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Review

Effect of tyrosine supplementation on clinical and healthy populations under stress or cognitive demands—A review

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ABSTRACT

Consuming the amino-acid tyrosine (TYR), the precursor of dopamine (DA) and norepinephrine (NE), may counteract decrements in neurotransmitter function and cognitive performance. However, reports on the effectiveness of TYR supplementation vary considerably, with some studies finding beneficial effects, whereas others do not. Here we review the available cognitive/behavioral studies on TYR, to elucidate whether and when TYR supplementation can be beneficial for performance. The potential of using TYR supplementation to treat clinical disorders seems limited and its benefits are likely determined by the presence and extent of impaired neurotransmitter function and synthesis. Likewise, the potential of TYR supplementation for enhancing physical exercise seems minimal as well, perhaps because the link between physical exercise and catecholamine function is mediated by many other factors. In contrast, TYR does seem to effectively enhance cognitive performance, particularly in short-term stressful and/or cognitively demanding situations. We conclude that TYR is an effective enhancer of cognition, but only when neurotransmitter function is intact and DA and/or NE is temporarily depleted.

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1. Introduction

The amino-acid L-Tyrosine (TYR) is the biochemical precursor of the catecholamines dopamine (DA) and norepinephrine (NE). Given the right circumstances TYR supplementation can enhance DA and NE levels in the brain (Cuche et al., 1985; Gibson and Wurtman, 1977; Tam et al., 1990) and this possibility has led numerous studies to investigate whether administration of TYR can positively influence cognitive or behavioral performance that relies on catecholamine function. Unfortunately, reports on the effectiveness of TYR supplementation have varied greatly, with some studies showing a marked positive effect, whereas others report no

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significant changes. Here we provide a summary review of the available cognitive and behavioral TYR studies and their main results, to gain a better understanding of the conditions under which TYR has a positive effect and whether TYR may be useful in a clinical context. Further, we hope to help inform future studies on how to best design and analyze experiments regarding TYR.

Before we review the behavioral and cognitive studies on TYR, we will first elaborate on the mechanism through which TYR presumably enhances brain physiology. As we will argue, the nature of this mechanism might play a crucial role in determining whether and to what extent supplementation can benefit performance. Plasma TYR levels peak between 1 and 2 h after consumption and can remain significantly elevated up to 8 h (Glaeser et al., 1979). Correspondingly, in rats it was shown prefrontal DA increased 1 h after TYR administration, but not earlier (Tam et al., 1990). Once it has passed the blood–brain barrier (BBB) and is taken up by the appropriate brain cells, TYR is converted into L-DOPA through an enzyme called tyrosine-hydroxylase (TH; Daubner et al., 2011). TH activity initially increases upon consumption of TYR, but it is regulated by end-product inhibition (Daubner et al., 2011; Tam et al., 1990), preventing large increases in catecholamine release. L-DOPA is converted into DA, resulting in an increase in DA level. In turn, DA can be converted into NE through the enzyme dopamine beta-hydroxylase (DBH; Kaufman and Friedman, 1965).

Importantly, TYR has been found to enhance neurotransmitter synthesis only in actively firing neurons (Fernstrom and Fernstrom, 2007; Lehnert et al., 1984; Tam et al., 1990). This suggests TYR can reverse a process called neurotransmitter depletion, in which increased brain activity leads to decreased DA and NE levels, with behavioral performance levels declining accordingly. This role as a depletion reverser is best illustrated by the following example. When exposed to stress or a cognitively challenging task, catecholamine neurons become more active and their synthesis rate increases (Kvetnansky et al., 2009; Lehnert et al., 1984; Mahoney et al., 2007). As more neurotransmitters are synthesized to meet the situational demands, the resource from which they are synthesized, namely TYR, is expended. Synthesis becomes limited once TYR runs low, leading to less neurotransmitter availability and corresponding decrements in performance (Goldman-Rakic et al., 2000; Muly et al., 1998). In this situation TYR might benefit brain function by providing the resources necessary to allow neurotransmitter synthesis to continue and maintain catecholamine levels needed to ensure optimal performance (Wurtman et al., 1981). On the contrary, one may assume when the rate of synthesis is not elevated then TYR supplementation amounts to providing unnecessary extra resources from which to synthesize DA and NE, which should not impact these neurotransmitters levels or their associated performance. Indeed, in rats it was shown that TYR administration only enhanced DA synthesis in the striatum when this region was pharmacologically activated (Tam et al., 1990). In other words, TYR supplementation seems to have a beneficial effect only in situations that stimulate neurotransmitter synthesis, i.e., situations that are sufficiently stressful or challenging. Indeed, in the present review we will demonstrate that TYR's role as a depletion reverser fits well with the pattern of results found in the literature.

