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Effect of oral intake of L-carnitine and L-arginine supplements on Growth hormone and Dopamine level in Sportsmen pre- and post-exercise

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Abstract. The present study was conducted to study the effect of L-carnitine and L-arginine supplements on GH and Dopamine level pre- and pose-exercise in Sportsmen, the groups were divided in five groups (1st group control, 2nd group received L-carnitine 1000 mg daily for 14 days, 3rd group received L-arginine 1000 mg daily for 14 days, 4th group received L-carnitine 1000 mg every other day for 14 days, 5th group received L-arginine 1000 mg other day for 14 days). L-carnitine induced a high significant ($P<0.05$) increase in serum Growth hormone in pre- exercise and post and L-arginine induced a high significant ($P<0.01$) increase in serum Growth hormone in pre- exercise and post. For the Dopamine the L-carnitine a high significant ($P<0.01$) increase in serum pre-exercise and a high significant ($P<0.01$) decrease post-exercise , while in L-arginine a

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significant decrease ($p \leq 0.01$) of dopamine concentration in serum in pre- and post exercise.

L-carnitine and L-arginine determined to increase an improving and enhancement of male growth.

تأثير التناول الفمي للمكملان الغذائيان الكارنتين والارجنين على مستوى هرمون النمو والموصل العصبي دوبامين للرياضيين قبل وبعد التمرين

الدراسة الحالية تضمنت دراسة تأثير المكملان الغذائيان الكارنتين والارجنين على مستوى هرمون النمو والدوبامين قبل وبعد التمرين في الرياضيين ، تم تقسيم المجاميع الى خمسة مجاميع (المجموعة الاولى : مجموعة السيطرة ، المجموعة الثانية : استلمو الكارنتين 1000 ملغم يوميا لمدة 14 يوم ، المجموعة الثالثة : استلمو الارجنين 1000 ملغم يوميا لمدة 14 يوم ، المجموعة الثالثة : استلمو الكارنتين 1000 ملغم كل يومين لمدة 14 يوم و المجموعة الرابعة : استلمو الارجنين 1000 ملغم كل يومين لمدة 14 يوم). الكارنتين ادى الى تحفيز عالي المعنوية ($p<0.05$) في مصل هرمون النمو قبل وبعد التمرين والارجنين ادى الى تحفيز عالي المعنوية ($p<0.01$) في مصل هرمون النمو قبل وبعد التمرين . بينما في الدوبامين ادى الكارنتين الى تحفيز عالي ($p<0.01$) المعنوية قبل التمرين و انخفاض عالي المعنوية ($p<0.01$) بعد التمرين ، و ادى الارجنين الى انخفاض عالي المعنوية ($p<0.01$) قبل وبعد التمرين وعليه يؤدي الكارنتين الارجنين الى تحسين نمو الرياضيين

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Introduction:

L-Carnitine is synthesized from the essential amino acids (lysine and methionine) with the assistance of vitamin C and other secondary compounds produced in the body (Harpaz, 2005). L-Carnitine is needed for transmission of medium- and long-chain fatty acids from the cytosol into the mitochondria for energy production (Harpaz, 2005, Ozório *et al.*, 2002). As a result, this compound stimulates the rate of fatty acid oxidation, metabolic flux in the tricarboxylic acid (TCA) cycle, protein synthesis via gluconeogenesis. L-arginine plays an important role in multiple physiological phenomena, including the production of nitric oxide, creatine, ammonia, urea, protein and growth hormone (GH) release (Schaefer, 2002). In healthy adults with adequate protein intake, endogenous synthesis insufficient to meet physiological needs (Visek, 1986). However, the metabolic demand for L-arginine may exceed the body's ability to synthesize L-arginine under the conditions of intensive exercise or other severe stress; therefore, L-arginine is considered a semiessential or conditional amino acid. (Appleton, 2002: May *et al*, 2002: Wilmore, 2004), and strategies with L-arginine supplementation

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have been documented to provide functional benefits in such cases (Wilmore, 2004: Lind, 2004). L-arginine stimulates the release of growth hormone (Colloer *et al*, 2005) as well as the release of pancreatic insulin, glucagon, pituitary prolactin (Boger *et al*, 2001) and an improving and enhancement of male fertility.

