UNIVERSITI PUTRA MALAYSIA

INTERRELATIONS OF PLEASURE DEFICIENCY, DOPAMINE HIGH SECRETION AND OVERCONSUMPTION OF SACCHARIN ON SPRAGUE DAWLEY RATS

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By

TOUMI ZAKARIA

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science

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Emotional eating is an overeating, for compensating emotional deficiency or for relieving negative emotions that is activated by dopamine. Dopamine neurons are known for their strong responses to rewards like foods and their critical role in positive motivation. Emotional hunger elicits overeating. However, a link between emotional deficiency, dopamine activation, and overeating has not been established yet. The goal of this research is to identify the relation between the previous parameters by focusing on pleasure deficiency as a type of emotional deficiency, beta-endorphin as a pleasure neurotransmitter, and overconsumption of saccharin as an eating disorder. ELISA method was used for dopamine measurements during hunger, fullness, before tasting saccharin, and after tasting saccharin in rats' striatum homogenate, while it was used for Beta-endorphin before and after tasting liquid saccharin in rats' striatum homogenate, to assess their contributions in this type of emotional eating. Results showed that less dopamine is released in full rats and less beta-endorphin is released before liquid saccharin tasting and vice versa. It is proposed that dopamine is involved in the motivation of food intake, while beta-endorphin is involved in pleasure emotion of saccharin intake. Subsequently, full rats were injected subcutaneously with dopamine agonist (quinpirole) and antagonist (raclopride). Quinpirole increased liquid saccharin intake while raclopride decreased it. Food preference was observed in rats during food deprivation and satiety by using two choices of food, Mazuri high fat diet that contains fats without sweet taste represents the caloric part, and liquid saccharin as non-nutritive sweetener that contains sweet taste without any calories represents the pleasure part. Here, two different choices of food with opposite properties were used to compare between caloric and pleasure needs. All hungry rats chose Mazuri high-fat diet to compensate their caloric needs, while all full rats chose liquid saccharin to compensate their pleasure needs. These results suggest that pleasure deficiency stimulates striatum dopamine secretion, that leads to overconsumption of saccharin even though rats are full, to compensate the deficiency.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

SALING KAITAN DI ANTARA KEKURANGAN KESERONOKAN, REMBESAN TINGGI DOPAMIN DAN PENGAMBILAN BERLEBIHAN SAKARIN BAGI TIKUS SPRAGUE DAWLEY

Oleh

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Pengerusi : Profesor Madya Dr Mohamad Aris bin Mohd Moklas, PhD
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Emosi pemakanan ditakrifkan sebagai suatu pengambilan makanan yang berlebihan, bertujuan untuk pengimbangan emosi ataupun kelegaan terhadap emosi yang negatif. Pengambilan makanan yang berlebihan ini adalah disebabkan berlakunya pengaktifan dopamin dan ianya mempunyai suatu tindak balas yang kuat terhadap sesuatu yang bersifat pemperolehan (ganjaran) seperti makanan. Selain itu juga, neuron dopamin turut memainkan peranan yang penting dalam mewujudkan aspek motivasi yang positif. Emosi kelaparan merupakan pemangkin kepada pengambilan makanan yang berlebihan. Walau bagaimanapun, hubungan antara kekurangan emosi, pengaktifan reseptor dopamin dan pengambilan makanan yag berlebihan masih belum dapat dihubungkan secara langsung. Oleh itu, antara objektif utama dalam kajian ini ialah untuk mengenalpasti hubungan antara parameter-parameter tersebut. Untuk tujuan itu, aspek kekurangan keinginan digunakan sebagai suatu bentuk kekurangan emosi iaitu dalam "mekanisma yang sama". Kaedah ELISA digunakan dalam kajian ini bagi mengukur tahap dopamin dan beta-endorphin pada homogenat striatum (pusat ganjaran) pada tikus apabila dalam keadaan lapar dan kenyang (bagi pengukuran dopamin), sebelum dan selepas pengujian sakarin (bagi pengukuran beta-endorphin). Keputusan menunjukkan bahawa, kadar dopamin yang dikeluarkan oleh tikus yang dalam keadaan kenyang adalah kurang, manakala, kadar beta-endorfin yang dikeluarkan adalah rendah sebelum ujian sakarin. Hubungan terbalik yang sama dapat dilihat pada tikus yang lapar. Penggunaan suntikan subkutaneus bagi dopamin agonis (quinpirole) dan antagonis (raclopride) digunakan terhadap tikus yang kenyang bagi mendapatkan hasil keputusannya. Pemerhatian yang dibuat mendapati bahawa quinpirole meningkatkan pengambilan cecair sakarin manakala raclopride mengurangkat pengambilan cecair sakarin. Selain itu, pemerhatian terhadap keutamaanmakanan turut dibuat terhadap tikus semasa dalam keadaan kekurangan makanan dan kekenyangan dengan menggunakan dua pilihan makanan iaitu, diet Mazuri berlemak tinggi bagi mewakili bahagian kalori dan "sakarin" pemanis tanpa kalori mewakili bahagian aspek seronok bagi menentukan samada, kekurangan keseronokan adalah

