

## EFFECT OF MONDAY THURSDAY FASTING ON WORKING MEMORY AFTER ACUTE STRESS EXPOSURE

Abdullah Faqih<sup>1\*</sup>, Sinu Andhi Jusup<sup>2</sup>, Nanang Wiyono<sup>3</sup>, Isna Qadrijati<sup>2</sup>

<sup>1</sup>Medical Faculty of Sebelas Maret University

<sup>2</sup>Departement of Physiology of Medical Faculty of Sebelas Maret University

<sup>3</sup>Departement of Anatomy of Medical Faculty of Sebelas Maret University

Email: [Abdafaqih111@gmail.com](mailto:Abdafaqih111@gmail.com)

---

### ABSTRAK

Memori kerja merupakan bagian dari fungsi kognitif yang berhubungan dengan proses pembelajaran dan menghubungkan perilaku manusia dengan sistem saraf. Stres dapat menyebabkan terganggunya sistem homeostatis tubuh. Puasa Senin-Kamis dapat digunakan untuk melawan efek negatif stres dengan menghambat jalur mediator stres. Penelitian ini bertujuan untuk membuktikan bahwa puasa senin-kamis dapat mempertahankan fungsi memori kerja setelah mengalami stres akut. Penelitian ini merupakan penelitian *quasi experimental* dengan rancangan post test only control group design pada 124 mahasiswa kedokteran Universitas Sebelas Maret laki-laki, berusia 18-25 tahun, IMT normal, dan tidak mengkonsumsi obat kortikosteroid atau psikofarmaka yang dibagi menjadi 4 kelompok. Kontrol tidak mendapat perlakuan, kelompok perlakuan 1 (TG1) diberikan induksi stres akut berupa ujian akademik, *sing a song steess test* (SSST), dan tes berhitung, kelompok perlakuan 2 (TG2) merupakan kelompok yang telah melaksanakan puasa minimal 3 bulan terakhir dan diberikan induksi stres akut. Pengukuran memori kerja dilakukan secara serentak di ruang tutorial setelah masing-masing kelompok mendapat perlakuan. Data memori kerja dianalisis dengan uji MANOVA dan Bonferroni ( $\alpha = 0,05$ ). Working memory tertinggi terdapat pada TG2 diikuti oleh kontrol, dan TG1. Hasil uji MANOVA menunjukkan perbedaan bermakna antara keempat kelompok dengan  $p = 0,000$ . Hasil uji Bonferroni menunjukkan perbedaan bermakna antara kontrol-TG1 dan TG1-TG2 dengan masing-masing  $p < 0,05$ . Puasa pada aktivitas senin-kamis dapat menjaga fungsi memori kerja saat tubuh mengalami stres akut.

**Kata kunci:** puasa senin-kamis, stres, *working memory*, digit-span test

### ABSTRACT

Working memory is part of cognitive function relates to the learning process and associates human behavior with the nervous system. Stress can cause a disruption to the body's homeostasis system. Monday-Thursday fasting can be used to counter the negative effects of stress by inhibiting stress mediators pathways. This study aims to prove that monday-thursday fasting can maintain working memory function after getting acute stress. This study was quasi experimental with post test only control group design in 124 medical students of Sebelas Maret University, aged 18-25 years, normal BMI, and not taking corticosteroid or psychopharmaceutical drugs. Samples were taken by purposive sampling method divided into 4 groups. The control did not get treatment, treatment group 1 (TG1) was given acute stress induction in the form of academic examinations, *sing a song stress test* (SSST), and arithmetic test, treatment group 2 (TG2) carried out fasting at least 3 months and was given acute stress induction. Dependent variables are Monday-thursday fasting and acute stressors in the form of nominal categorical data. Independent variables in the form of working memory measured using digit-span tests in the form of numerical-interval data. Measurements of working memory were carried out simultaneously in the tutorial room after each group received treatment. Working memory data were analyzed by MANOVA and Bonferroni tests ( $\alpha = 0.05$ ). The highest working memory is found in TG2 followed by control, and TG1. The results of the MANOVA test showed significant differences between the four groups with  $p = 0,000$ . The Bonferroni test results show significant differences between the control-TG1 and TG1-TG2 with each  $p < 0.05$ . Fasting on Mondays-Thursdays activity can maintain a working memory function when the body gets acute stress.

