Tyrosine supplementation mitigates working memory decrements during cold exposure ☆

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Abstract

In rats, dietary supplementation with the amino acid tyrosine (TYR) prevents depletion of central catecholamines observed during acute environmental stress. Concomitant changes in the animals' behavioral responses to stress suggest that TYR might have similar effects on central catecholamines and cognition in humans exposed to environmental stress. This study aimed to determine if severe cold exposure impairs human cognition and if dietary supplementation with TYR would ameliorate such deficits. Volunteers ($N=19$) completed three test sessions on different days (35 °C control/placebo, ~10 °C/placebo, ~10 °C/TYR) using a double-blind, within subjects design. During each session, volunteers completed two 90-minute water immersions and consumed a food bar (150 mg/kg TYR or placebo) before each immersion (total TYR 300 mg/kg). Cognitive performance, mood, and salivary cortisol were assessed. Cortisol was elevated in the cold ($p<.01$). Volunteers made fewer correct responses on a Match-to-Sample memory measure ($p<.05$) and reaction time (RT) and errors increased on a choice RT test ($p<.01$) in the cold. Self-reported tension ($p<.01$), depression ($p<.05$) and confusion ($p<.01$) also increased in the cold. When volunteers consumed TYR, correct responses increased on a Match-to-Sample memory measure ($p<.05$) and study time for the sample was shorter ($p<.05$), indicative of more rapid and accurate information processing. Finally, RT on the memory measure revealed a similar pattern across immersions for TYR and thermoneutral conditions, but not cold/placebo ($p<.05$). This study demonstrates cold exposure degrades cognitive performance and supplementation with TYR alleviates working memory decrements.
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1. Introduction

Environmental stress can impair performance and produce adverse changes in behavior and mood. Animals exposed to high or prolonged levels of environmental stressors, such as extreme cold, show significant impairment on performance tasks [1]. In humans, significant decrements have been observed on several types of cognitive measures following cold stress, including vigilance, reaction time, reasoning skills, and short-term memory [2–6].

Reported changes in performance associated with environmental stress may result from the depletion of catecholamine neurotransmitters in the central nervous system following acute cold exposure. Exposure to cold increases brain catecholamine activity, e.g., norepinephrine, in animals [7–10]. Since tyrosine is a substrate for catecholamine biosynthesis in the brain, under

cold conditions, tyrosine availability might be a limiting factor for optimal central nervous system function. Consequently, dietary tyrosine supplementation might reduce some of the adverse effects of stress and central nervous system activation.

Tyrosine, a large amino acid found in substantial quantities in many animal and plant protein foods, is the metabolic precursor for synthesis of the catecholamine neurotransmitters, dopamine and norepinephrine, in the central and peripheral nervous systems [11,12]. In rodents, administering tyrosine can increase catecholamine levels in the brain, under certain conditions. When catecholaminergic neurons are highly active, they release more neurotransmitter, causing tyrosine to be metabolized at an accelerated rate to sustain catecholamine synthesis. As the brain stores of tyrosine are depleted, the synthesis of catecholamines may become limited. Supplementing the diet with exogenous tyrosine may therefore be efficacious in restoring brain synthesis and release of catecholamines.

Supplementation with tyrosine has been shown, in animals, to limit or prevent the depletion of brain catecholamines that results from acute environmental stress [7,9,10,13] and mitigate the associated behavioral deficits [13–15]. Studies with human volunteers have not consistently shown positive performance effects with tyrosine supplementation [12,16]. The lack of conclusive evidence in human studies may be due to differences in the severity of stress (and consequently differences in brain catecholamine depletion) produced by the experimental paradigm or individual responses to acute stress. Previous work suggests that tyrosine reduces performance decrements in situations of high environmental stress [5] but has little effect under conditions of lower or moderate environmental stress [12].

The principle goal of this investigation was to evaluate the efficacy of the nutrient tyrosine as a countermeasure to cold-induced cognitive performance decrements. The study was designed using an environmental stressor previously shown to induce cognitive impairment in an effort to maximize the likelihood of stress-induced depletion of brain catecholamines and hence the potential for tyrosine administration to have significant beneficial impact. Participants were immersed to the chest in cold-water to decrease core body temperature, induce substantial cold stress and produce unambiguous performance decrements. Past work has demonstrated that cold-water immersion creates a stressful condition suitable for observing the effects of tyrosine [17]. The use of cold stress as an environmental manipulation is also of interest due to a lack of systematic information on the effects of body core cooling on cognitive performance in humans. We hypothesized that supplemental tyrosine could reduce the associated decrements in cognitive performance during cold stress.

