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Working memory reloaded: tyrosine repletes updating in the *N*-back task

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In this study we tested the idea that the food supplement L-Tyrosine (TYR) repletes resources required for cognitive-control operations. We investigated whether the "updating" (and monitoring) of working memory (WM) representations, a key cognitive-control function, can be promoted by administering TYR, the biochemical precursor of dopamine. Participants performed an *N*-back task where we compared the WM-demanding 2-back condition with the WM-undemanding 1-back condition. As expected, TYR promoted performance in the more demanding (2-back) but not in the easier (1-back) condition, suggesting that TYR selectively targets cognitive-control operations. This result suggests that TYR can replete cognitive resources when more control is needed and, more generally, that food can act as a cognitive enhancer.

Keywords: working memory, tyrosine, dopamine, updating

INTRODUCTION

In a seminal essay (1862/1960), the German philosopher Ludwig Feuerbach claimed that "Der Mensch ist, was er ißt" (you are what you eat). Feuerbach was probably the first intellectual to promote the idea that the food one eats has a bearing on one's state of mind. This idea later became the motto of the hippie culture, which promoted eating organic and healthy food. Since then, the idea that the food we eat modulates the way we think and perceive the world has been very suggestive in popular culture and the focus of scientific research. One of the most investigated amino acids (building blocks of proteins) is tyrosine (TYR), which is contained in food such as fish, soy, eggs, milk, and bananas. In healthy population the average daily intake of TYR is 7 mg/kg, one half of the (World Health Organization) WHOs upper requirement of 14 mg/kg (see Deijen, 2005). Importantly, tyrosine is the biochemical precursor of two important brain catecholamine neurotransmitters: norepinephrine (NE) and dopamine (DA). The supplementation of TYR, or TYR-containing diets, increase plasma TYR and enhance brain DA and NE release (Lehnert et al., 1984; Reinstein et al., 1984; Acworth et al., 1988; During et al., 1988; see Deijen, 2005, for a comprehensive review). Glaeser et al. (1979) found, after the administration of a single oral dose of 100 mg/kg TYR, that mean plasma TYR levels were maximal after 2 h, rising from 69 ± 3.9 to 154 ± 9.5 nmol/ml. Previous literature has mainly focused on the role of TYR as "counteractor" of conditions that cause brain DA and NE depletion, such as stress (Deijen and Orlebeke, 1994; Shurtleff et al., 1994; Mahoney et al., 2007). Only in one study TYR has been administered without exposure to stress (Thomas et al., 1999), using a multiple task battery (SYNWORK1; Elsmore, 1994) designed to measure working memory (WM), arithmetic skills, and visual and auditory monitoring simultaneously, and a simple task battery consisting of only two of the subtasks: the Sternberg Memory task (Sternberg, 1966) and the Visual Monitoring task (Loeb and Binford, 1968). The results revealed beneficial effects of TYR supplementation when competing requirements to perform other tasks simultaneously degrade performance (Thomas et al., 1999). This indicates that TYR may replete cognitive resources, but only under sufficiently demanding conditions.

Interestingly, executive control has been considered to emerge from the interplay between cognitive stability (defined as the maintenance of task-relevant representations) and flexibility (defined as the ability to adapt, update, and shift between informational states) – two major, but partially antagonistic functions of cognitive control, related correspondingly to the prefrontal cortex (PFC) and the striatum, which both are modulated by DA (Cools, 2006; Cools and D'Esposito, 2010) – the precursor of which is TYR. According to Cools (2006), the same high DA levels in the PFC that are beneficial for the stability of representations may reduce the ability to flexibly alter cognitive representations. Low DA levels in the PFC may in turn be beneficial for the flexible updating of cognitive representations, but at the same time impair the ability to maintain representations in the face of intervening distractors. Several studies have shown that striatal dopamine plays a crucial role in WM updating. According to Moustafa et al. (2008), the nigrostriatal dopaminergic pathway serves as a gate to signal when and when not to update information in prefrontal WM. Consistent with this idea, Siessmeier et al. (2006) found that administering DA agents to healthy subjects led to a correlation between DA uptake in the striatum and BOLD activity in the dorsolateral PFC, suggesting that the striatum might drive WM activity in the PFC. Moreover, a PET study showed that individual WM capacity predicts the striatal dopamine synthesis capacity: subjects with low WM capacity have a low synthesis capacity while subjects with high WM capacity have a high synthesis capacity (Cools et al., 2008).

The current study focused, for the first time, on the acute effect of TYR supplementation on the updating (and monitoring) of WM representations – a key cognitive-control function (Miyake