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Review

Behavioral and cognitive effects of tyrosine intake in healthy human adults

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ABSTRACT

The amino acid tyrosine is the precursor to the catecholamine neurotransmitters dopamine and norepinephrine. Increasing tyrosine uptake may positively influence catecholamine-related psychological functioning. We conducted a systematic review to examine the effects of tyrosine on behavior and cognition. Fifteen studies were reviewed. All studies except one involved tyrosine loading during a single test session. In most behavioral studies, there were no significant effects of tyrosine on exercise performance. In contrast, cognitive studies employing neuropsychological measures found that tyrosine loading acutely counteracts decrements in working memory and information processing that are induced by demanding situational conditions such as extreme weather or cognitive load. The buffering effects of tyrosine on cognition may be explained by tyrosine's ability to neutralize depleted brain catecholamine levels. There is evidence that tyrosine may benefit healthy individuals exposed to demanding situational conditions. For future research we recommend moving from studying the acute effects of a single tyrosine load in small samples to studying the behavioral and cognitive effects of tyrosine in larger groups over multiple weeks.

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1. Introduction

In recent years, nutrition science has been gaining influence on hobby athletes and people concerned with an effective diet, as they have increasingly focused on nutritional factors to augment their personal performance and well-being. This has led the dietary supplement industry to grow, and offer various products designed to improve physical and mental performance (Bucci and Unlu, 2000). For example, interest in protein mixtures has increased, particularly thanks to the ability of whey protein to support gains in lean muscle mass after exercise (Volek et al., 2013). These muscular gains can improve performance in sports, and in occupations that demand strength.

Supplement producers have also been marketing products that contain specific amino acids, either added to whey protein mixtures or in isolation (Bucci and Unlu, 2000). Amino acids are the building blocks

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of proteins. Some amino acids also act as neurotransmitter precursors, meaning that certain neurotransmitters are directly or indirectly synthesized from specific amino acids (Young, 1996). Altering the intake of these amino acids may influence the function of their respective neurotransmitters. At the blood–brain barrier, many amino acids compete for uptake into the brain. For these amino acids, the effect of a specific amino acid supplement on brain function may be more predictable than the effect of a supplement containing a mixture of different amino acids (Strüder et al., 1998). One relevant neurotransmitter precursor is the amino acid L-tyrosine (tyrosine from here onwards). A 1996 review on dietary neurotransmitter precursors reported beneficial effects of tyrosine on cognitive task performance, fatigue, and general alertness under various stressful conditions (Young, 1996). There were no consistent effects on mood, although some case reports and small studies suggested that tyrosine might potentiate the action of antidepressant drugs. The present review integrates all placebo-controlled studies on the effects of tyrosine intake on behavior and cognitive (i.e., neuropsychological) task performance, most of which were published after 1996.

Increased tyrosine intake has the potential to influence the catecholamine neurotransmitters dopamine and norepinephrine via its conversion into L-3,4-dihydroxyphenylalanine (L-DOPA), the direct precursor to dopamine, which in turn gets converted to norepinephrine (Fernstrom and Fernstrom, 2007). Tyrosine hydroxylase, the enzyme involved in the conversion from tyrosine to L-DOPA, is about 75% saturated with tyrosine under typical physiological conditions (Carlsson and Lindqvist, 1978). As the other enzymes involved in catecholamine synthesis have low saturation rates, there is a modest but significant potential to increase brain catecholamine synthesis by increasing local tyrosine levels. This brings the question whether increased tyrosine intake can have significant effects on human behavior and cognition.

The most commonly adopted hypothesis about stress-induced performance decrements holds that reduced brain catecholamine levels account for this phenomenon (O'Brien et al., 2007; Colzato et al., 2013). In line with this, tyrosine depletion experiments, in which participants consume an amino acid mixture devoid of tyrosine and its precursor, phenylalanine, suggest that acute reductions in brain catecholamine levels lead people to behave in a less motivated way (McLean et al., 2004; Roiser et al., 2005; Cawley et al., 2013) or develop cognitive impairments (Harmer et al., 2001). Moreover, reduced brain catecholamine levels seem to make mood more vulnerable to the negative effects of low light exposure (Cawley et al., 2013). Consequently, positive effects of increased tyrosine intake in demanding situations could be explained by the replenishment of brain catecholamines.