Growth Hormone (GH) is secreted and regulated in a complex pattern by two hypothalamic peptides; a stimulating hormone, GH releasing hormone (GHRH), and an inhibiting hormone, somatostatin (Winer *et al.,* 1990). Growth-hormone secretagogues (GHSs) are small 36 synthetic molecules that stimulate the release of GH through a G-protein-coupled receptor in the pituitary. (Kamegai, *et al*., 2004). GH secretion is influenced by several normal and pathophysiological conditions, such as gender, age, physical exercise, nutritional state and other metabolic factors. The most powerful external physical stimuli are exercise and sleep (Catherine , 2012).

The acute relationship of GH to aerobic exercise is well characterized. The relationship of growth hormone to aerobic exercise time is direct and positive; the rate of GH release increases at or close to the onset of aerobic exercise and peaks at or close to its cessation (Kramer *et al.,* 2010).

The catecholamine dopamine is a part of the monoamine neurotransmitter family and can be re-uptake by specific transporters from the synaptic spaces back into cytosol and activated by mechanism mediated through G protein-coupled receptors (GPCRs) (Lin & Kuo, 2013). The physiological actions of dopamine are mediated by at least five distinct G protein coupled receptor subtypes. These receptors classified into two classes, the D1-like receptor subtypes (D1 and D5) which couple to the G protein and activate adenylyl cyclase, the D2-like receptor subfamily that inhibit adenylyl cyclase and activate K+ channels (Ebadi & Pfeifferm, 2005; Shiner, 2011).

The aim of this study termination of Growth hormone and dopamine in sportsmen.

MATERIALS AND METHODS

Subjects

Seventy five healthy students were as a volunteers from Tikrit University, College of Physical Education and Sports Science (mean age 20.8±1.85 yr) . Subjects were asked to maintain their normal physical training throughout the duration of the study to ensure completion of the exercise challenge without induction of severe muscle damage. Subjects were randomly assigned by simple drawing to five groups, each group contains 15 subjects and received two different types of supplement in two different doses for two weeks : control group, received L-carnitine group 1000 mg daily, received L-arginine 1000 mg daily, received L-carnitine group 1000 mg every other day and received L-arginine group 1000 mg every other day.

L-carnitine :

This amino acid manufactured by AMERICAN NATURES'S BOUNTY, INC. COMPANY . Each tray contains 30 tablets and its concentration is 500 mg which used in two doses (one tablet, twice daily for 14 day) & (one tablet, twice daily for every other day for two weeks).

L-arginine:

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This amino acid manufactured by AMERICAN NATURES'S BOUNTY, Amazing AN Nutrition COMOANY. Each tray contains 120 tables its concentration is 500 mg which used in two doses (one tablet, twice daily for 14 day) & (one tablet, twice daily for every other day for two weeks).

experimental design:

The experimental protocol required that each subject of these second and third groups were take a blood sample before exercise and given tables of L-carnitine or L-arginine and take another blood sample after exercise and then giving 28 tablet of L-carnitine or L-arginine (one tablet, twice daily) for 14 days and then take a blood sample before and after exercise and after 14 day of leaving L-carnitine or L-arginine another blood sample were taken from the subject before and after exercise. While the forth and the fifth groups of the subject were take a blood sample before exercise and given tablets of L-carnitine or L-arginine and take another blood sample after exercise and then giving 28 table of L-carnititne or L-arginine (one tablet, twice daily for every other day) for 14 days and then take a blood sample before and after exercise and after 14 day of leaving L-carnititne or L-arginine another blood sample were taken from the subject before and after exercise.

Blood collection :

To every subject in this study were taken six sample of blood in period of 4 week 5 ml of blood were taken from each subject before and after the exercise, and the blood were put in test tubes without anticoagulant, then it lets in room temperature for period (15) minutes, after this centrifuged for (10) minutes at 3000 rpm, then separate the serum and kept temporarily in (-20) °C in clean plane tubes so that using later for determination of GH and concentration.

Hormone assay

Serum GH and Dopamine concentration was determined by kits of American Monobind company, depending on Enzyme Linked Immunosorbant Assay (ELISA) techinque (Tietz, 1995).

Result

Results showed in figure (1) showed a significant increase ($p \leq 0.05$) of Growth hormone concentration in serum of sportsmen groups that received L-carnitine (daily/every two days) in comparison with control group.

It also found a high significant increase ($p \leq 0.01$) of GH concentration in serum of sportsmen group that received L-arginine (daily/every two days) in comparison with control group.