2. Method

2.1. Participants

Male and female volunteers ($N=19$), between the ages of 18–35 years, were recruited from the local research volunteer test pool of military members. Their physical characteristics were age 20.5 ± 2.5 years, height 174.0 ± 6.6 cm, weight $77.0\pm$ 11.1 kg, and body fat 18.7 ± 5.4%. Volunteers were screened to identify any medical conditions contraindicating cold exposure. Written informed consent was obtained from each individual who volunteered to participate after being informed of the purpose, experimental procedures, and known risks of the study. This protocol was approved by the Natick Soldier Center Scientific Review Committee and the U.S. Army Research Institute of Environmental Medicine Human Use Review Committee.

2.2. Materials

An immersion pool was used to administer the cold exposure. It holds approximately 36,000 l of water and temperature is controlled within .5 °C of the desired temperature with a thermostatic control system.

2.3. Cognitive tests and questionnaires

Volunteers were evaluated using multiple, dependent measures of symptoms, mood, and cognitive performance. Measures were administered on IBM compatible lap-top computers, except for the Environmental Symptoms Questionnaire which was administered by paper and pencil. Volunteers completed 5 practice sessions with the test battery in a thermoneutral environment to familiarize themselves with the task and minimize practice effects.

2.3.1. Visual vigilance
This test of visual vigilance was designed to resemble military tasks requiring sustained scanning of the visual environment for infrequent, difficult to detect stimuli such as those during sentry duty[18]. The task required the participant to detect a small, faint stimulus that randomly appeared for a second at various locations on the computer screen. On the average, presentation of a stimulus occurred once a minute. The participant was told to respond as quickly as possible when a stimulus was detected. Dependent measures included correct detections and the response time. Responses made before (or after) stimulus occurrence were recorded as false alarms. The duration of this test was 20 min.

2.3.2. 4-choice visual reaction time
Volunteers were presented with a series of visual stimuli at one of the four different spatial locations on the computer screen [15,19]. The volunteer's task was to indicate the correct spatial location of each stimulus by striking one of the four corresponding keys on the computer keyboard. Dependent measures included the response latency for each trial, premature errors (responding before the presentation of the stimulus), errors of omission (response latency >1 s) and errors of commission (hitting the wrong key). The duration of this test was approximately 5 min.

2.3.3. Delayed match-to-sample
During this test, a sample pattern of 36 red and green grid squares was presented on the computer display. The volunteer

studied this pattern and then pressed a key on the keyboard. The sample pattern disappeared and the screen was blank for either 8 or 16 s ("delay"). Next, two patterns were presented and the volunteer selected the pattern that matched the previous sample pattern. Dependent measures included correct responses, incorrect responses, time out errors, study time for the sample, and response time. The delayed match-to-sample test consisted of 20 trials and required about 12 min to complete.

2.3.4. Profile of Mood States Questionnaire

The questionnaire is an inventory of self-reported mood states [20]. Each volunteer was asked to rate a series of 65 mood-related adjectives on a five point scale, using the response set of "How are you feeling right now?" The adjectives factor into six mood subscales (tension, depression, anger, vigor, fatigue, and confusion) [21]. The POMS is sensitive to a wide variety of environmental factors; sleep loss, nutritional manipulations and sub-clinical doses of various drugs [16,18,22,23]. The POMS required about 5 min to complete.

2.3.5. Environmental Symptoms Questionnaire

The Environmental Symptoms Questionnaire was administered to assess symptoms of cold stress, as well as alertness, muscle discomfort, and distress [24]. The items used to determine cold stress include statements like "My hands are shaking or trembling," "I feel weak," "I feel chilly," and "I'm shivering." Volunteers rate each statement using a 6-point scale with discrete anchor points that vary from "NOT AT ALL" to "EXTREME." This questionnaire required about 5 min to complete.

2.4. Procedure

Volunteers completed all three test conditions on separate days; thermoneutral/placebo (CON), cold/placebo (PLAC) and cold/tyrosine (TYR). Only one volunteer was tested at a time and the order of treatment was counterbalanced. There was a minimum three-day washout period between testing days. Volunteers were instructed to refrain from alcohol, smoking, and exercising 12 h prior to the start of each test day and could not eat or drink anything except water after 2200 h the evening before the test day.

