

## ORIGINAL ARTICLE

## Fatigue, Sleepiness, Anxiety-Depression Score, Calories and BDNF Serum Level, Quality of Life Alteration During Holy Ramadhan Month

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### ABSTRACT

**Introduction:** Ramadhan fasting increases mental and physical health. The study aims to evaluate the effect of Ramadhan fasting on fatigue, sleepiness, depression and anxiety mood, quality of life (QoL), calories consumed and Brain-derived neurotrophic factor (BDNF) serum level.

**Methods:** Twenty participants are included in the fasting group (FG), and nineteen participants are included in the non-fasting group (NFG). Fatigue severity scales (FSS), fatigue VAS, Epworth sleepiness scale (ESS), hospital depression and anxiety score (HADS), Beck depression inventory (BDI)-II, Short form 12 (SF-12), and BDNF in both groups were assessed at five-time points: one week before Ramadhan (T1), in the middle of Ramadhan (T2), the last days of Ramadhan (T3), one week after Ramadhan fasting (T4) two weeks after Ramadhan (T5).

**Results:** We found no significant differences across the time points between FG and NFG groups in all variables ( $p > 0.05$ ). There is a significant correlation between fatigue VAS with BDNF serum levels ( $r > r_{table}$ ), SF-12 PCS ( $r > r_{table}$ ) with BDNF, SF-12 MCS ( $r > r_{table}$ ). There is no correlation between fatigue, depression and anxiety intensity, sleepiness, QoL, BDI-II, and BDNF serum levels with calories consumed, BDI-II, and BDNF of fasting group in Ramadhan ( $r < r_{table}$ ).

**Conclusions:** Ramadhan fasting has positive effects on fatigue and mood. Ramadhan fasting does not have a significant effect on sleepiness, physical exercise, and calories consumed. Fatigue VAS and SF-12 PCS can replace the serum BDNF examination

**Keywords:** BDNF, depression, fatigue, quality of life, ramadhan fasting

## ABSTRAK

**Pendahuluan:** Puasa Ramadhan meningkatkan kesehatan mental dan fisik. Penelitian ini bertujuan untuk mengevaluasi pengaruh puasa Ramadhan terhadap kelelahan, rasa kantuk, mood depresi dan kecemasan, kualitas hidup, dan tingkat serum Brain-derived neurotrophic factor (BDNF)

**Metode:** Dua puluh peserta termasuk dalam kelompok puasa dan sembilan belas peserta termasuk dalam kelompok tidak puasa. Kedua kelompok dinilai *Fatigue severity scales (FSS)*, *fatigue VAS*, *Epworth sleepiness scale (ESS)*, *hospital depression and anxiety score (HADS)*, *Beck depression inventory (BDI)-II*, *Short form 12 (SF-12)*, dan *BDNF* pada lima waktu: satu minggu sebelum Ramadhan (T1), di tengah Ramadhan (T2), hari terakhir Ramadhan (T3), satu minggu setelah puasa Ramadhan (T4), dan dua minggu setelah Ramadhan (T5).

**Hasil:** Tidak ditemukan perbedaan yang signifikan antara kelompok puasa dan tidak puasa di semua variabel ( $p > 0,05$ ). Ada hubungan yang signifikan antara *fatigue VAS* dengan kadar serum BDNF ( $r > r$  tabel), SF-12 PCS ( $r > r$  tabel) dengan BDNF, SF-12 MCS ( $r > r$  tabel). Tidak ada hubungan antara *fatigue*, depresi dan kecemasan, rasa kantuk, kualitas hidup, BDI-II, dan kadar BDNF serum dengan kalori, BDI-II, dan BDNF pada kelompok puasa ( $r < r$  tabel).

**Kesimpulan:** Puasa Ramadhan mempunyai efek positif pada *fatigue* dan mood. Puasa Ramadhan tidak mempunyai efek yang signifikan terhadap rasa kantuk, latihan fisik, dan kalori yang dikonsumsi. *Fatigue VAS* dan SF-12 PCS dapat digunakan untuk mengganti serum BDNF.

**Kata Kunci:** BDNF, depresi, *fatigue*, kualitas hidup, puasa ramadhan

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## INTRODUCTION

According to Sural Al-Baqarah: 183, fasting is an act conducted by Muslims to achieve righteousness (*taqwa*).<sup>1</sup> Fasting during the month of Ramadhan is one of the five main pillars of Islam.<sup>2</sup> Surah Al-Baqarah:187

mentions all adult Muslims who are not acutely sick, pregnant, menstruating, or breastfeeding must refrain from eating, drinking, smoking, violence, anger, and sex from dawn (*fajr*) to sunset (*maghrib*) for 29 to 30 days of the fasting period.<sup>1</sup> The duration of Ramadhan fasting depends on geographic location and season—ranging between 10 to 18 hours per day.<sup>3</sup> The length of Ramadhan fasting in Indonesia is about 14 hours, from 4 am to 6 pm local time.

