Relationship between calorie intake, physical activity, and dopamine D2 receptor Taq1A gene polymorphism in normal-weight, overweight, and obese students of the faculty of medicine of university of Sumatera Utara

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INTRODUCTION

Obesity is defined as an excessive fat accumulation deposited in subcutaneous tissue, around organ, and sometimes distributed into visceral organ. Increased fat accumulation is a risk factor that causes degenerative diseases such as diabetes mellitus, coronary heart disease, and hypertension.1 Obesity is caused by an imbalance of energy between consumed calories and expended calories in a long term, influenced by environmental and genetic factors.2 Imbalance of energy due to excess input of kilocalories compared to the output to support body energy expenditure will cause excess energy stored as triglyceride in fat tissue. Calorie intake for body is obtained from carbohydrate, fat, and protein nutrition in food. Study about the relationship between calories intake and obesity had been conducted before, but the result is still controversial because different outcomes were obtained in different populations.3-5

The quantity of physical activity in energy expenditure clearly has a role in maintaining body weight. Physical activity helps with maintaining energy imbalance and thus obesity is prevented. Lack of physical activity causes lack of energy burned and this excess energy causes obesity. Earlier studies showed that there is relationship between physical activity and obesity.4,6

Energy imbalance that causes obesity is also influenced by genetic factor. Genome-wide association studies (GWAS) have identified more than 40 common polymorphisms that are associated with BMI variability in humans.7 Genetic factor is a genetic disorder that changes the function of the protein.8 Various studies have proven that D2 dopamine receptor, especially Taq1A polymorphism, as the gene that is involved in obesity risk factors. Dopamine receptor normally acts as a dopamine activity controller.9 Taq1A polymorphism decreases the amount of D2 dopamine receptor in the brain.

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and as a result functions of dopamine decrease, which is the ability to inhibit negative behavior, such as eating and reduced motivation to engage in activities.\(^\text{10}\)

The current study aims to see the relationship between calorie intake, physical activity, and dopamine D2 receptor (DRD2) Taq1 gene polymorphism in normal weight, overweight, and obese students in the Faculty of Medicine of University of Sumatera, Utara.

**RESEARCH DESIGN AND METHODS**

Consent to conduct this study was obtained from the Ethical Committee of the Faculty of Medicine of University of Sumatera, Utara. Subjects who agreed to participate were asked to fill out and sign an informed consent; the target study population were given an explanation about the purpose and benefits of the research. This cross-sectional study involves 139 subjects. Nutrition intake is measured using a 24-hour Food Recall Questionnaire; appropriate calculations were made using the Nutrisurvey software. Body height and weight were measured using a digital scale with maximum capacity of 150 kg and a microtoise maximum length of 200 cm. Body Mass Index was calculated by dividing weight and square of height to classify body weights as normal, overweight, and obese. Physical activity was measured using the International Physical Activity Questionnaire (IPAQ).

DNA was extracted from buffy coats peripheral blood leukocyte. PCR product used 5’-ACCCTTCCTGAGTGTCATCA-3’ (Forward) and 5’-ACGGCTGGCCAAGTTGTCTA-3’ (Reverse). The 310 bp amplicons were then visualized with 3% agarose gel. Amplicon digestion was then done using Taq1A restriction enzyme incubated at 37°C for 2 hours. The digested DNA (Taq1A CC: 180bp, 130bp; Taq1A CT: 310bp, 180bp, 130bp; Taq1A TT: 310 bp) was then visualized using 3% agarose gel using gel documentation system.

Hardy–Weinberg Equilibrium was used to assess the polymorphism. Bivariate chi-square test is used to analyze the distribution of normal data to see the relationship within the study variables, which was carried out with SPSS software (version 14).

**RESULTS**

This study was done on 139 students of the Faculty of Medicine of University of Sumatera, Utara; the students were recruited after they had fulfilled the inclusion criteria, and other characteristics of the participants were as follows: age: 16–23 years, gender distribution: 55 males and 84 females; weight distribution: 48 participants were normal weight, 16 overweight, and 75 obese.

PCR amplification showed a 310 bp amplicon and the RFLP electrophoresis of DRD2 Taq1A genotype on agarose 3% can be seen in Figure 1.