Each test session consisted of two, 90-minute water immersions, with a rewarming and recovery period (or rest if thermoneutral) between immersions. During the cold treatment, the water temperature was approximately 10 °C, but varied systematically according to individual percent body fat. The exact water temperature (to the nearest whole degree) for each participant was calculated using the Tikuisus Cold Water Survival Model [25] to induce a fall in core temperature from 37 °C to 35 °C in approximately 90 min. During the thermoneutral condition, the water was 35 °C.

When volunteers arrived for testing, they were instrumented with a rectal temperature thermistor, skin temperature sensors, and heart rate electrodes and then rested in a seated position for 15 min while baseline measurements were taken. Once baseline physiological measures were obtained, a baseline battery of cognitive tasks and questionnaires was completed. Volunteers

then consumed either tyrosine or placebo. Following consumption, volunteers were immersed while seated to the chest in circulated water (either 35 °C or 10 °C) for 90 min. For safety reasons, immersion was terminated before the 90 minute period was complete if the participant's core temperature fell below 35 °C, or dropped .6 °C in 5 min, or the participant asked to stop testing. Following the first immersion, the cognitive tests were completed and then the volunteer began the rewarm/recovery phase. The core temperature at the beginning of the second immersion during each test day was similar to the temperature observed prior to immersion during the first trial. In order to ensure this, participants were warmed (within .5 °C of the pre-immersion temperature) in warm water (38.9 °C) after the first immersion. A second dose of tyrosine or placebo was consumed during the rewarming period. Following the rewarming period, participants completed an identical second 90 minute immersion and cognitive testing took place immediately after immersion.

2.4.1. Measurements and calculations

Rectal temperature was measured by a thermistor inserted 10 cm past the anal sphincter. Heat flow disks, used to measure skin temperature, were secured on 10 sites (right side of the body): foot, calf, thigh, chest, triceps, anterior aspect of the forearm, subscapular, forehead, and hand (dorsal). Mean skin or heat flow was calculated as follows: $T_{sk} = .06 T_{foot} + .17 T_{calf} + .28 T_{thigh} + .14 T_{chest} + .07 T_{tricep} + .07 T_{forearm} + .14 T_{subscapular} + .07 T_{hand}$. (40). Temperature and heat flow measurements were made continuously using a data acquisition system (National Instruments). Heart rate (HR) was monitored from three chest electrodes (CM-5 configuration) and radio-telemetered to an oscilloscope-cardiotachometer (Hewlett-Packard).

2.4.2. Tyrosine or placebo administration

A low fat, high-energy nutrient bar was the matrix used for delivery of tyrosine (see Table 1). The bars were matched for taste and texture to ensure volunteers could not distinguish tyrosine from placebo bars. Volunteers received a tyrosine dose of 150 mg/kg of body weight before each immersion. Thus, each participant received a total of 300 mg/kg of body weight of

Table 1
Characteristics of the nutrient bar (supplemental tyrosine and placebo configurations)

Constituents	Tyrosine bar		Placebo bar	
	grams	% (weight)	grams	% (weight)
Total fat	5.8	8.7	5.8	8.7
Saturated fat	2.3	3.4	2.3	3.4
Cholesterol	0	0	0	0
Sodium	.112	.17	.112	.17
Total carbohydrate	50	75	59.3	88.5
Sugars	27	40	27	40
Maltodextrin	0	0	9.3	13.9
Dietary fiber	1.8	2.7	1.8	2.7
Total protein	9.3	13.9	0	0
Tyrosine	9.3	13.9	0	0