sebab yang utama akan mengambil sakarin secara berlebihan. Hasil kajian mendapati semua tikus yang lapar memilih "Diet lemak Mazuri tinggi" dan semua tikus yang dalam keadaan kenyang memilih sakarin. ini menunjukkan bahawa, keutamaan makanan ini dikira pada keperluan kalori dan emosi. Keputusan kajian menunjukkan bahawa kekurangan keseronokan merangsang rembesan dopamin di striatum yang membawa kepada pengambilan berlebihan sakarin, walaupun tikus dalam keadaankekenyangan. Ia merupakan suatu tingkah laku maladaptif untuk keseimbangan emosi.

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LIST OF ABBREVIATIONS

DA	Dopamine
SD	Sprague Dawley
Q	Quinpirole
R	Raclopride
BCR	Brain stimulating reward
PET	Positron emission tomography
NAc	Nucleus Accumbens
6-OHDA	Hydroxydopamine
UPM	University Putra Malaysia
AUP	Acceptable Use Policy

CHAPTER 1

INTRODUCTION

The reward system is a group of neuronal substances that are stimulated, through sensory organs such as ears, eyes, and tongue, by rewarding or reinforcing stimuli suchas food, sex, and alcohol. It drives our behaviour towards pleasurable stimuli or away from painful ones like homework that require more energy or effort (Arias, 2010). It modulates and process emotions to start or stop action. This system is in charge of craving or motivation for a reward, learning, and pleasure. It consists of a group of brain structures at the core of the brain, they weigh up whether or not to repeat a behaviour and form a habit (Berridge, 2013).

The reward system is composed of three subsystems involving learning, emotional and motivational processing (Robinson, 2013). Respectively, these components are responsible for reward learning, liking through endogenous opioid system and wanting through dopaminergic system (Berridge , 2009). Each component has its own pathways, when this system exposed to a rewarding stimulus through sensory organs, the brain responds by increasing release of the neurotransmitter dopamine along the major dopamine pathways.

Dopamine is an organic chemical that refers to catecholamine families. It is an amine synthesized by its precursor chemical L-DOPA, which is synthesized in the brain and kidneys. Dopamine functions as a neurotransmitter, a chemical released by neurons to send signals to other neurons. The dopaminergic system located in the brain plays an important role in the motivational component of reward-motivated behaviour. The expectation of rewards stimulate dopamine secretion in the brain, also drugs of abuse increase dopamine release or block its reuptake into neurons following release. Other brain dopamine pathways are involved in motor control and in controlling the release of various hormones (Schultz, 2015). The current opinion in pharmacology is that dopamine gives motivational salience, which means it drives us to rewards that we need for survival like food and sex. For instance, people with Parkinson's Disease do not process enough dopamine (Meder, 2019). This shows up as jerky movements. Repeated spurts of dopamine strengthen neural pathways to make us want to repeat a behaviour. It is a key factor in how we learn anything, that's why it is very carefully balanced in the brain. Dopamine released prior to an action is related to its pleasure properties. Drugs activate the reward system and make high levels of opioids and dopamine. A user is always chasing the experience and memory of the first pleasurablescene (Volkow, 2007). The primary source of dopamine is the ventral tegmental area (VTA). It then goes to the nucleus accumbens (NAc), an area found in the striatum thatis related to reward and motivation (Robbins, 1992).