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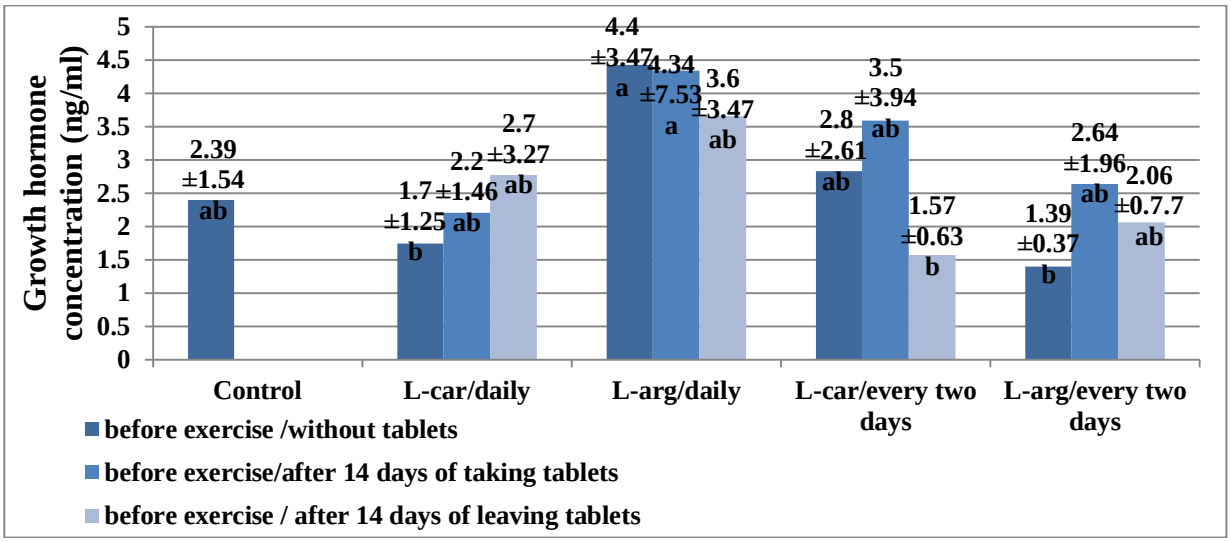

Figure(1): Effect of receiving L-carnitine (daily / every two days) and L-arginine (daily / every two days) on Growth hormone concentration in sportsmen for 14 days before exercise.

The results showed in figure (2) showed a significant increase ($p \leq 0.05$) of Growth hormone concentration in serum of sportsmen groups that received L-carnitine (daily/every two days) in comparison with control group.

It is also found a high significant increase ($p \leq 0.01$) of GH concentration in serum of sportsmen group that received L-arginine (daily/every two days) in comparison with control group.

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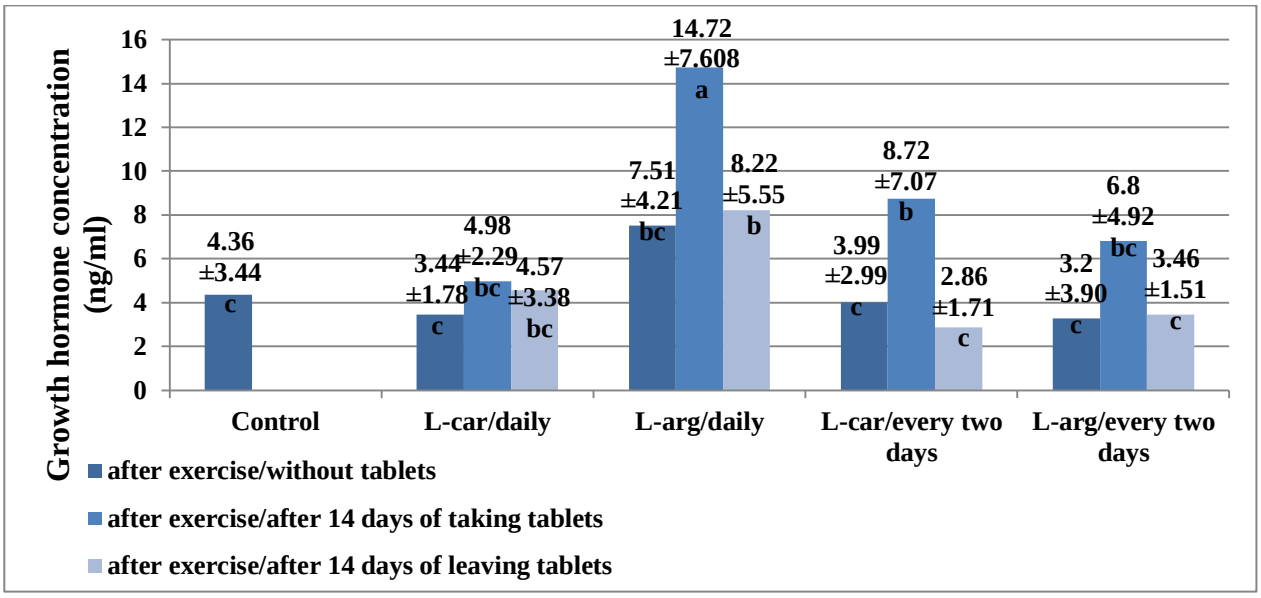