Ramadhan fasting has been known to have a health improvement effect.<sup>4</sup> Ramadhan fasting improves spiritual as it can also greatly affect physical health such as blood pressure, lipid profile, oxidative stress and antioxidant status.<sup>5</sup> A study by Amin et al. found various positive

impacts of Ramadhan fasting on mental health, including depression, anxiety, and stress. However, the changes in drinking and eating habits, mental and physical activities can cause several problems such as fatigue and increased sleepiness for those who undergo fasting.<sup>6-8</sup>

A study from Alessio et al, patients with major depression appeared to have lower Brain-derived neurotrophic factor (BDNF) levels in whole blood, serum, or plasma.<sup>9</sup> Therefore, based on the known positive effects of fasting in improving mood states, we are interested in evaluating whether the serum BDNF can assess the depression value during this holy month of fasting.

Based on these considerations, this study aims to evaluate the effect of Ramadhan fasting on fatigue, sleepiness, mood, quality of life, and BDNF serum levels and its correlation to further explore the benefits of fasting.

## METHODS

Prior to the study, ethical clearance was obtained from the Profession and Research Ethics Committee of Medical Committee Faculty of Medicine, Padjadjaran University (ethical clearance number: 251/UN6.KEP/EC/2021). As required, procedures and ethical aspects of current research have been conducted in full accordance with the World Medical Association Declaration of Helsinki. All participants agreed to participate based on informed consent. All participants completed 30 days of fasting starting from 27 May 2017 to 24 June 2017.

Thirty-nine healthy men are included in this study and divided into two groups. Twenty healthy men performed fasting during Ramadhan (fasting group, FG) and nineteen healthy men served as a control group by not fasting (non-fasting group, NFG). The inclusion criteria for the fasting group are: (1) be healthy, (2) be older than 18 years of age, (3) intend to fast the 86 whole month of Ramadan, (4) have fasted during Ramadhan at least once before, (5) can understand a command and communicate in Bahasa Indonesia.

Both groups were then measured at five-time points. The first measurement (T1) was taken one week before the beginning of Ramadhan, the second measurement was in the middle of Ramadhan (T2: two weeks after T1), the third measurement was during the last days of Ramadhan (T3), the fourth measurement was one week after the end of Ramadhan (T4), and the last measurement was two weeks after the end of Ramadhan (T5).

Fatigue is measured by the fatigue severity scale (FSS) and fatigue visual analog scale (VAS). FSS is a questionnaire consisting of 9 items that evaluate the fatigue level with a linear score of 1 (strongly disagree) to 7 (strongly agree). This questionnaire can evaluate the impact of fatigue and VAS with a score from 0 (no fatigue) to 10 (the worst imaginable fatigue).<sup>10</sup>

Mood intensity in this study is measured using the Hospital Depression and Anxiety Score (HADS) and Beck's Depression Inventory (BDI)-II questionnaire. HADS consists of fourteen items divided into two domains: seven

items of anxiety scales and another seven items to assess depression level. The score of each parameter is between 0 to 21. If the score is 8 or more than 8, it indicates the symptoms of anxiety or depression.<sup>11</sup> BDI-II consists of 21 items to measure the severity of depression and scored between 0 to 63. The higher the BDI-II score is, the more severe the depression.<sup>12</sup>

Day sleepiness is measured using Epworth Sleepiness Scale (ESS) questionnaires and Sleepiness VAS. ESS consists of 8 items, and each item is rated between 0 to 3. ESS score is the sum of 8 items and scored between 0 to 24. High ESS values indicate a high tendency of average daily life sleepiness in individuals.<sup>13</sup>

Short Form 12 questionnaire (SF-12) is used to measure both mental and physical functioning.<sup>14</sup> There are 12 items in the SF-12 questionnaire comprising 8 domains: physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. A higher score indicates better quality of life.<sup>14</sup>

Brain-derived neurotrophic factor (BDNF) serum samples are collected during each of the five-time points in both groups. 5 mL of blood was collected from the subjects' serum blood by laboratory personnel. BDNF serum levels are then analyzed using a quantitative sandwich enzyme immunoassay technique by Quantikine ELISA Human CXCL-8/IL-8 HS.<sup>15</sup>