**Keyword:** monday-thursday fasting, stress, *working memory*, digit-span test

## 1. INTRODUCTION

Stress is a condition that basically everyone can experience from time to time. Human needs are increasing with intense competition in meeting these needs, causing humans experience stress more easily. Based on data from the Ministry of Health of the Republic of Indonesia in 2013 it was stated that around 1.33 million residents of Jakarta, 608,000 residents of Central Java, 13,000 residents of West Kalimantan experienced stress. Stress is an imbalance between the body's ability to meet the demands made both physically and psychologically which can have a crucial impact. When the body receives stress, an adaptation mechanism will occur to maintain homeostatic conditions, but this adaptation will fail when the stress received exceeds the adaptability and causes disturbances in physiological and psychological systems.

The negative impact of the failure of these adaptation mechanisms can be in the form of working memory disorders, obesity, mood disorders, hypo-immune dysfunction, structural changes in the central nervous system, and premature death<sup>1</sup>.

Disturbances in working memory due to exposure to sustained stress are caused by increased secretion of the hormone cortisol which causes a reduction in the number of glucocorticoid receptors. The cortisol produced will bind to glucocorticoid and mineralocorticoid receptors in the amygdala and hippocampus which play a role in the regulation of working memory<sup>2</sup>. As a result of the reduced number of glucocorticoid and mineralocorticoid receptors and an increase in the hormone cortisol from normal levels, it will cause disturbances in the processing of working memory<sup>1</sup>.

Intermittent fasting can affect the human body both physiologically and psychologically. Physiologically, fasting can affect autonomic nervous regulation such as regulation of heart rate and blood pressure. Fasting can also affect brain function, such as spatial memory, working memory, and cognitive function<sup>3</sup>. Psychologically, fasting can affect emotional status<sup>3</sup>. So that fasting can be used as an intervention against stressful conditions in a person<sup>4</sup>.

Intermittent fasting can stimulate the brain to downregulate inflammatory response pathways with different molecular mechanisms<sup>5,6</sup>. This stimulus is especially transmitted to IL-6 and TNF- $\alpha$  which are responsible for the regulation of cortisol secretion that occurs under stress conditions<sup>7,8</sup>. This causes cortisol levels, which initially increase, to decrease significantly. So that intermittent fasting can tightly suppress cortisol regulation and its adverse effects on the body and also cause significant improvements in learning function and working memory<sup>9</sup>.

Monday Thursday fasting is a type of fasting performed by Muslims on Mondays and Thursdays. Monday Thursday fasting is also a type of intermittent fasting, because there are fasting and non-fasting periods within one week.

This research was conducted because there is a uniqueness in fasting Monday Thursday, where there is a difference in the time span of the non-fasting period between Monday to Thursday (two days) and Thursday to Monday (three days). This difference was used as the basis for conducting research to find out whether Monday Thursday fasting has an effect on working memory after exposure to acute stress.

## 2. METHOD

This research is a quasi-experimental study using the Post-test control only Group Design. The aim is to determine the effect of Monday Thursday fasting on working memory after acute stress induction.

The research subjects were selected using a purposive sampling technique and also adjusted to the predetermined inclusion and exclusion criteria. The researcher determined that the number of subjects was 93 people out of a total population of 972 people, which was obtained from the Lemeshow sample size formula. The total number of samples was then divided into 3 research groups consisting of the control group (control) which did not get acute stress induction or fasting Monday Thursday, the stress group (TG1) which only got acute stress induction, the fasting group with stress induction (TG2). ) who fast Monday Thursday and get acute stress induction. The number of samples in each group consisted of 31 samples.