Figure(2): Effect of receiving L-carnitine (daily / every two days) and L-arginine (daily / every two days) on Growth hormone concentration in sportsmen for 14 days after exercise.

The results in figure (3) showed a high significant increase ($p \leq 0.01$) of dopamine concentration in serum of sportsmen group that received L-carnitine daily in comparison with control group, and there was a high significant decrease of dopamine concentration in serum of sportsmen group that received L-carnitine (every two days) in comparison with control group.

It is also found that there was a high significant increase ($p \leq 0.01$) of dopamine concentration in serum of sportsmen group that received L-argininie daily in comparison with control group, and there was a high significant decrease of dopamine concentration in serum of sportsmen group that receiving L-arginine every two days in comparison with control group.

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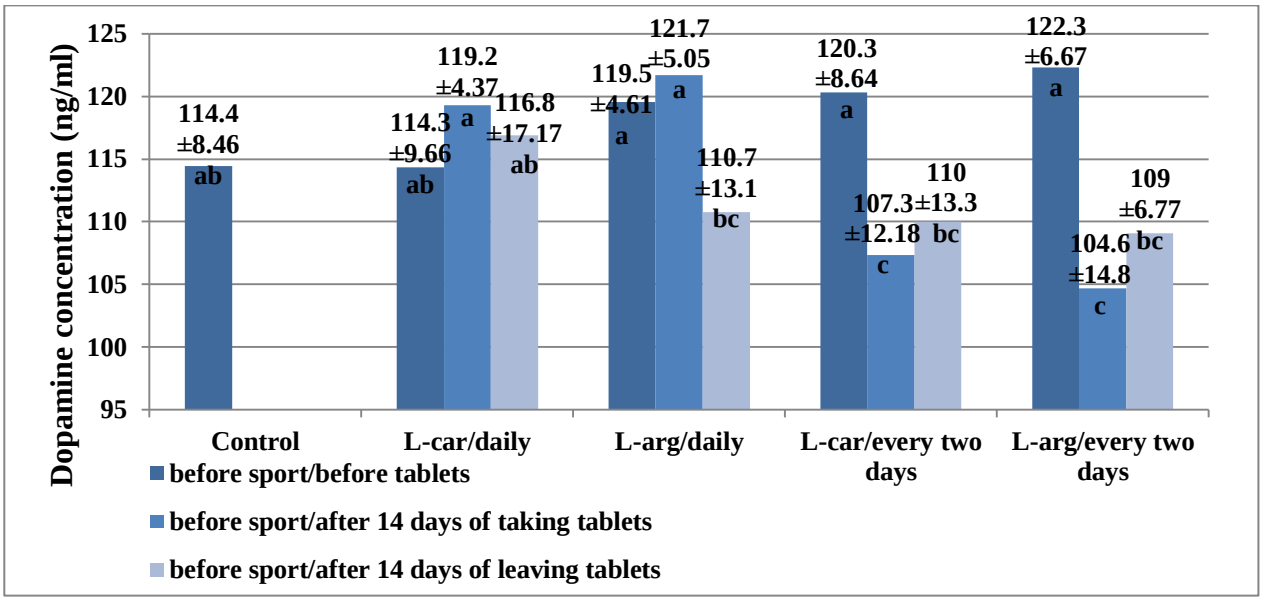

Figure(3): Effect of receiving L-carnitine (daily / every two days) and L-arginine (daily / every two days) on Dopamine concentration in sportsmen for 14 days before exercise.

The results in figure (4) showed a high significant increase ($p \leq 0.01$) of dopamine concentration in serum of sportsmen group that received L-carnitine daily in comparison with control group, and there was a high significant decrease of dopamine concentration in serum of sportsmen group that received L-carnitine every two days in comparison with control group.