24-hour Food Recall is a method that focuses on the subject's ability to recall all the food and drinks an individual consumed during the last

24 hours. This method is also used to screen individual nutritional intake. The advantage of this method is it requires only minimal tools and can be done at any time.<sup>16</sup> All subjects were instructed to record their daily dietary intake and calculate it using household measurements (spoon, slice, glass, plate, and bowl). Food recall results represent the average of food calories consumed in breakfast, lunch, and dinner. The recall is conducted twice a week for each measurement (T1 - T5). However, because the FG was fasting during T1-T3, they only conducted the Food Recall at dawn and dinner and calculated the average between the two.

Numerical data analysis is tested using the unpaired T-test if the data are normally distributed and the alternative Mann Whitney test if the data are not normally distributed, namely Age. A paired T-test is used to compare T1 and T2, T1 and T3, T1 and T4, and T1 and T5 in FG and NFG. Pearson and Spearman's analysis performed a correlation between fatigue, sleepiness, depression intensity, and QoL with BDNF. Statistical analysis is performed using SPSS version 22 (IBM, New York USA). Significant is set at  $p < 0.05$ .

## RESULTS

The mean ( $\pm$  SD) age of the fasting group (FG) patients is  $29.65 \pm 4,209$  years old. The FG is consisted of 20 people who are all men (100%) and of mongoloid race (100%). The mean ( $\pm$  SD) age of the patients in the non-fasting group (NFG) is  $25.26 \pm 5,162$  years old. The NFG consists of 19 people who are all men (100%) and of mongoloid race (100%) (Table 1).

**Table 1. Demographic characteristics in fasting group and non-fasting group**

Variable	Group		P
	Fasting Group (FG) N=20	Non-Fasting Group (NFG) N=19	
<b>Age</b>			
Mean $\pm$ Std	29.65 $\pm$ 4.209	25.26 $\pm$ 5.162	0.005**
Median	31.00	23.00	
Range (min-max)	22.00-36.00	18.00-39.00	
<b>Gender</b>			1.000
Men	20(100.0%)	19(100.0%)	
Women	0(0.0%)	0(0.0%)	
<b>Race</b>			
Mongoloid	20(100.0%)	19(100.0%)	1.000

\*p<0.05, \*\*p<0.01

We found no significant differences across the time points between FG and NFG groups in all variables ( $p > 0.05$ ) (Table 2). However, in Table 3, we found a significant difference in FG between T1 and T3 BDNF serum levels ( $5.93 \pm 5.135$  to  $6.82 \pm 4.946$ ,  $p < 0.05$ ) and T1 with T2 Fatigue VAS ( $4.86 \pm 2.148$  to  $5.72 \pm 2.077$ ,  $p < 0.05$ ). The significant differences of HADS-Depression in FG can be seen by comparing T1 with T3 ( $3.45 \pm 2.139$  to  $1.90 \pm 1.804$ ,  $p < 0.05$ ), T1 with T4 ( $3.45 \pm 2.139$  to  $1.80 \pm 1.989$ ,  $p < 0.05$ ), and T1 with T5 ( $3.45 \pm 2.139$  to  $1.65 \pm 1.980$ ,  $p < 0.05$ ). There are significant differences in HADS-Anxiety score in FG when comparing T1 with T3 ( $4.75 \pm 3.226$  to  $2.90 \pm 2.337$ ,  $p < 0.05$ ), T1 with T4 ( $4.75 \pm 3.226$  to  $2.95 \pm 3.605$ ,  $p < 0.05$ ), and T1 with T5 ( $4.75 \pm 3.226$  to  $2.50 \pm 3.204$ ,  $p < 0.05$ )

and significant BDI-II when comparing T1 with T3 ( $4.80 \pm 4.099$  to  $3.05 \pm 3.531$ ,  $p < 0.05$ ), T1 with T4 ( $4.80 \pm 4.099$  to  $2.85 \pm 4.557$ ,  $p < 0.05$ ), and T1 with T5 ( $4.80 \pm 4.099$  to  $3.05 \pm 4.148$ ,  $p < 0.05$ ). There is a significant difference of calories in FG between T1 with T4 ( $1470.10 \pm 438.875$  to  $1638.20 \pm 419.021$ ,  $p < 0.05$ ) and T1 with T5 ( $1470.10 \pm 438.875$  to  $1694.85 \pm 431.892$ ,  $p < 0.05$ ).