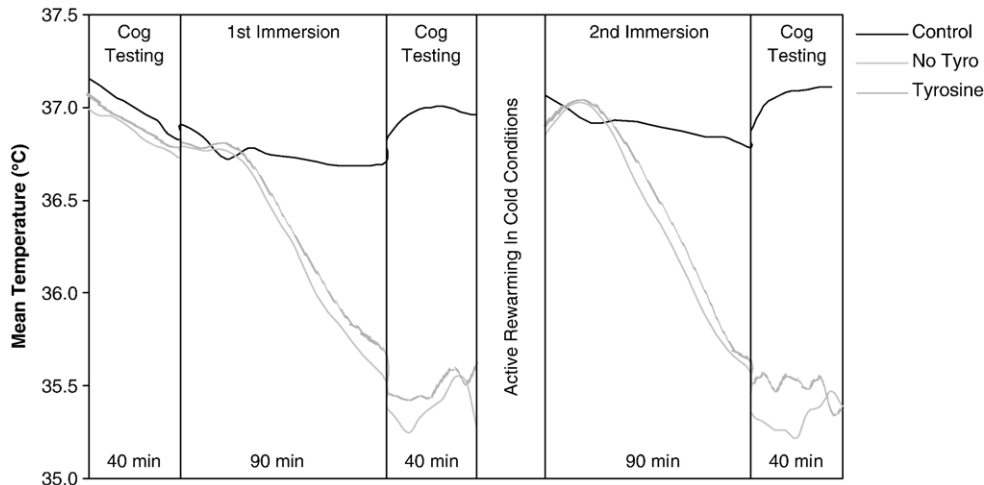Serving size: 65 g; total calories: 285; calories from fat: 52.

Fig. 1. Mean body core temperature (°C) for each treatment condition.

tyrosine over the course of the test day. Each nutrient bar contained 9.3 g of tyrosine. The quantity of the bar given to each participant was adjusted based on individual body weight. Participants consumed the bar and 1/2 glass of water 30 min before the start of each immersion.

2.4.3. Salivary measures of stress

Saliva was collected to evaluate two established biochemical markers of stress, cortisol and testosterone. Saliva was collected in 5 mL salivette tubes (Sarstedt; Newton, NC) from all volunteers on 5 occasions per test day. The first sample was collected upon arrival at the laboratory, a second sample was collected immediately preceding the first water immersion, a third immediately upon conclusion of the first immersion, a fourth immediately preceding the second immersion, and a fifth sample was collected upon conclusion of the second immersion.

2.4.4. Statistical analyses

Analyses consisted of repeated measures Analysis of Variance (ANOVA) with treatment (CON, PLAC, and TYR) and time (immersion 1 and immersion 2) as within subject

variables. An effect was deemed statistically significant if the likelihood of its occurrence by chance was $p \leq .05$. In those instances in which ANOVA yielded a significant main effect, post-hoc analyses in the form of Bonferroni were performed with the significance level again set at $p < .05$. All statistical analyses were performed using SPSS 12.0. Data are reported as a change from baseline performance. Change scores were calculated by subtracting the baseline score from each test score. Results are given for only those tasks that yielded significant effects.

2.5. Results

2.5.1. Core temperature and skin temperature

Analyses of temperature data revealed a main effect for treatment, such that both core temperature and skin temperature were significantly lower in the cold, relative to baseline, for both the first (Tcore: $F(2, 36) = 23.19$, $p < .001$; Tskin: $F(2, 36) = 913.32$, $p < .001$) and second immersion (Tcore: $F(2, 34) = 32.12$, $p < .001$; Tskin: $F(2, 34) = 1094.58$, $p < .001$; see Figs. 1 and 2).
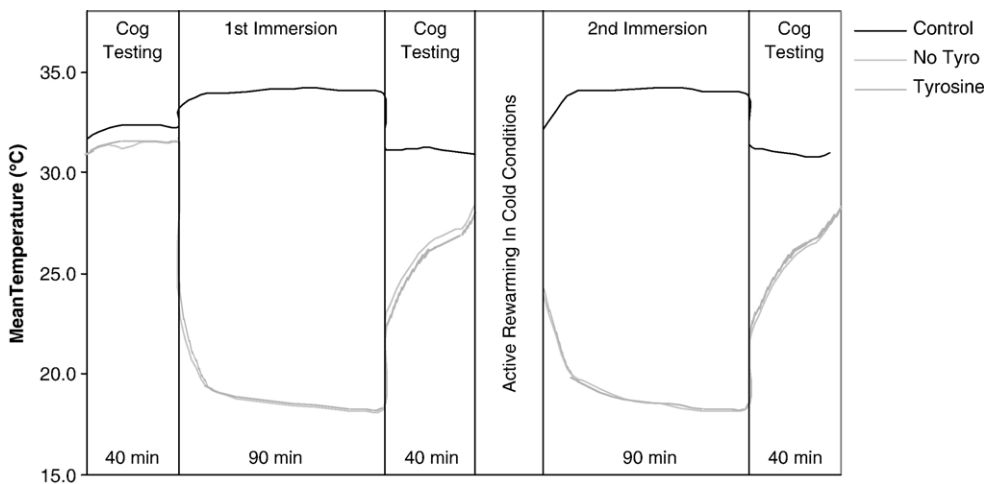