It is also found that there was a significant decrease ($p \leq 0.01$) of dopamine concentration in serum of sportsmen group that received L-argininie (daily / every two days) in comparison with control group.

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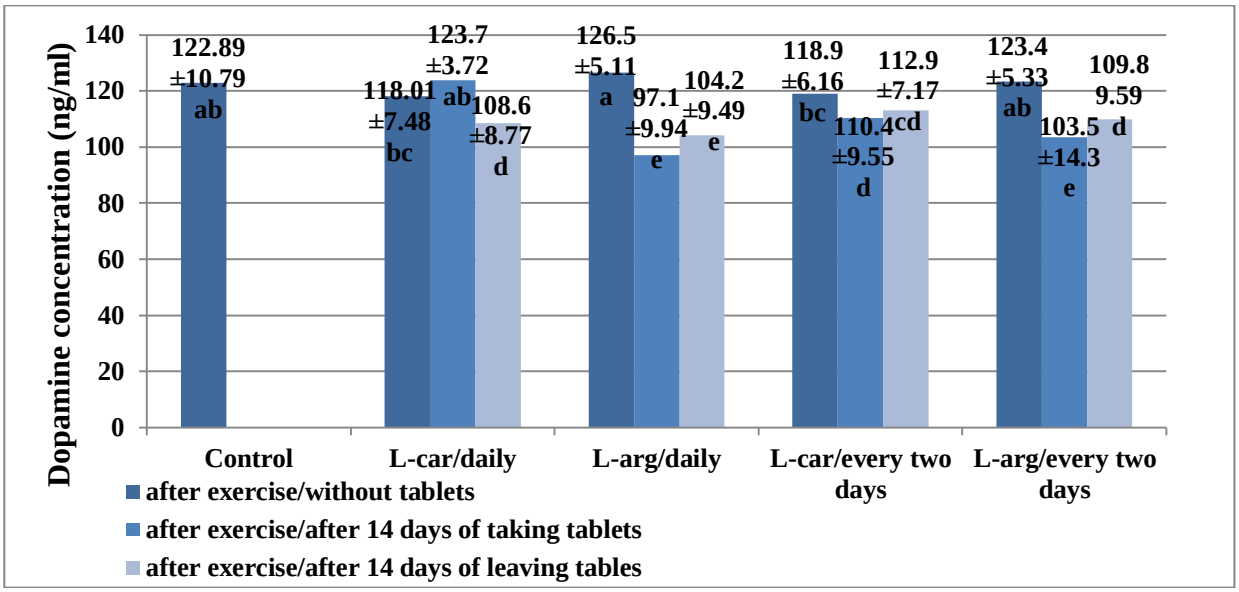

Figure(4): Effect of receiving L-carnitine (daily / every two days) and L-arginine (daily / every two days) on Dopamine concentration in sportsmen for 14 days after exercise.

Discussion

The increase in L-carnitine 1000 mg (daily/every other day) pre-exercise as shown in figure (1) can be explained either by the direct effect of L-carnitine on GH or by its indirect relation to IGF-1.

Directly, L- carnitine supplementation increase the level of GH in patients have a deficiency in GH (El-Beshlawy., et al.,2010).

Indirectly, Carnitine has a modulating effect on the function of acetylcholine excitatory neurotransmitter, glutamate excitatory amino acid, insulin growth factor-1 (IGF-1) and NO (Khalil et al., 2013), and high-dose L-carnitine may promote liver regeneration by increasing IGF-1 (Pehlivan et al .,2009).

Certain metabolic functions including lipolysis are mediated directly by GH, many of the observed effects of GH are the result of IGF-I generation, at higher levels of GH secretion IGF-I generation is maximally stimulated with no further increase in circulating IGF-I (Parkinson et al.,2001).

L-arginine observed facilitates muscle growth (by inhibiting muscle loss) and is required for the transport of the nitrogen used in muscle metabolism (Barbul, 1986), few studies explain how L-arginine lead to muscle growth, the present study is supposing this may be due to increase production of GH. In addition, L-arginine may be led to increase the release of GH (Chromiak & Antonio, 2002; Kanaley, 2008).

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Exercise is a potent stimulus to GH release and there is some evidence that the acute increase in GH is important in regulating substrate metabolism post-exercise. (Widdowson et al.,2009).