There are no significant differences between the time points in most of the variables in NFG ( $p > 0.05$ ), except the comparison of T1 with T4 in HADS-Anxiety ( $4.75 \pm 3.226$  to  $2.95 \pm 3.605$ ,  $p < 0.05$ ) and T1 with T3 ( $33.84 \pm 7.812$  to  $31.21 \pm 10.147$ ,  $p < 0.05$ ) also T1 with T4 ( $33.84 \pm 7.812$  to  $30.37 \pm 10.838$ ,  $p < 0.05$ ) in FSS (Table 3).

Table 2. Fatigue, Mood and health-related QoL and significant difference between fasting group and non-fasting group

Variable	Group	T1			T2			T3			T4			T5		
		Mean ± SD	P	Mean ± SD	Mean ± SD	P	Mean ± SD	Mean ± SD	P	Mean ± SD	Mean ± SD	P	Mean ± SD	Mean ± SD	P	Mean ± SD
Fatigue Severity Scale (FSS)	FG (n=20)	36.00 ± 12.716	0.525	36.30 ± 8.962	0.321	34.30 ± 8.517	0.309	34.45 ± 9.248	0.213	34.20 ± 7.716	0.517					
	NFG (n=19)	33.84 ± 7.812		33.37 ± 9.221		31.21 ± 10.147		30.37 ± 10.838		32.27 ± 9.691						
Fatigue VAS	FG (n=20)	4.86 ± 2.148	0.495	5.72 ± 2.077	0.167	4.78 ± 1.651	0.368	5.36 ± 1.833	0.193	5.52 ± 2.054	0.437					
	NFG (n=19)	4.44 ± 1.525		4.78 ± 2.042		4.22 ± 2.127		4.51 ± 2.186		5.08 ± 1.307						
HADS-Anxiety	FG (n=20)	4.75 ± 3.226	0.874	4.10 ± 2.511	0.255	2.90 ± 2.337	0.235	2.95 ± 3.605	0.365	2.50 ± 3.204	0.101					
	NFG (n=19)	4.58 ± 3.469		5.37 ± 4.085		4.68 ± 4.151		3.68 ± 3.433		3.79 ± 3.066						
HADS - Depression	FG (n=20)	3.45 ± 2.139	0.461	2.50 ± 1.821	0.309	1.90 ± 1.804	0.336	1.80 ± 1.989	0.607	1.65 ± 1.980	0.478					
	NFG (n=19)	3.26 ± 2.978		3.95 ± 3.865		3.21 ± 3.537		3.37 ± 5.283		3.16 ± 4.764						
Beck Depressing Inventory II	FG (n=20)	4.80 ± 4.099	0.835	4.30 ± 4.067	0.607	3.05 ± 3.531	0.158	2.85 ± 4.557	0.235	3.05 ± 4.148	0.444					
	NFG (n=19)	6.79 ± 8.522		7.89 ± 12.449		6.89 ± 9.826		5.79 ± 10.570		5.63 ± 10.166						
Epworth Sleepiness Score (ESS)	FG (n=20)	9.25 ± 3.712	0.787	11.20 ± 5.064	0.302	10.30 ± 4.156	0.503	10.35 ± 4.283	0.992	10.37 ± 6.978	0.846					
	NFG (n=19)	9.63 ± 4.991		9.42 ± 5.551		9.26 ± 5.373		9.90 ± 4.154		9.58 ± 6.003						
Sleepiness VAS	FG (n=20)	5.40 ± 1.818	0.567	5.27 ± 1.690	0.817	4.92 ± 1.809	0.224	5.37 ± 1.895	0.226	5.23 ± 1.964	0.644					
	NFG (n=19)	5.06 ± 1.826		5.11 ± 2.493		4.28 ± 2.000		4.52 ± 2.396		4.91 ± 2.245						
SF-12 PCS	FG (n=20)	52.67 ± 6.105	0.444	52.63 ± 3.046	0.689	52.62 ± 3.498	0.683	49.81 ± 7.485	0.134	51.60 ± 5.905	0.627					
	NFG (n=19)	51.88 ± 6.136		51.96 ± 6.527		52.88 ± 6.548		52.69 ± 7.273		52.09 ± 6.492						
SF-12 MCS	FG (n=20)	49.91 ± 7.053	0.728	47.42 ± 7.458	0.901	48.36 ± 7.319	0.380	47.26 ± 8.155	0.824	49.76 ± 7.775	0.835					
	NFG (n=19)	46.56 ± 10.762		45.52 ± 13.380		44.14 ± 11.756		47.85 ± 8.275		49.98 ± 8.675						
BDNF	FG (n=20)	5.93 ± 5.135	0.569	5.67 ± 4.463	0.380	6.82 ± 4.946	0.771	5.67 ± 4.737	0.771	5.43 ± 3.736	1.000					
	NFG (n=19)	5.83 ± 3.783		6.70 ± 4.560		6.46 ± 4.927		5.94 ± 4.358		5.67 ± 3.316						
Calories	FG (n=20)	1470.10 ± 438.875	0.158	1397.55 ± 343.553	0.649	1543.00 ± 385.723	0.936	1638.20 ± 419.021	0.302	1694.85 ± 431.892	0.116					
	NFG (n=19)	1560.53 ± 263.057		1443.00 ± 268.003		1533.74 ± 327.189		1501.11 ± 397.812		1503.05 ± 296.074						