In Figure 1, it can be seen that after the digestion with Taq1A restriction enzyme, homozygous CC showed up at bands indicating 180 bp and 130 bp; heterozygous CT showed bands at 310 bp, 180 bp, and 130 bp; and homozygous TT showed bands at 310bp. Results showed 30 subjects with variant Taq1A CC (22%), 78 subjects with the variant Taq1A CT (56%), and 31 subjects with variant TT (22%).

The consistency of genotype frequencies was tested with Hardy–Weinberg equilibrium (HWE). HWE analysis of this population can be seen in Table 1. In Table 1, based on an analysis using HWE calculator in normal weight, overweight, and obese group of students, it was seen that the total HWE frequencies were 100%. In normal-weight subjects, C allele frequency is found highest compared to T allele (63% vs. 37%), but in overweight and obese subjects T allele is found highest compared to C allele (66% vs. 34% and 57% vs. 43%). The results of HWE analysis and chi-square test show that there are no significant relationships in Taq1A DRD2 gene frequency between normal-weight, overweight, and obese students, yielding significance at \(p > 0.05\); this means this study does not deviate from the HWE law.
Table 1  Genotype and allelic frequency of DRD2 Taq1A polymorphism in normal-weight, overweight, and obese students in HWE calculations

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>CC</th>
<th>CT</th>
<th>TT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight</td>
<td>Observed</td>
<td>19</td>
<td>23</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Expected</td>
<td>18.75</td>
<td>22.50</td>
<td>6.75</td>
</tr>
<tr>
<td></td>
<td>H-W frequency</td>
<td>(39.06%)</td>
<td>(46.88%)</td>
<td>(14.06%)</td>
</tr>
<tr>
<td></td>
<td>Allele frequencies</td>
<td>C = 61 (63%)</td>
<td>T = 35 (37%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Observed</td>
<td>1</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Overweight</td>
<td>Expected</td>
<td>1.89(11.81%)</td>
<td>7.22(45.12%)</td>
<td>6.89(43.07%)</td>
</tr>
<tr>
<td></td>
<td>H-W frequency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Allele frequencies</td>
<td>C = 12 (34%)</td>
<td>T = 20 (66%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Observed</td>
<td>10</td>
<td>45</td>
<td>20</td>
</tr>
<tr>
<td>Obese</td>
<td>Expected H-W frequencies</td>
<td>14.08(18.78%)</td>
<td>36.83(49.11%)</td>
<td>24.08(32.11%)</td>
</tr>
<tr>
<td></td>
<td>Allele frequencies</td>
<td>C = 65 (43%)</td>
<td>T = 85 (57%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2  Relationship between research variables and students’ body weight

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Overweight</th>
<th>Obese</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calorie</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>30</td>
<td>7</td>
<td>50</td>
<td>0.011</td>
</tr>
<tr>
<td>Adequate</td>
<td>7</td>
<td>7</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>11</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>10</td>
<td>5</td>
<td>18</td>
<td>0.032</td>
</tr>
<tr>
<td>Moderate</td>
<td>16</td>
<td>3</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>22</td>
<td>8</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>DRD2 Taq1A polymorphism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>19</td>
<td>1</td>
<td>10</td>
<td>0.004</td>
</tr>
<tr>
<td>CT</td>
<td>23</td>
<td>10</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td>6</td>
<td>5</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

Relationship between calorie intake, physical activity, and dopamine D2 receptor gene polymorphism in terms of students’ body weight are displayed in Table 2.

In Table 2, we evaluated whether calorie intake, physical activity, and DRD2 Taq1A polymorphism were associated with normal weight, overweight, and obesity. Based on chi-square test, it was found that there are significant relationships between calorie intake and physical activity in normal-weight, overweight, and obesity groups (p = 0.011 and p = 0.032).

DRD2 Taq1A polymorphisms in this study showed CC genotype (homozygous variant wild type) was found higher in normal-weight subjects compared to overweight and obese subjects, but CT genotype and TT genotype were found higher in obese subjects compared to normal-weight and overweight subjects.

There is a significant relationship in DRD2 Taq1A polymorphism between normal-weight, overweight, and obese groups (p < 0.05).

DISCUSSION

In this study three variants of DRD2 taq1A—30 subjects with Taq1A CC (22%), 78 subjects with Taq1A CT (56%), and 31 subjects with TT (22%)—were obtained. This study is in accordance with Yeh et al’s study11 that found three variants of DRD2 Taq1A gene, higher CT frequencies compared to TT, and CC genotypes in Asians students. Pinto et al’s.12 They have been found TT genotype frequencies more than CC and CT. DRD2 gene polymorphisms in population arises from the differences between genotypes and alleles according to the ethnicity. These effects could be occurred by the differences in race and diet.