The independent variables in this study were Monday Thursday fasting and acute stressors in the form of categorical-nominal data (categorical data that did not have a rating between categories) in the form of distribution based on the condition of the sample who fasted Monday Thursday or not, and whether or not to get an acute stressor.

The dependent variable in this study is working memory data. Working memory data is obtained from the results of the digit-span test which is numerical-interval data (numeric data that does not have an absolute zero) in the form of a standard value which is the conversion result of the raw value (the sum of the most series of forward and backward tests) and age. sample.

This research began with conducting a survey to group samples who had never fasted and had fasted for at least 3 months in a row.

Then proceed with carrying out acute stress induction in the form of sing a song stress test (SSST) and arithmetic test combined with the Medical Faculty of Sebelas Maret University academic exam in the research group with stress induction (TG1) and the research group that has carried out fasting Monday-Thursday and received stress induction ( TG2). Acute stress induction given to research subjects using the sing a song stress test (SSST) method is one of the acute stress induction methods where research subjects will be given the task of singing a song in front of at least two audience members. The task was given shortly after the research subject entered the experimental room, so that before entering the room the research subject did not get any information regarding the mechanism of stress induction that would be given.

After the acute stress induction using the SSST method is complete, then proceed with the arithmetic test in the form of a math task given orally (subtracting the number 2023 from the number 17 continuously to 0 which will be repeated from the beginning if you make a mistake). Then the research was continued by collecting working memory data in all research groups.

Retrieval of working memory data in this study used the digit-span test method which was carried out with the help of the Inquisit 5 millisecond application for windows. The results or values obtained from the digit span test measurements will then be processed into standard scores 16.

The working memory data will then be processed statistically using the SPSS-20 for Windows application with the significance degree used is  $p < 0.05$ .

Statistical analysis for working memory data includes the Lilliefors normality test and Levene's homogeneity as a descriptive test to find out whether the data is feasible for a parametric test (MANOVA) or a statistical test must be performed using a non-parametric test (Kruskall-Wallis).

### 3. RESULTS

Working memory data that is statistically processed remains in the form of numerical-interval data. The average working memory data for each study group is shown in table 1.

**Table 1. Post-stress working memory level data**

	<b>Group</b>	<b>N</b>	<b>Mean</b>	<b>St. Deviation</b>
	Control <sup>a</sup>	31	86,33	6,211
	Treatment Group 1 (TG1) <sup>b</sup>	31	74,90	9,998
	Treatment Group 2 (TG2) <sup>c</sup>	31	89,50	6,027
a:	P<0,05 against TG1 P>0,05 against TG2			
b:	P<0,05 against TG2			
c:	P<0,05 against TG1 P>0,05 against control			

A series of analytical tests were conducted to test the effect of Monday-Thursday fasting on working memory. The working memory data was first subjected to the Lilliefors normality test because the number of data was more than 50 and less than 200, and the Levene homogeneity test was carried out to see the distribution of the data. The Lilliefors test results are shown in table 2.

**Table 2. Results of the Lilliefors Test on Working Memory Data**

	<b>Group</b>	<b>N</b>	<b>p<sup>a</sup></b>
	Control	31	0,056
	Treatment Group 1 (TG1)	31	0,060
	Treatment Group 2 (TG2)	31	0,123
a:	Normal data if $p > 0.05$		

The results of the Lilliefors test showed that the distribution of data was normal for working memory data because in each group the value was  $p > 0.05$ , while the Levene

homogeneity test obtained a homogeneous distribution of data with the result  $p = 0.073$  ( $p > 0.05$ ) so that it meets the requirements for the test Parametric Multivariate ANOVA.

Multivariate ANOVA test was conducted to see the effect of Monday Thursday fasting on working memory in 3 research groups. The results of the Multivariate ANOVA test gave a value of  $p = 0.000$  ( $p < 0.05$ ) meaning that there was a statistically significant difference in working memory between the three groups. Next, a Bonferroni test will be carried out to find out where there are significant differences between the sample groups.