VAS = Visual Analogue Scale, Hospital Depression and Anxiety Score (HADS), SF-12 PCS = Short Form 12 Physical Component Score; MCS = Mental Component Score; BDNF = Brain-derived neurotrophic factor; \*p<0.05

**Table 3. Comparison between Time Points in fasting group and non-fasting group**

Variable	Group	P <sup>a</sup>	P <sup>b</sup>	P <sup>c</sup>	P <sup>d</sup>
Fatigue Severity Scale (FFS)	FG (n=20)	0.878	0.500	0.542	0.469
	NFG (n=19)	0.667	0.025*	0.028*	0.064
Fatigue (VAS)	FG (n=20)	0.048*	0.877	0.391	0.270
	NFG (n=19)	0.443	0.625	0.922	0.094
HADS-Anxiety	FG (n=20)	0.203	0.006*	0.022*	0.003*
	NFG (n=19)	0.131	0.848	0.078	0.046*
HADS-Depression	FG (n=20)	0.053	0.009*	0.015*	0.006*
	NFG (n=19)	0.070	0.904	0.428	0.223
Beck Depressing Inventory II	FG (n=20)	0.374	0.023*	0.019*	0.030*
	NFG (n=19)	0.527	0.906	0.246	0.211
Epworth Sleepiness Score	FG (n=20)	0.113	0.224	0.215	0.449
	NFG (n=19)	0.830	0.667	0.557	0.953
Sleepiness VAS	FG (n=20)	0.628	0.177	0.923	0.666
	NFG (n=19)	0.882	0.014	0.95	0.503
SF-12 PCS	FG (n=20)	0.823	0.737	0.173	0.457
	NFG (n=19)	0.929	0.370	0.215	0.897
SF-12 MCS	FG (n=20)	0.770	0.800	0.789	0.398
	NFG (n=19)	0.493	0.159	0.332	0.053
BDNF	FG (n=20)	0.502	0.042*	0.526	0.287
	NFG (n=19)	0.071	0.509	0.655	0.808
Calories	FG (n=20)	0.411	0.588	0.037*	0.023*
	NFG (n=19)	0.180	0.756	0.564	0.484

*Pa* = T1vsT2 significant difference; *Pb* = T1vsT3 significant difference; *Pc* = T1vsT4 significant difference; *Pd* = T1vsT5 significant difference; *VAS* = Visual Analogue Scale, Hospital Depression and Anxiety Score (HADS), SF-12 PCS = Short Form 12 Physical Component Score; MCS = Mental Component Score; BDNF = Brain-derived neurotrophic factor; \**p*<0.05

**Table 4. Correlation between fatigue, mood, sleepiness, and quality of life with BDI-II, BDNF serum levels, and calories in the fasting group**

	BDI-II		BDNF		Calories	
	r	P	r	P	r	P
FFS	-0.304	0.193	0.261	0.267	-0.091	0.702
Fatigue VAS	0.345	0.136	-0.518	0.017**	0.092	0.701
HADS-Anxiety	0.110	0.643	-0.086	0.718	0.159	0.504
HADS-Depression	0.009	0.971	-0.335	0.149	-0.012	0.959
SF-12 PCS	0.182	0.442	0.519	0.019**	-0.125	0.598
SF-12 MCS	-0.574	0.008**	-0.191	0.420	0.176	0.458
ESS	0.316	0.175	-0.175	0.635	-0.113	0.635
Sleepiness VAS	0.304	0.193	0.324	0.163	0.311	0.182
BDI-II			0.036	0.892	0.032	0.892
BDNF					0.338	0.145

*BDI-II* = Beck depression inventory II; *VAS* = Visual Analogue Scale; *HADS* = hospital depression and anxiety score; *ESS* = Epworth sleepiness scale; *SF-12 PCS* = Short Form 12 Physical Component Score; *MCS* = Mental Component Score; *BDNF* = Brain-derived neurotrophic factor; \*\**p*<0.05