Fig. 2. Mean weighted skin temperature (°C) for each treatment condition

2.5.2. Salivary cortisol and testosterone

Analyses of salivary cortisol revealed a main effect for temperature exposure $F(1, 15) = 9.37$, $p < .01$. Salivary cortisol (µg/dL) was higher in the cold (PLAC $\bar{x} = -.10$, SEM = .04) than CON ($\bar{x} = -.23$, SEM = .04). There were no significant differences between treatment conditions for testosterone.

2.5.3. Environmental Symptoms Questionnaire

Analyses of the "cold symptom" measure on the ESQ revealed a main effect of temperature, $F(2, 40) = 49.82$, $p < .01$, such that volunteers felt a greater change in symptoms of cold stress following cold (TYR $\bar{x} = 1.75$, SEM = .25; PLAC $\bar{x} = 1.85$, SEM = .26) compared to CON ($\bar{x} = .07$, SEM = .08). A main effect of temperature on the muscle discomfort measure was also observed, $F(2, 40) = 20.04$, $p < .01$. Post-hoc analyses revealed that volunteers felt a greater change in muscle discomfort following cold (TYR $\bar{x} = 1.11$, SEM = .23; PLAC $\bar{x} = 1.01$, SEM = .20) than CON ($\bar{x} = -.09$, SEM = .10).

2.5.4. Profile of Mood States

A main effect of temperature for the tension subscale was observed, $F(2, 28) = 14.30$, $p < .01$, with volunteers scoring higher in the cold, relative to baseline, (TYR $\bar{x} = 2.33$, SEM = .92; PLAC $\bar{x} = 2.07$, SEM = .58) than CON ($\bar{x} = -1.76$, SEM = .65). A main effect of temperature for the depression subscale was also present, $F(2, 28) = 3.67$, $p < .05$. Post-hoc analyses revealed that volunteers scored higher in the cold (TYR $\bar{x} = 2.37$, SEM = 1.16; PLAC $\bar{x} = 2.37$, SEM = .93) than CON ($\bar{x} = .33$, SEM = .76).

Analyses of the confusion subscale revealed a main effect of treatment, $F(2, 28) = 6.89$, $p < .01$. Post-hoc analyses demonstrated that volunteers scored significantly higher with PLAC ($\bar{x} = 1.60$, SEM = .56) compared to CON ($\bar{x} = -.53$, SEM = .54), but TYR was not significantly different than CON.

In addition, there was a main effect of temperature for total mood disturbance, $F(2, 28) = 7.76$, $p < .01$, such that volunteers scored higher in the cold (TYR $\bar{x} = 8.83$, SEM = 3.45; PLAC $\bar{x} = 10.1$, SEM = 3.54) than CON ($\bar{x} = -.37$, SEM = 3.07).

2.6. Cognitive performance measures

2.6.1. Match-to-sample

Analyses of correct responses on the match-to-sample memory measure revealed a main effect of treatment on correct responses following the 16 second delay, $F(2, 20) = 3.69$, $p < .05$. Post-hoc analyses showed that fewer correct responses, relative to baseline, were made with PLAC ($\bar{x} = -2.36$, SEM = .77) compared to TYR ($\bar{x} = .14$, SEM = .80) and CON ($\bar{x} = .18$, SEM = .67).

Analyses of RT (seconds) for hits following a 16 second delay revealed a treatment by time interaction, $F(2, 20) = 4.08$, $p < .5$ (see Fig. 3). Post-hoc analyses revealed that volunteers responded more quickly with TYR ($\bar{x} = -1.11$, SEM = 6.13) compared to PLAC ($\bar{x} = 19.38$, SEM = 5.37) following the first cold immersion, but there was no difference in RT following the second immersion (TYR $\bar{x} = 12.24$, SEM = 9.34; PLAC
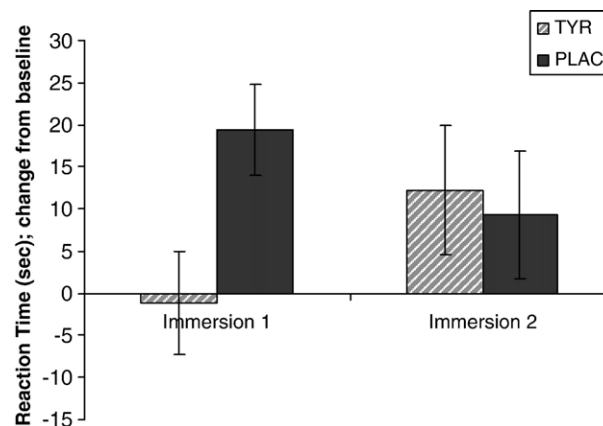