In short, selective increases in the intake of tyrosine may benefit those aspects of human behavior and cognition that are under the catecholaminergic control (Young, 1996). To test this idea further, we systematically reviewed tyrosine administration studies conducted in healthy human adults. Our main research question was which aspects of human behavior and cognition improve following increased tyrosine intake. Given the above, these would be expected to include alterations in behavioral and cognitive responses to physical and mental stressors. Beneficial effects of tyrosine could be relevant for a range of target populations, including sportsmen, university students, manual laborers, office workers, and patients with psychological problems.

2. Materials and methods

The search for and selection of relevant studies was conducted in the electronic databases MEDLINE and PsycINFO according to the PRISMA guidelines for systematic reviews (Liberati et al., 2009). We entered ("tyrosine" AND "load*" OR "supplement*") into the search field. To be selected by the first two authors (AH and SEJ), a study needed to be published in an academic journal and have used a placebo-controlled experimental design with healthy human adults that involved single or multiple dosing with tyrosine in one day (loading) or repeated dosing over multiple days (supplementation). Studies in which tyrosine was mixed with other compounds of experimental interest were excluded, because our objective was to examine the effects of increased tyrosine intake in isolation.

3. Results

The search, last conducted in November 2014, yielded 3059 results. The first two authors (AH and SEJ) then selected 72 studies that met the selection criteria based on the title. In the next step, they independently read the abstracts of these studies and considered whether they should remain included based on the information in the abstract. In the final step, they retrieved full-text versions of the 17 remaining studies and determined whether appropriate methods were used. One study was then excluded based on the full text because it had tested the effects of a mixture with various amino acids yet labeled it as a tyrosine intervention in title and abstract. Another study was excluded because it used a non-experimental design without adult participants.

Characteristics and main outcomes of the 15 reviewed studies are presented in Table 1. Ten studies involved a single tyrosine load, three studies involved two loads in one day, and one study involved two loads in the hour prior to testing and additional loads every 10 min during the 1.5-hour experiment (on average 8 loads). One study supplemented tyrosine daily for 3–4 months.

Dosages of tyrosine also varied across studies. Six studies involved fixed amounts of tyrosine, ranging from 2 to 20 g. The remaining nine studies used a dosage adjusted to the body weight of the participants, ranging from 25 to 150 mg/kg. Some studies administered tyrosine in solid form, namely in a nutrient bar (O'Brien et al., 2007; Mahoney et al., 2007; Kishore et al., 2013) or in apple sauce (Thomas et al., 1999; Sutton et al., 2005; Palinkas et al., 2007; Shurtleff et al., 1994). The remaining studies offered tyrosine in water (Strüder et al., 1998; Chinevere et al., 2002; Tumilty et al., 2011, 2014), orange juice (Colzato et al., 2013, in press), or a sugar-free fruit drink (Watson et al., 2012).

All seven studies in which plasma tyrosine levels were measured (Strüder et al., 1998; Sutton et al., 2005; Shurtleff et al., 1994; Chinevere et al., 2002; Tumilty et al., 2011, 2014; Watson et al., 2012) found these levels to be significantly elevated after tyrosine intake compared to placebo. All studies were placebo-controlled and conducted under double-blind conditions. In most studies, the food or drink in the placebo condition contained no protein. In one study, the placebo was an isocaloric whey protein drink, which means it contained some tyrosine, though less than the amount of tyrosine in the active condition (Tumilty et al., 2014). All studies except one (Palinkas et al., 2007) used a within-subjects design with a counterbalanced treatment order.

3.1. Behavioral effects

While one study found tyrosine to enhance endurance exercise performance (Tumilty et al., 2011), five studies found no significant differences between tyrosine and the placebo (Strüder et al., 1998; Sutton et al., 2005; Chinevere et al., 2002; Tumilty et al., 2014; Watson et al., 2012). All six studies involved physically trained young men in sample sizes ranging from 7 to 20 participants. Two studies operationalized endurance exercise performance as the time spent on a cycling time trial, three studies operationalized it as the time cycled until exhaustion, and one study operationalized it as the time spent on a treadmill until exhaustion. Three studies investigated endurance exercise performance in a warm environment and the other three used normal temperatures. The study in which participants performed better on tyrosine than on placebo was similar in methodology to the other five behavioral studies.