To date there is not yet a single, agreed upon effective dose for TYR supplementation and thus administered doses have varied

Table 1
Characteristics and main outcomes of the reviewed studies.

Authors	Sample	Dose of TYR	Findings
Banderet and Lieberman (1989)	Healthy, cold exposure ($N = 23$)	100 mg/kg	Reduced symptoms, improved mood, reaction times and vigilance
Chinevere et al. (2002)	Healthy, physically exerted ($N = 9$)	150 mg/kg	No effect of TYR
Colzato et al. (2013)	Healthy, cognition challenged ($N = 22$)	2.0 g	Improved working memory
Colzato et al. (2014a)	Healthy, cognition challenged ($N = 22$)	2.0 g	Improved inhibitory control
Colzato et al. (2014b)	Healthy, cognition challenged ($N = 32$)	2.0 g	Improved convergent thinking
Deutsch et al. (1994)	Schizophrenia patients ($N = 11$)	10.0 g	Increased saccadic intrusions, no effect on behavior or cognition
Deijen and Orbleke (1994)	Healthy, auditory stress ($N = 16$)	100 mg/kg	Improved working memory and Stroop performance
Deijen et al. (1999)	Healthy, intensive combat training ($N = 21$)	2.0 g	Improved memory and tracking performance
Eisenberg et al. (1988)	ADHD patients ($N = 7$)	100 mg/kg	No effect of TYR
Gelenberg et al. (1980)	Depressive patients ($N = 1$)	100 mg/kg	Self-rated improvement of depression
Gelenberg et al. (1990)	Depressive patients ($N = 65$)	100 mg/kg	No effect of TYR
Goldberg et al. (1980)	Depressive patients ($N = 2$)	100 mg/kg	Improvement of symptoms
Growdon et al. (1982)	Parkinson's patients ($N = 23$)	100 mg/kg	Increased levels of TYR and homovanillic acid.
Kishore et al. (2013)	Healthy, heat exposure ($N = 10$)	6.5 g	Reduced delay in event related potentials
Leathwood and Pollet (1983)	Healthy, no manipulation ($N = 60$)	500 mg	No effect of TYR on mood
Lemoine et al. (1989)	Parkinson's patients ($N = 10$)	1.6–4.0 g	Improvement of symptoms
Lieberman et al. (1983)	Healthy, no manipulation ($N = 16$)	100 mg/kg	No effect of TYR on mood
Magill et al. (2003)	Healthy, sleep deprivation ($N = 76$)	150 mg/kg	Improved working memory, reasoning and vigilance
Mahoney et al. (2007)	Healthy, cold exposure ($N = 19$)	150 mg/kg	Improved working memory
Nemzer et al. (1986)	ADHD patients ($N = 14$)	140 mg/kg	No effect of TYR
O'Brien et al. (2007)	Healthy, cold exposure ($N = 15$)	300 mg/kg	Improved working memory
Palinkas et al. (2007)	Healthy, in Antarctica ($N = 43, 42$)	12 g	Improved mood during winter
Pietz et al. (1995)	Phenylketonuria patients ($N = 24$)	100 mg/kg	No effect of TYR
Pollin et al. (1961)	Schizophrenia patients ($N = 12$)	285 mg/kg	No effect of TYR
Posner et al. (2009)	ADHD patients ($N = 1$)	100 mg/kg	Improvement of symptoms
Reimherr et al. (1987)	ADHD patients ($N = 12$)	50–150 mg/kg	Short term, unsustained clinical response
Shurtleff et al. (1994)	Healthy, cold exposure ($N = 8$)	150 mg/kg	Improved working memory
Smith et al. (1998)	Phenylketonuria patients ($N = 21$)	100 mg/kg	No effect of TYR
Steenbergen et al. (2015)	Healthy, cognition challenged ($N = 22$)	2.0 g	Improved cognitive flexibility
Sutton et al. (2005)	Healthy, physically exerted ($N = 20$)	150 mg/kg	No effect of TYR
Thomas et al. (1999)	Healthy, cognition challenged ($N = 20$)	150 mg/kg	Improved working memory
Tumilty et al. (2011)	Healthy, heat exposure ($N = 8$)	150 mg/kg	Increased endurance capacity
Tumilty et al. (2014)	Healthy, heat exposure ($N = 7$)	150 mg/kg	No effect of TYR
Watson et al. (2012)	Healthy, heat exposure ($N = 8$)	150 mg/kg	No effect of TYR
Wood et al. (1985)	ADHD patients ($N = 12$)	150 mg/kg	Short term, unsustained clinical response

Studies reviewed in the present article, listing author names, publication years, type and size of sample, as well as potential stressor, dose of L-Tyrosine and the study's main outcomes. TYR, L-Tyrosine.