Fig. 3. Reaction time for hits during the match-to-sample task (16 second delay) following cold exposure.

$\bar{x} = 7.62$, SEM = 7.51). This is the only significant difference in performance found between the first and second cold-water immersions across all tests.

A main effect of treatment for study time across both delays was also observed $F(2, 30) = 5.61$, $p < .05$. Post-hoc analyses revealed that volunteers studied the sample for a shorter amount of time (seconds) with TYR ($\bar{x} = -2.18$, SEM = .47) than PLAC ($\bar{x} = -.80$, SEM = .34) and CON ($\bar{x} = -.61$, SEM = .41).

2.6.2. 4-choice reaction time

Analyses of the 4-choice reaction time task revealed a main effect of temperature on the reaction time (ms) measure, $F(1, 19) = 35.85$, $p < .001$, such that volunteers responded more rapidly, relative to baseline in the CON ($\bar{x} = -28.15$, SEM = 6.29) than in the cold (TYR $\bar{x} = 12.91$, SEM = 9.34; PLAC $\bar{x} = 17.38$, SEM = 7.63).

Analyses of errors revealed a main effect of temperature for premature errors $F(2, 32) = 5.52$, $p < .05$. Post-hoc analyses show that more premature errors were made following cold exposure (TYR $\bar{x} = .97$, SEM = .42; PLAC $\bar{x} = 1.18$, SEM = .35) than CON ($\bar{x} = .38$, SEM = .19). Analyses of errors also show a main effect for temperature on total errors $F(2, 32) = 5.53$, $p < .05$, such that the total error score was higher following cold exposure (TYR $\bar{x} = 2.47$, SEM = .85; PLAC $\bar{x} = 3.29$, SEM = .90) compared to CON ($\bar{x} = .74$, SEM = .58).

3. Discussion

The principle goals of this investigation were to determine how exposure to cold resulting in significant core body cooling influences cognitive performance and to evaluate the efficacy of the amino acid tyrosine to alleviate cold-induced performance decrements. The results of this study demonstrate that core body cooling produces adverse changes on multiple measures of cognitive performance, mood and symptomology and that dietary supplementation with the amino acid tyrosine prior to cold exposure alleviates cold-induced decrements in working memory. The dose of tyrosine used in the present study was

150 mg/kg prior to each immersion, totaling 300 mg/kg a session. This dose is considerably higher than those used in previous work in which doses of 100 or 150 mg/kg have been used [16,26]. Given the repetitive immersion paradigm used in the present study to maximize the level of stress produced, supplementing with multiple doses of tyrosine prior to each exposure was appropriate. No negative side effects were observed.

Results of previous work on the efficacy of tyrosine as a countermeasure for stress-induced cognitive performance decrements have been mixed. It is hypothesized that tyrosine only has a beneficial impact in situations of significant stress and relatively little effect on conditions resulting in only mild physiological stress [27]. Therefore, it was important to ensure that our paradigm created the appropriate amount of physiological stress. Core hypothermia, resulting from cold exposure, was used because it has been previously established that this type of stress results in decrements in cognitive performance [3]. Analyses confirmed that the cold treatment acted as a significant physiological stressor as evidenced by the elevated salivary cortisol and decreased body core and skin temperatures during repeated cold exposures. Salivary cortisol was an important marker because it provided confirmation that significant physiological stress was induced by cold exposure. Increased release of the hormone cortisol is the most widely accepted biological marker of activation of the hypothalamus–pituitary–adrenal axis (HPA) in humans [28,29]. Pre-clinical and clinical research demonstrates the HPA axis is sensitive to most types of physical and psychological stress [30]. Saliva cortisol is accepted as an excellent measure of plasma cortisol, frequently used to assess the impact of psychological and physical stress on humans in laboratory and military field studies [30–32].