Striatum is a region of the brain that produces feelings of reward or pleasure. It coordinates multiple aspects of thinking like movement reinforcement, motivation, reward perception, and action planning. It's where the brain weighs up the value of a stimulus in a nanosecond, sending go for it or stay away signals (Robbins, 1992); also considered as the main responsible for addictive behaviours. Feelings of pleasure comes from opioids secretion in the brain like beta-endorphin. These opioids formed innucleus accumbens, orbitofrontal cortex, parabrachial cortex, and ventral palladium.

Survival, on the other side, means maximizing links with helpful stimuli and minimizing links with painful ones, and reward awareness serves to increase the chance of survival by causing learning and inducing seeking and consummatory behaviour. Rewards are crucial objects for life, they drive people to eat and to meet for survival (Schultz, 2015).

Primary homeostatic rewards are liquids and foods that contain survival elements, the important activities to produce offspring, to mate, and care about them. They are attractive to all animals and humans (du Hoffmann, 2016). Non-primary rewards including all other rewards that increase the function of primary rewards in order to increase the chance for survival. They can be objects like money, specific ingredients like spices, or particular beauty like red foliage of Japanese trees for humans. It's right that we need sensory receptors to detect these rewards, but their pleasing or motivating properties require more investigations on the brain (Aharon, 2001). Particular beauty is based on physical geometric properties (Schultz, 2015). The monetary value is determined by the subjective value that follow the sensory processing and identification of asymmetry. Although we sense a great smell or taste, we appreciate them as pleasing and motivating based on our subjective valuation (Li, 2019). For Humans, Other social rewards include friendship, altruism, general social encounters, and social activities that promote group coherence, cooperation, and competition whichare mutually beneficial for group members and thus evolutionarily advantageous (Schultz, 2015). Nonphysical rewards, such as jokes and gambling novelty are attractive but intangible rewards. They don't have a homeostatic basis or nutrient value,but they may help to find new food sources. People with schizophrenia tend to have an overproduction of dopamine and this can lead to mental storms and extreme emotions like bingeing on food.

1.1 Problem statement

Overeating is excessive food consumption that leads to obesity. It considered as an eating disorder induced by multiple factors and one of them is emotional eating. Emotional eating considered as a form of disordered eating, expressed by an excess in food intake as a result of negative emotions as a maladaptive strategy (Spoor, 2007). Emotional eating would classified as a form of emotion-focused coping, which try to prevent, regulate, and minimize distress. Emotional eating can also occur when one is eating for social reasons such as family or friends. Stress can cause shame, guilt, or regret, on the other hand, negative feelings are not related with fulfilment of physical hunger with calories that body needs (Spoor, 2007). Emotional eating In some cases

can leads "mindless eating" when people are eating without knowing what or how much they are consuming (Eisenstein, 2015). Our aim is to prove that pleasure deficiency increases dopamine level as a positive reinforcement to get the missing pleasure emotion by overconsuming palatable foods such as saccharin, at satiety condition, as a maladaptive procedure to maintain pleasure homeostasis in SD rats.

1.2 Hypothesis

Our hypothesis is that pleasure hunger signals activate the striatum, and this activation will increase dopamine secretion to motivate liquid saccharin intake, even though at fullness condition, for compensating pleasure deficiency.

1.3 General objective

To prove that Hedonic hunger increases dopamine level that is responsible for positive reinforcement to get the missing pleasure by overconsuming saccharin.

1.4 Specific objectives

1. To determine the effects of dopamine agonist and antagonist administration on saccharin intake in Sprague Dawley rats
2. To determine the effects of hunger and satiety on dopamine level in the striatum of Sprague Dawley rats.
3. To determine the effects of saccharin intake on dopamine level in the striatum of Sprague Dawley rat.

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