Table 4 shows the results of the Spearman correlation test statistical analysis between the fatigue, mood, sleepiness, and quality of life with depression parameters BDI-II and BDNF. Thus, we found a significant correlation between fatigue VAS with BDNF serum levels with moderate correlation strength ( $r > r$  table). There is a moderate correlation between SF-12 PCS ( $r > r$  table) and BDNF, but not with SF-12 MCS ( $r < r$  table). On the other hand, SF-12 MCS ( $r > r$  table) has a moderate correlation with BDI-II but not with SF-12 PCS ( $r < r$  table). There is no correlation between fatigue, depression and anxiety intensity, sleepiness, QoL, BDI-II and BDNF serum levels with calories, and BDI-II and BDNF of fasting group in Ramadhan ( $r < r$  table).

## DISCUSSION

This study aims to evaluate the effects of Ramadhan fasting on fatigue, mood, sleepiness, quality of life, calories, and BDNF serum levels and the correlation with BDI-II and BDNF, especially in healthy men. We found no significant differences between the FG and NFG in all-time points of this current study. These results are in agreement with other studies conducted by Nugraha et al., which found no differences in mood, fatigue, sleepiness, and quality of life in Ramadhan fasting during summertime in Germany between the FG and NFG.<sup>17</sup>

Fatigue is assessed using FSS and fatigue VAS, where their high scores indicated higher fatigue values. Ramadhan fasting appears to increase the levels of fatigue in previous studies significantly.<sup>8</sup> However, we found no significant

improvement in fatigue values before and after fasting, but there is a slight increase of FSS and VAS scores from T1 to T2, but it decreased again at T3. The increase in fatigue value at T2 could be due to the adaptation during fasting.<sup>17</sup> The relationship of this fasting adaptation is acceptable because it is followed by the decline of the value of fatigue scales until the last day of fasting (T3), which indicates that adaptation against fatigue may be needed during the initial two weeks of fasting in these study participants.

ESS and sleepiness VAS is used to assess the possibility of the subject falling asleep during his/her daily activities.<sup>13</sup> Several studies found in a systematic review that perception of sleepiness increased during the daytime of Ramadhan fasting.<sup>18</sup> Although there is an increase of ESS values in this fasting group, the increase of the values proved to be statistically non-significant and have no correlation with other parameters.

SF-12 is selected as an instrument to assess the quality of life in general and specific populations because it is substantially shorter than SF-36.<sup>19</sup> However, the results are the same as in the previous study that showed no significant improvement of QoL between FG and NFG as well as in all-time points during fasting.<sup>17</sup> This result is in contradiction with other studies that find a better health-related quality of life in diabetic patients who perform fasting during Ramadhan compared to the non-fasting diabetics.<sup>20</sup>

Several studies suggest that fasting for a long time can reduce symptoms of depression and relieved negative moods. However, other studies have shown an increase in depression



scores in depressed patients during Ramadhan.<sup>21</sup> Significant decrease of anxiety and depression values measured using HADS can be seen at the end of fasting up to two weeks after fasting even though there is no significant difference between the NFG and FG group. BDI-II, which also assessed depression, found a significant decrease of values similar to HADS results. This is then compared to the non-fasting group, where there are no significant changes in all-time point measurements. This result contradicts other studies that found lower anxiety and depression levels in nurses after Ramadhan fasting—although these results are statistically non-significant.<sup>22,23</sup> However, a study conducted by Kadri et al. found increased anxiety levels in healthy men during Ramadhan due to refraining from smoking.<sup>24</sup> However, in this study, we did not exclude the subjects who smoked.

BDNF concentration in serum is about 100 folds higher than plasma levels.<sup>25</sup> Therefore, we used the BDNF serum to measure the BDNF levels in this study. BDNF, a secretory protein that helps maintain existing neurons and the growth and differentiation of new neurons and synapses<sup>26</sup> involved in depression pathogenesis. BDNF serum and plasma have been lower in patients with depression than people with healthy mental status.<sup>27</sup> We also found significant changes in BDNF serum levels in the first week (T1) of fasting compared to the serum levels on the last day of fasting (T3). Thus, we can conclude that there is a tendency for depression value to increase during fasting, although there are no significant differences while comparing it to the non-fasting group. We recommend fasting BDNF assessments to be carried out in patients who are diagnosed with depression to differentiate the better significance.