Based on the results of the Bonferroni test, it can be seen that there was a significant difference in working memory ( $P < 0.05$ ) between the control group and the stress group (control and TG1) and the stress group and the fasting group with stress induction (TG1 and TG2). However, the control group and the stress-induced fasting group (control and TG2) did not show a significant difference ( $P > 0.05$ ) indicating that the stress intervention in the stress-induced fasting group could be inhibited the negative effects by fasting activity, so that working memory between control and TG2 only has a slight difference (the difference is not significant). The results of data analysis which showed no significant difference showed that fasting activity given along with stress induction can counteract the negative effects of stress and maintain working memory.

#### 4. DISCUSSION

The difference in working memory levels in this study was influenced by the presence or absence of Monday-Thursday fasting activity and interventions in the form of acute stress induction in each group. The cause of the stress group (TG1) was to get the lowest working memory score because of the acute stress induction that was given without being accompanied by Monday Thursday fasting activity. This will cause the activation of stress mediators which will interfere with the processing of working memory<sup>10</sup>. One of the stress mediators that can affect working memory is through the HPA axis and SAM axis pathways<sup>11</sup>.

When the body is exposed to a stressor, there will be an activation process from the SAM axis which will cause an increase in catecholamine secretion both from the adrenal medulla and in the locus coeruleus in the brain. Catecholamines secreted in excess will have an inhibitory effect on the amygdala, especially on the basolateral side. This inhibition will cause a decrease in mitogen-activated protein kinase (MAPK) in the basolateral amygdala, thereby reducing the activity of the medial prefrontal cortex (mPFC) which is responsible for several cognitive functions such as thinking processes, decision-making processes, and working memory<sup>12</sup>. Inhibition of the basolateral amygdala will also have an impact in the form of decreased activation of the glucocorticoid receptors in the hippocampus which are responsible for processing working memory<sup>12</sup>.

Stressors received by the body will cause the process of activating another pathway, namely the HPA axis pathway which causes an increase in cortisol secretion from the adrenal cortex<sup>11</sup>. Secreted cortisol will bind to glucocorticoid receptors and mineralocorticoid receptors in the brain which function to regulate human cognitive function. The mechanism resulting from the bond between cortisol and the two receptors is in the form of a decrease in the expression of both receptors so that the brain's ability to process working memory is reduced.

The fasting group with stress induction (TG2) got the highest working memory results due to the influence of Monday Thursday fasting activity. This will lead to an increase in cognitive function, neural plasticity, resistance to stress, working memory, and stimulate neurogenesis<sup>13</sup>. The mechanism of fasting that can improve brain function is obtained through the dopaminergic pathways in the brain<sup>12</sup>. Fasting activities will cause eustress stimulation in the body so that there will be an increase in cortisol secretion in the body to the optimum limit, namely the limit where cortisol can have a positive impact on the body. The secreted cortisol binds to glucocorticoid receptors and  $\delta$ -opioid receptors in the brain. The result of the bonding mechanism between cortisol in optimum amounts and these two receptors is an increase in the secretion of Brain Derived Neurotropic Factor (BDNF) and Nerve Growth Factor (NGF) by the nervous system which is spread throughout all areas of the brain<sup>8,14</sup>. Increased BDNF secretion will lead to increased dopamine secretion in the mesolimbic circuit<sup>15</sup>. The released dopamine will cause a decrease in inflammatory pathways that can interfere with the processing of working memory<sup>16</sup>, in addition, secreted dopamine will increase the activity of the nucleus accumbens, ventral tegmental area (VTA), hypothalamus, and insula cortex which will have an impact on the regulation of autonomic and physiological pathways in the form of increased tone of the parasympathetic nervous system<sup>17</sup>. BDNF can also increase the plasticity of the brain's nerves so that it can improve the brain's ability to perform memory processing<sup>17</sup>.