During more intensive exercise (with accumulation of lactate at 70% Maximum oxygen consumption (VO2 max) for a short term period such as 10–20 minutes) GH will increase by 5–10-fold. With short exercise durations, levels of GH will generally peak at 15– 30 minutes after the exercise (Saugy et al ., 2006). Furthermore, it appears that GH response is more closely related to the peak intensity of exercise than the total work output. Endurance training generally amplifies the pulsatile release GH, elevating the GH amplitude. (Jessica et al ., 2012).

In the post-exercise (figure 2) the increase in GH was found immediately after exercise ,as mention above either by direct effect of L-carnitine on GH level and the indirect effect through IGF-1 .

The GH/ IGF-I exerts short-and long-term metabolic effects that are potentially important during exercise (Widdowson et al.,2009).

It is well documented that the infusion of arginine stimulated GH secretion from the anterior pituitary (Hembree and Ross, 1969). This increase in GH secretion from arginine infusion has been attributed to the suppression of endogenous somatostatin secretion (Alba-Roth et al, 1988). Colombani et al,(1999) has found that supplemented marathon runners with arginine for 14 days before a marathon run. On the day of the marathon, blood samples were taken shortly before the run, at the end of the run, and after a recovery period of two hours, found that growth hormone concentrations were elevated during a marathon run to a greater degree than exercise would elicit alone (Colombani et al,1999). Also highlighted several factors that appeared to modify the growth hormone response to amino acid administration (Chromiak and Antonio,2002). These include training status, age, sex, diet, and time since last meal. Also, the growth hormone response to amino acid ingestion may be reduced in exercise-trained individuals (Campbell et al,2004).

In the per-exercise (figure 3) the dopamine level was found to be near normal after the supplementation of L-carnitine because L-carnitine is able to enhance the glutathione level due to its energy-promoting property (Rani and Panneerselvam ,2001).

A study showed that animals treated for seven days with L-carnitine had levels of extraneuronal dopamine in the nucleus accumbens shell (NAcS) significantly higher than the control group, and the accumulation of the monoamine after uptake inhibition in this area exceeded that of control rats. (Tolu et al., 2002).

L-carnitine has long been reported to affect the dopaminergic and GABAergic systems, but the mechanisms involved were mostly unknown. (Summaville et al., 2011).

L-arginine is the precursor of NO, stereospecifically increased the release of Dopamine and its major metabolites (Lorrain and Hull, 1993). Also, another study [Lechin, et al., 2006], has found that increase dopamine concentration in healthy subjects.

L-Arginine has been shown to induce dopamine release from the striatum and increase the extracellular levels of dopamine in the medial preoptic area in vivo (Lorrain & Hull, 1993;Strasser et al., 1994).

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L-arginine stimulate NO production which may also inhibit the dopamine transporter (Lonart and Zigmond, 1991; Pogun et al., 1994; Chaparro-Huerta et al., 1997; Kiss and Vizi, 2001), thereby prolonging dopamine's presence in extracellular fluid. In addition, NO may increase extracellular dopamine indirectly by increasing the release of glutamate or via other neurotransmitter systems (Prast and Philippu, 2001; West et al., 2002). The decrease in dopamine concentration may due to partially masked by citalopram. In accordance with the effects of NOS inhibitors, perfusion with the endogenous NO-precursor, L-arginine, decreased the extracellular level of Dopamine. This probably represents the true effect of facilitated NO synthesis as L-arginine has been shown to increase NOS activity in the hippocampus (Vallebuona & Raiteri, 1994).

In the post-exercise (figure 4) the control group was found that dopamine content and release is increased during physical activity (Foley amd Fleshner, 2008).

Interestingly, the increase in dopamine during exercise is dependent on the speed and postural direction (Hattori et al. 1994), yet it is independent of training status (trained versus untrained)(Lim et al. 2001) mode of exercise (swim versus treadmill versus wheel run)(Hoffmann et al. 1994) , or gender of the human (male versus female) (Bailey et al. 1992).

The increasing of release of dopamine and decreasing the catabolism of dopamine as long as the exercise persist (Bailey et al. 1993), so increase of dopamine in L-carnitine received group after exercise was in addition to physical activity , L-carnitine act by enchancing glutatione level which reduce uptake and metabolism of Dopamine leading to an in increase in circulating dopamine and thereby delaying muscle to fatigue and enhance physical performance (Packiasamy et al., 2003).

while for the decrease in L-arginine, this may be due to the L-arginine effect on dopamine concentration, this probably represents the true effect of facilitated NO synthesis as L-arginine has been shown to increase NOS activity in the hippocampus (Vallebuona & Raiteri, 1994).

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