Interestingly, we found a correlation between BDNF and fatigue in the fasting group. These correlations showed the same results as prostate cancer patients in that fatigue may have mutual psychological and shared neuroanatomical pathways with other symptoms such as depression.<sup>28</sup> Although BDI-II and BDNF both measure a person's depression levels, and there are contradictory results in relation to the quality of life scores as measured by SF-12 in this study where BDI-II had a correlation with only SF-12 MCS, which assesses mental status but not with BDNF. On the other hand, BDNF correlates with SF-12 PCS but not with BDI-II. It is necessary to study further whether BDNF, which correlates with the VAS Fatigue, has a relationship with the correlation between BDNF and SF-12 PCS.

Diet habits are known to activate BDNF and sustain brain neuronal plasticity, playing an essential role in neurogenesis.<sup>21</sup> Other study argues that BDNF can be modulated by dietary composition on dietary restriction in overweight and obese patients.<sup>29</sup> Therefore, we wanted to find out whether the number of calories consumed had a relationship with the BDNF value in Ramadhan fasting. However, in this research, we found that there is no correlation between these two. This may affect the subjects we take are healthy people, and the food that each person eats is neither defined nor uninformed.

There is no significant difference between the number of calories consumed by the fasting and non-fasting groups. This is due to the increased intake consumed, especially when breaking the fast after sunset (Iftar).<sup>30</sup> However, other studies found a decrease in daily calorie intake by 103

Kcal / d, albeit not statistically significant.<sup>31</sup> This may also be influenced by differences in diet depending on location and family habits.<sup>30</sup> The types of food consumed after Ramadhan that are typically rich in fat and carbohydrates coupled with an increase in food consumption may cause weight gain after Ramadhan.<sup>32</sup> Due to inadequate data, the effect of calorie restriction during Ramadhan remains unclear.

## CONCLUSION

Ramadhan fasting has positive effects on fatigue and mood, as indicated by HADS and BDI score at some time points. Ramadhan fasting does not significantly affect sleepiness, quality of life, and calories consumed between FG and NFG. The serum BDNF can measure the value of depression at the end of fasting and show us improvement results. Fatigue VAS and SF-12 PCS can replace BDNF examination since it correlates them. Further studies are required more selective criteria for inclusion, such as the equal level of the subject's daily activities, which will affect the assessment parameters.

## REFERENCES

- Departemen Agama RI. Al-Quran and its translation. Bandung: CV Dipenogoro; 2008. Available at: <https://repository.uin-suska.ac.id/3128/7/EM.pdf>. Accessed June 28<sup>th</sup>, 2022.
- Jahromi SR, Sahraian MA, Ashtari F, Ayromlou H, Etemadifar M, Ghaffarpour M, et al. Islamic fasting and multiple sclerosis. *BMC Neurol* 2014; 14: 56.
- Azizi F. Islamic fasting and health. *Ann Nutr Metab* 2010; 56: 273–82.
- Rouhani MH, Azadbakht L. Is Ramadan fasting related to health outcomes? A review on the related evidence. *J Res Med Sci* 2014; 19: 987-92.
- Trepanowski JF & Bloomer RJ. The impact of religious fasting on human health. *Nutr J* 2010; 9: 57.
- Tas F, Karabulut S, Ciftci R, Yildiz R, Keskin I, Kilic S, et al. The behavior of Turkish cancer patients in fasting during the holymonth of ramadan. *Jpn J Clin Oncol* 2014; 44: 705-10.
- Alabed H, Abuzayan K, Waterhouse J. Changes in subjective and objective measures of performance in ramadan. *Int J Sci Res Innov* 2013; 7(5): 1174-83.
- Ovayolu O, Ovayolu N, Tasan E. Does ramadan fasting affect fatigue in nurses. *Holist Nurs Pract* 2016; 30: 222-6.
- Alessio P, Giuliana M, Ruggiero F, Baj G, Florean M, Mascaretti LG, et al. A method for reproducible measurements of serum BDNF: comparison of the performance of six commercial assays. *Sci Rep* 2015; 5: 17989.
- Valet M, Stoquart G, Glibert Y, Hakizimana JC, Lejeune T. Is fatigue associated with cardiorespiratory endurance among patients suffering from multiple sclerosis. *Ann Phys Rehabil Med* 2016; 59: 41.
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67(6): 361-70.
- Wang YP, Gorenstein C. Psychometric properties of the beck depression