The increase in NGF due to induced eustress by fasting activity will lead to an increase in the proliferation of nerve cells in the brain which will make it easier for the brain to process information and process information into memory<sup>18</sup>. Acute stress induction interventions that stimulate the activation of stress-mediated pathways, namely the HPA axis and SAM axis, cause an increase in catecholamine secretion, which can cause a distress response in the body<sup>11</sup>. One form of this distress response is in the form of an inhibitory mechanism in the basolateral part of the amygdala which under normal circumstances plays a very important role in the mechanism of thinking processes, decision making, and working memory<sup>19,20</sup>. In addition, when the body receives a stressor, there is also an increase in the secretion of the hormone cortisol which exceeds its optimum limit so that it can cause a mechanism to decrease the expression of glucocorticoid receptors in the brain which under normal conditions functions as a regulator of the memory consolidation process. The form of response to the stressor above will eventually cause disruption of the thinking process and processing of working memory<sup>20</sup>.

Negative responses caused by stressors or stressful conditions above can be inhibited by interventions in the form of fasting activities. This is because fasting activities can stimulate several body systems that can inhibit negative responses caused by stressors.

Monday Thursday fasting activity will stimulate macrophage cells to decrease the secretion of IL-6 and TNF-a which can interfere with brain function and are cytokines that can cause increased activity of HPA axis<sup>21</sup>. In addition, fasting activity can also inhibit the SAM axis pathways by increasing the tone of the parasympathetic nervous system which is obtained through processes mediated by the hippocampus<sup>26</sup>. Fasting activity will stimulate the hippocampus to inhibit the sympathetic nervous system through the medial prefrontal cortex (mPFC), inhibition signals from the hippocampus will be sent to the nucleus tractus solitarius (NTS). Inhibitory impulses to the NTS will reduce sympathetic nerve stimulation and will cause a decrease in the secretion of catecholamines and cortisol hormone<sup>18,20</sup>. This

provides benefits for the brain to prevent the occurrence of neuroinflammatory and neurotoxic processes that can cause cognitive dysfunction and disturbances in working memory processing<sup>21</sup>. The control group (Control) obtained lower working memory measurements than the fasting group with stress induction (TG2) and higher than the stress group (TG1). This is because in the control group (Control) no intervention was carried out, either fasting activity or stress induction, so there was no stimulus that could cause activation of the HPA axis and SAM axis which could cause a decrease in memory function, and there was no stimulus that could cause memory loss. activation of the dopaminergic system which can improve memory function.

## 5. CONCLUSION

Monday-Thursday fasting activities have the potential to significantly maintain working memory function and the body's resistance to acute stress. So MondayThursday fasting can be used as a reference to maintain body condition so that it is always in optimal condition.

## REFERENCES

1. Gagnon SA, Wagner AD. Acute stress and episodic memory retrieval: Neurobiological mechanisms and behavioral consequences. *Annals of the New York Academy of Sciences*. 2016;1369(1):55–75. doi:10.1111/nyas.12996
2. Lovallo WR, Robinson JL, Glahn DC, Fox PT. Acute effects of hydrocortisone on the human brain: An fmri study. *Psychoneuroendocrinology*. 2010;35(1):15–20. doi:10.1016/j.psyneuen.2009.09.010
3. Cheng G, Huang C, Deng H, Wang H. Diabetes as a risk factor for dementia and mild cognitive impairment: A meta-analysis of longitudinal studies. *Internal Medicine Journal*. 2012;42(5):484–91. doi:10.1111/j.1445-5994.2012.02758.x
4. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Research Reviews*. 2017;39:46–58. doi:10.1016/j.arr.2016.10.005
5. Kelly KA, Miller DB, Bowyer JF, O'Callaghan JP. Chronic exposure to corticosterone enhances the neuroinflammatory and neurotoxic responses to methamphetamine. *Journal of Neurochemistry*. 2012;122(5):995–1009. doi:10.1111/j.1471-4159.2012.07864.x
6. Moro T, Tinsley G, Bianco A, Marcolin G, Pacelli QF, Battaglia G, et al. Effects of eight weeks of time-restricted feeding (16/8) on basal metabolism, maximal strength, body composition, inflammation, and cardiovascular risk factors in resistance-trained males. *Journal of Translational Medicine*. 2016;14(1). doi:10.1186/s12967-016-1044-0
7. Azevedo FR, Ikeoka D, Caramelli B. Effects of intermittent fasting on metabolism in men. *Revista da Associação Médica Brasileira*. 2013;59(2):167–73. doi:10.1016/j.ramb.2012.09.003
8. Australian Psychology Society. (2017). *Symptom of Stress*. Sydney.
9. Marks WN, Fenton EY, Guskjolen AJ, Kalynchuk LE. The effect of chronic corticosterone on fear learning and memory depends on dose and the testing protocol. *Neuroscience*. 2015;289:324–33. doi:10.1016/j.neuroscience.2015.01.011