Under law of HWE, DRD2 Taq1A in normal-weight, overweight, and obese subjects are in equilibrium, which means this study does not deviate from HWE law. This analysis is functioning as an evolutionary parameter in a population. If the gene frequency in a population is always constant from generations to generations, then the population will not evolve. This analysis is needed to confirm that no gene mutation took place in the population. HWE law does not apply in the imbalance in population. It can happen because there is a genotype that has inability in fertility and same viability; un-random mating, and massive migration in a population or mutation.13

This study found a significant relationship between calorie intake in normal-weight, overweight, and obese groups. According to National Health and Nutrition Examination Survey (NHANES), which surveyed 4381 Americans in 1971–2006, there was a relationship between calorie intake and the amount of calorie in which increased calorie intake is related to increased body weight.14
Humans need a certain amount of calories to have a healthy lifestyle. The nutrients obtained through food consumption must enable an individual to be fit and be sufficient for their well-being. Energy consumption from obtained nutrients is needed to preserve health, to support growth, and to do physical activity. Excess energy consumption and diminished energy expenditure or less energy utilized for physical activity in long term will potentially cause obesity because excess energy will be deposited in the body as fat.  

In this study, it was found that there is a relationship between physical activity in normal-weight, overweight, and obese subjects. Relationship between physical activity and body weight showed a contrary relationship. Decreased physical activity will increase body weight. This study's subjects are medical students of the University of North Sumatera, and most of their daily activity consists of sitting and studying in the classroom. Medical students in general do not spend time in sports activities and other recommended physical activities because they have a tight lecture schedule from morning to evening.

Previous studies showed that medical students are two times less active physically than students from other faculties. Another study of adolescents in America showed that low physical activity has a relationship with obesity. According to Jayamani et al., women who engage in only moderate physical activity have a 3.87 times higher risk of becoming obese than women who engage in high physical activity. Women who engage in high physical activity are found to be underweight, whereas women who engage in low or moderate physical activity are at an increased risk of becoming overweight or obese.

Physical activity is body movement requiring contraction of skeletal muscles that increases energy expenditure. Physical activity can be done at work place, house, and physical inactivity is associated with other sedentary times, even traveling. Physical inactivity means no significant energy expenditure took place. When people are sedentary the energy expended is less than 1.5 kcal/kg/day. Physical inactivity signifies that body movement is minimal and can also be referred to as sedentary behavior, which includes watching television, reading, using a computer, reading, and even talking with friends on the phone.

The Taq1A allele D2 dopamine gene receptor polymorphism in this study showed that it has a significant relationship with normal weight than with overweight and obesity. A previous study showed that there is a relationship between body weight and dopamine receptor availability in the caudate region of the brain. Another study showed that the evidence for lower striatal D2/D3 availability in obesity confirms the role of the striatal dopaminergic reward system in obesity. People with D2 dopamine receptor gene polymorphism present lower amounts of dopamine receptor. Disorder in the dopamine system causes addictive, impulsive, and compulsive behavior which causes someone not being able to make a good judgment in food consumption. This cause lots of fat deposition in the adipose tissue of obese individuals. Dopamine also has a greater role in the arrangement of movement control, which is associated with pleasure system in the brain, gives a feeling of pleasure, and provides source of motivation to proactively engage in certain activities. This theory links obesity and physical inactivity with Taq1A allele D2 dopamine receptor gene polymorphism.

The gene has a role in causing obesity depends on environment, food, and daily activity. Without the environment factor, people with genetic tendency to become obese may not actually become obese. It is often suggested that reduced D2R generates a reward deficiency (“Reward Deficiency Syndrome”) and altered appetitive motivation that induces compulsive eating and contributes to obesity. Although dopamine is known to regulate physical activity, the question still remains whether reduced D2R contributes to obesity through alterations in energy expenditure and physical activities. Research conducted by Beeler et al. on a D2R knockdown (KD) mouse line showed that contribution of altered D2R signaling to obesity lies in altered energy expenditure rather than in the induction of compulsive overeating.

**CONCLUSION**

This result indicates that calorie intake, physical activity, and DRD2 Taq1A gene polymorphism modulate overweight and obesity in students’ of the Faculty of Medicine of University of Sumatera, Utara, with equilibrium population from time to time in this population.

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**REFERENCES**


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