- inventory-II: A comprehensive review. *Braz J Psychiatry* 2013; 35(4): 416-31.
13. Xiong Y, Zhou XJ, Nisi RA, Martin KR, Karaman MM, Cai K, et al. Brain white matter changes in CPAP-treated obstructive sleep apnea patients with residual sleepiness. *J Magn Reson Imaging* 2017; 45: 1371-8.
14. Ware JJr, Kosinski M, Keller SD. A 12-item short-form health survey: Construction of scales and preliminary tests of reliability and validity. *Med Care* 1996; 34: 220e233.
15. Gejl AK, Enevold C, Bugge A, Andersen MS, Nielsen CH, Andersen LB. Association between serum and plasma brain-derived neurotrophic factor and influence of storage time and centrifugation strategy. *Sci Rep* 2019; 9: 9655.
16. Astuti T. Metode food recall. In: Sirajuddin, Surmita & Astuti T. *Survey Konsumsi Pangan*. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018. p. 110.
17. Nugraha B, Ghashang SK, Hamdan I, Hamdan I, Gutenbrunner C. Effect of Ramadan fasting on fatigue, mood, sleepiness, and health-related quality of life of healthy young men in summer time in Germany: A prospective controlled study. *Appetite* 2017; 111: 38-45.
18. Faris MAE, Jahrami HA, Alhayki FA, Alkhawaja NA, Ali AM, Aljeeb SH, et al. Effect of diurnal fasting on sleep during ramadan: a systematic review and meta-analysis. *Sleep Breath* 2020; 24: 771-82.
19. Ware JE, Kosinski M, Keller SD. SF-12: How to score the SF-12 physical and mental health summary scales. 2nd ed. Boston: The Health Institute, NEMC; 1995.
20. Mahgoub AO, Abdekgadir E. The association between health-related quality of life and ramadan fasting in diabetic patients: a survey using a structured D-39 assessment tool. A sudanese cohort. *J Fasting Health* 2017; 5: 24-30.
21. Zhang Y, Liu C, Zhao Y, Zhang X, Li B, Cui R. The effects of calorie restriction in depression and potential mechanisms. *Curr Neuropharmacol* 2015; 13(4): 536-42.
22. Koushali An, Hajiamini Z, Ebadi A, Bayat N. Effect of Ramadan fasting on emotional reactions in nurses. *Iran J Nurs Midwifery Rese* 2013; 18: 232-6.
23. Harder-Lauridesn N, Rosenberg A, Benatti FB, Damm JA, Thomsen C, Mortensen EL, et al. Ramadan model of intermittent fasting for 28 d had no major effect on body composition, glucose metabolism, or cognitive function in healthy lean men. *Nutrition* 2017; 37: 92-103.
24. Kadri N, Tilae A, Batal ME, Taltit Y, Tahiri SM, Moussaoui D. Irritability during the month of Ramadhan. *Psychosom Med* 2000; 62: 280-5.
25. Radka SF, Holst PA, Fritsche M, Altar CA. Presence of brain-derived neurotrophic factor in brain and human and rat but not mouse serum detected by a sensitive and specific immunoassay. *Brain Res* 1996; 709: 122-301.
26. Acheson A, Conover JC, Fandl JP, DeChiara TM, Russell M, Thadani A, et al. A BDNF autocrine loop in adult sensory neurons prevents cell death. *Nature* 1995; 374: 450-3.

27. Kishi T, Yoshimura R, Ikuta T, Iwata N. Brain-derived neurotrophic factor and major depressive disorder: evidence from meta-analyses. *Front Psychiatry* 2018; 8: 308.
28. Saligan LN, Lukkahatai N, Holder G, Walitt B, Machado-Vieira R. Lower brain-derived neurotrophic factors level associated with worsening fatigue in prostate cancer patients during repeated stress from radiatic therapy. *World J Biol Psychiatry* 2016; 17: 608-14.
29. Araya AV, Orellana X, Espinoza J. Evaluation of the effect of caloric restriction on serum BDNF in overweight and obese subjects: preliminary evidences. *Endocrine* 2008; 33: 300-4.
30. Khaled MB, Belbraouet S. Ramadan fasting diet entailed a lipid metabolic disorder among type 2 diabetic obese women. *Am J Appl Sci* 2009; 6(3): 471-7.
31. Mafauzy M, Mohammed WB, Anum MY, Zulkifli A, Ruhani AH. A study of the fasting diabetic patients during the month of ramadan. *Med J Malaysia* 1990; 45: 14-7.
32. Bakhotmah, Balkess Abed. The puzzle of self-reported weight gain in a month of fasting (ramadan) among a cohort of Saudi families in Jeddah Western Saudi Arabia. *Nutr J* 2011; 10: 84.