10. Hadem IK, Majaw T, Kharbuli B, Sharma R. Beneficial effects of dietary restriction in Aging Brain. *Journal of Chemical Neuroanatomy*. 2019;95:123–33. doi:10.1016/j.jchemneu.2017.10.001
11. Pruessner JC, Dedovic K, Pruessner M, Lord C, Buss C, Collins L, et al. Stress regulation in the central nervous system: Evidence from structural and functional neuroimaging studies in human populations - 2008 curt richter award winner. *Psychoneuroendocrinology*. 2010;35(1):179–91. doi:10.1016/j.psyneuen.2009.02.016
12. Silva WCN, Köhler CC, Radiske A, Cammarota M. D1/D5 dopamine receptors modulate spatial memory formation. *Neurobiology of Learning and Memory*. 2012;97(2):271–5. doi:10.1016/j.nlm.2012.01.005
13. Longo VD, Mattson MP. Fasting: Molecular mechanisms and clinical applications. *Cell Metabolism*. 2014;19(2):181–92. doi:10.1016/j.cmet.2013.12.008
14. Park HR, Lee J. Neurogenic contributions made by dietary regulation to hippocampal neurogenesis. *Annals of the New York Academy of Sciences*. 2011;1229(1):23–8. doi:10.1111/j.1749-6632.2011.06089.x
15. Beste C, Schneider D, Epplen JT, Arning L. The functional BDNF VAL66MET polymorphism affects functions of pre-attentive visual sensory memory processes. *Neuropharmacology*. 2011;60(2–3):467–71. doi:10.1016/j.neuropharm.2010.10.028
16. Donzis EJ, Tronson NC. Modulation of learning and memory by cytokines: Signaling mechanisms and long term consequences. *Neurobiology of Learning and Memory*. 2014;115:68–77. doi:10.1016/j.nlm.2014.08.008
17. Zhao H, Alam A, San C-Y, Eguchi S, Chen Q, Lian Q, et al. Molecular mechanisms of brain-derived neurotrophic factor in neuro-protection: Recent developments. *Brain Research*. 2017;1665:1–21. doi:10.1016/j.brainres.2017.03.029
18. Christiansen AM, Herman JP, Ulrich-Lai YM. Regulatory interactions of stress and reward on rat forebrain opioidergic and GABAergic circuitry. *Stress*. 2011;14(2):205–15. doi:10.3109/10253890.2010.531331
19. Corbett B, Weinberg L, Duarte A. The effect of mild acute stress during memory consolidation on emotional recognition memory. *Neurobiology of Learning and Memory*. 2017;145:34–44. doi:10.1016/j.nlm.2017.08.005
20. Li L, Wang Z, Zuo Z. Chronic intermittent fasting improves cognitive functions and brain structures in mice. *PLoS ONE*. 2013;8(6). doi:10.1371/journal.pone.0066069
21. Shojaie M, Ghanbari F, Shojaie N. Intermittent fasting could ameliorate cognitive function against distress by regulation of inflammatory response pathway. *Journal of Advanced Research*. 2017;8(6):697–701. doi:10.1016/j.jare.2017.09.002
22. Vasconcelos AR, Yshii LM, Viel TA, Buck HS, Mattson MP, Scavone C, et al. Intermittent fasting attenuates lipopolysaccharide-induced neuroinflammation and memory impairment. *Journal of Neuroinflammation*. 2014;11(1). doi:10.1186/1742-2094-11-85