauma. The similar deposit was also found in children with acute TBI. In Alzheimer disease, deposit plaq of Amyloid- $\beta$  was also prominent in addition to neuronal loss and synaptic dysfunction.<sup>16</sup>

The severity of cognitive function disorder in TBI patients will depend on the severity of primary and secondary injury of TBI. Direct mechanical force to the head during primary injury causes mechanical problem to neuron, glial cell, vasculature and axons. The damage after primary injury is immediate and irreversible. Primary prevention is the best method to prevent this primary injury. Primary injury activates secondary injury which characterize with systemic complication and cell injury mechanism. Systemic disturbances such as oedema, increased intracranial pressure and bleeding. All of these will affect cerebral blood flow and lead to ischemia process. Once the ischemia was developed, biochemical cascade will be initiated. Glutamate exotoxicity, calcium overload, free radical over production, mitochondrial dysfunction, inflammation and apoptosis activation are several determinants for cell death. In addition to cell death, axonal degeneration and synaptic plasticity dysfunction are also contribute to cognitive function disorder after TBI.<sup>16</sup>

Executive function is one of the cognitive function disorder that commonly affected by TBI. National Center for Learning Disabilities (NCLD) defines executive function as a term that cover a lot of ability in cognitive, emotion and personality.<sup>14</sup> Another definition of executive function is mental ability to control and coordinate all of the cognitive, emotion and personality in order to reach the targeted objective. According to Tsaousides<sup>15</sup>, through this function, we are able to adapt our attitude appropriately with the current situation and condition. Neuroanatomically, executive function are related to frontal lobe. However, recently it is believed that dysfunction of other areas of the brain that related to frontal lobe will affect executive function.<sup>15</sup>

The present study revealed that based on distribution of mean of several executive function scores, there



were difference between TBI patients and control group significantly. The score of TMT-A test for TBI patients was 0.88 (SD  $\pm$  0.51) minute and 0.39 (SD  $\pm$  0.46) minute for the control group. The same result was calculated for mean score of TMT-B where the score of was 2.41 (SD  $\pm$  1.21) minute for TBI patients and for control group it was 0.86 (SD  $\pm$  0.93) minute. We also detected a difference of means of Stroop test 3 for both group. In TBI patient the mean score was 16.65 (SD  $\pm$  6.80) and for control group was 53.83 (SD  $\pm$  7.83). In statistic analysis we detected a significantly difference of mean between the two group ( $p < 0.05$ ) for all of the executive function test. TMT is an traditional executive function test to measure planning, reasoning, concentration, set shifting and problem solving. Stroop test is implemented to measure concentration, set shifting and inhibition.

According to Ardila<sup>17</sup> (2014), in post concussion disorder due to TBI, the most commonly symptom is concentration problems. Disorder of executive function and defect in speed processing are among the major etiologies of problem in concentration among TBI victims. Patients with executive function disorder may exhibit impaired judgement, abstraction, reasoning, planning, organizing, mental flexibility, impulse control, copying and anticipatory behavior. These deficit patterns are similar both in adult and children. A study revealed that executive function disorder would be the effect of reduce of hippocampal volume and enlargement of lateral ventricular system.

In this study we concluded that executive function disorder was significantly associated with acute TBI at our hospital. Patients with TBI exhibit poorer executive function test performance than normal healthy control group. Considering that executive function is a set of cognitive tool that creates our brain to be unique and sophisticated, prevention measures of TBI should be implemented consistently.

#### LIMITATION OF THE STUDY

First, in the present study the sample size was small which might influence the result. Second, we did not collect data about the recovery period between case and control group during acute period of TBI. Third,

there was no long term follow up for the patients in order to compare status of executive function from the baseline and to know daily complaints.

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