As anticipated, exposure to cold stress resulted in impaired performance on multiple cognitive measures. Cold exposure produced decrements on the 4-choice reaction time task. In particular, volunteers responded more slowly and committed a greater number of errors following cold exposure. In addition, performance was impaired on the working memory task at the longest delay interval (16 s). These results are consistent with the previous work showing that cold stress impairs working memory [1,5,33–35]. Previous work suggests that measures of working memory may be particularly susceptible to cold stress and is affected in the early stages of body cooling. Decrements in working memory have been seen with cold exposure resulting in relatively small reductions in core temperature [3] and exposure to cold air that are unlikely to have caused a reduction in core body temperature [5].

The effect of the cold stress was also validated by results from the ESQ and the POMS. As expected, when volunteers were exposed to cold, they had significantly higher symptoms of cold stress as well as increased muscle discomfort. In addition, when cold, volunteers report higher levels of tension, confusion and depression on these subscales of the POMS and have a significantly higher "total mood disturbance" score. These results are consistent with the previous work reporting increased scores of tension, confusion and total mood disturbance during cold air exposure [36].

Supplementation with tyrosine prior to cold exposure was effective in reducing cold-induced working memory decrements. In fact, administration of tyrosine prior to the cold exposure resulted in matching-to-sample accuracy comparable with that in the thermoneutral condition. This result is consistent with the previous work in both animals and humans demonstrating beneficial effects of tyrosine on working memory during stressful conditions [5,37] and again indicates that tyrosine mitigates working memory impairment when cold stress specifically affects memory retention, such that accuracy is impaired only at the longest delay interval [5]. This study extends previous work by showing that tyrosine is an effective countermeasure against cognitive decrements associated with larger changes in core body temperature, as well as multiple exposures to cold stress in humans. In addition, this study demonstrates that supplementation with the amino acid tyrosine prior to cold exposure reduced the amount of time taken to study the target compared to both the placebo condition and control. This is important because it indicates that when volunteers received tyrosine, they were not only protected against cold-induced memory deficits, but they were also able to process information more rapidly. Finally, results from the POMS questionnaire support these observations, as an increased score on the confusion subscale of the POMS following cold is mitigated with tyrosine supplementation.

The beneficial effects of tyrosine supplementation reported in the present study are consistent with the hypothesis that cold stress causes an increase in the firing rate of catecholaminergic neurons and tyrosine supplementation prior to stress increases syntheses of the catecholamines required for optimal working memory function. This hypothesis is supported by studies demonstrating that brain catecholamines, particularly norepinephrine and dopamine, are depleted in certain regions of the brain by exposure to a variety of stressors [9,38,39] and that this depletion is associated with decrements in cognitive performance [7,40]. Administration of tyrosine, a precursor for the synthesis of dopamine and norepinephrine [27] has been shown to prevent the stress-induced depletion of brain norepinephrine and dopamine in CNS regions associated with working memory [7,13,41].

The potential for tyrosine to have utility across multiple types of stressors is still unknown. Since many forms of stress induce brain depletion of catecholamines, tyrosine may be useful in counteracting stress-related performance decrements under a variety of conditions. Although it has been difficult to demonstrate conclusively that tyrosine has beneficial effects in humans, the literature suggests that tyrosine has the potential to be an effective countermeasure under such conditions as cold stress [5], exposure to cold and hypoxia [16], noise [42], extended wakefulness [11] and lower body negative pressure [43]. The lack of conclusive evidence in the human literature is likely related to inconsistencies in the amount of physiological stress produced, differences in the cognitive tasks employed and the amount and timing of the tyrosine dose.

The results of the present study indicate that tyrosine has beneficial effects on working memory in humans exposed to acute cold stress. To determine the feasibility of employing tyrosine as an effective countermeasure to stress, several key issues need to be addressed. Future research should attempt to determine the dose response function for the amelioration of stress-induced decrements in performance by tyrosine. Also, it will be necessary to determine the optimal time window of supplementation to maximize performance effects, the relative duration of beneficial effects, and if this amino acid provides protective effects through regular dietary supplementation or if acute supplementation is preferable. In addition, although we did not have enough female volunteers to make comparisons of sex differences valid, this is an issue that may warrant further study. Finally, since tyrosine supplementation can only be expected to have a beneficial impact on performance when stress is severe, it is necessary to determine the generalizability of tyrosine's effects across multiple stressful environments.

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