



## A Winning Combination among Polyphenols, Probiotics, Vitamins for Improved Memory and Cognitive Performance

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### ABSTRACT

*Intake of polyphenols, probiotics, and multivitamins has shown beneficial effects on spatial memory, learning, and cognition. However, the effect of various combinations of these nutrients as dietary intake on cognitive performance has remained unexamined. Knowing which antioxidant combination would be most effective is important, especially because regular intake of all nutraceuticals may not be possible. This study examined the best combination of nutrients that enhances spatial memory and cognitive performance. Since quality of nutrition can have a significant effect on memory and learning, the outcome of this study could be significant to improving cognitive function in humans, particularly in the context of childhood education. Especially with current disparities leading to food deserts and differing access to quality food, this may reveal changes to make in mass nutrition to better support cognitive performance and learning.*

**Keywords:** Cognitive performance, Nutrients, Spatial memory, Nutritional neuroscience, Polyphenols, Probiotics, Vitamins

### INTRODUCTION

Intake of polyphenols has been shown to have beneficial effects on memory and learning [1-3]. Polyphenols are secondary metabolites of plants, and they hold significant antioxidative properties [4,5]. Equipped with these properties, they protect cells against oxidative damage by scavenging free radicals [6]. Polyphenols also regulate mitochondrial function and enhance cerebrovascular blood flow [2,7]. Additionally, probiotics have also shown promise in improving spatial memory and cognition [8,9]. Probiotics are bacteria that support health, and they have particularly been shown to influence brain health [10]. Probiotics change composition of the gut microbiome, which influences brain health through the gut-brain axis, the bidirectional communication between the gut and the brain [11]. Through the gut-brain axis, probiotics can modulate the HPA axis involved in the stress response and alter levels of brain-derived neurotrophic factor (BDNF), which is crucial for learning and memory [12]. In addition, the intake of multivitamins (particularly vitamins ACE) has a well-demonstrated positive impact on spatial memory and cognitive function [13-15]. Vitamins are associated with neurological and cognitive health, especially in areas of free recall memory. Vitamins A, C, and E have antioxidant properties, counteracting oxidative stress by destroying free radicals [16,17]. In particular, Vitamin C has a high concentration in the brain since it is crucial for neuronal function, vascular function, and neurotransmitter synthesis, release, and reuptake [18]. However, the effect of various combinations of these nutrients on spatial memory and cognitive performance has remained unknown. This study examined the combination of nutrients among polyphenols, probiotics, and multivitamins that best enhances memory and cognitive performance. This study tested the hypothesis that a diet with a combination of polyphenols, probiotics, and multivitamins most strongly supports spatial memory and cognitive performance. Finding the best combination of nutrients for enhanced cognitive performance is beneficial in developing better strategies for improved learning and cognitive function in humans.

## METHODS

Based on the seven possible combinations of probiotics (Pro), polyphenols (Pol), and multivitamins (Vit), 32 house-cricket (*Acheta domesticus* [L.]) were divided into one control group and seven experimental groups (Pro, Pol, Vit, ProPol, PolVit, VitPro, ProPolVit; sample size of each group,  $n=4$ ). Throughout 7 weeks, crickets were fed their respective diets. Alternation Tests and Recognition Memory Tests were conducted every week using a Y-maze to assess spatial working memory. During the Alternation Test, crickets are allowed to explore all three arms of the Y-maze. Alternations are counted when the crickets explore a different arm each successive time, such as arm 1 → arm 2 → arm 3. If the cricket explores an arm twice in the set of three arm visits, such as arm 1 → arm 2 → arm 1, this is not counted as an alternation. The Alternation Test is dependent on the fact that crickets have the habit of exploring their least-recently visited location due to their curiosity; this relies on their working memory of where they have previously visited. During the Recognition Memory Test, crickets get access to only one of arms 2 or 3 (for example, arm 2) of the Y-maze, where food is placed. This arm is alternated among each of the six trials in one testing to avoid creating a bias for one arm. After obtaining the food, crickets are returned to arm 1. After a minute, all arms are opened, and the food is placed in the other arm of the Y-maze (arm 3 in this example). Due to their curiosity, crickets normally explore the unvisited arm, in which they would find the food. This indicates spatial memory by demonstrating whether they have a recollection of which arm they have previously visited. Data is analyzed using the Prism 8 data analysis tool by GraphPad Software Inc.

## RESULTS

All groups experienced improvement in performance over time in both the Alternation Test and the Recognition Memory Test, as shown in Figure 1. A two-way between-subjects analysis of variance (ANOVA) showed that there was a significant effect of nutrients on performance measured by the number of correct leg choices in both tests ( $p<0.0001$ ).

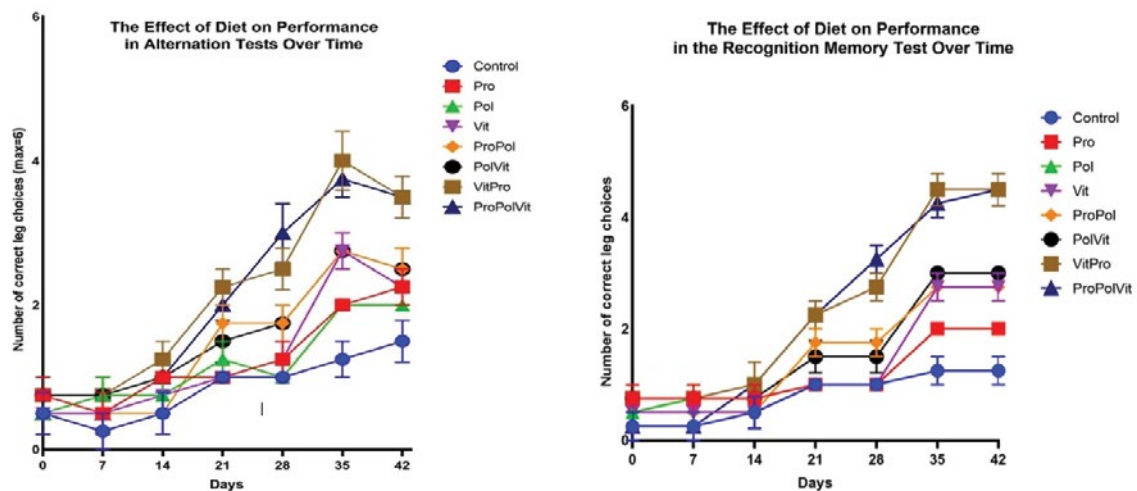


Figure 1 The effect of diet on performance in the alternation test and the recognition memory test over time

Post-hoc Tukey tests were run to further determine the significance of differences among individual means of improvement, which are shown in Figure 2. Improvement was defined as the difference between the final number of correct leg choices after 42 days and the initial number during the first testing. In the Recognition Memory Test, there was an extremely significant difference between the improvement of the control group and the groups fed probiotics and multivitamins (VitPro) ( $p<0.0001$ ), and probiotics, polyphenols, and vitamins (ProPolVit) ( $p<0.0001$ ). However, there was no significant difference between the improvement of the groups VitPro and ProPolVit ( $p=0.9988$ ). Similarly, in the Alternation Test, there was a significant difference between the improvement of the control group and the group ProPolVit ( $p=0.0255$ ), but there was no significant difference between the improvement of the groups VitPro and ProPolvit ( $p=0.9997$ ).

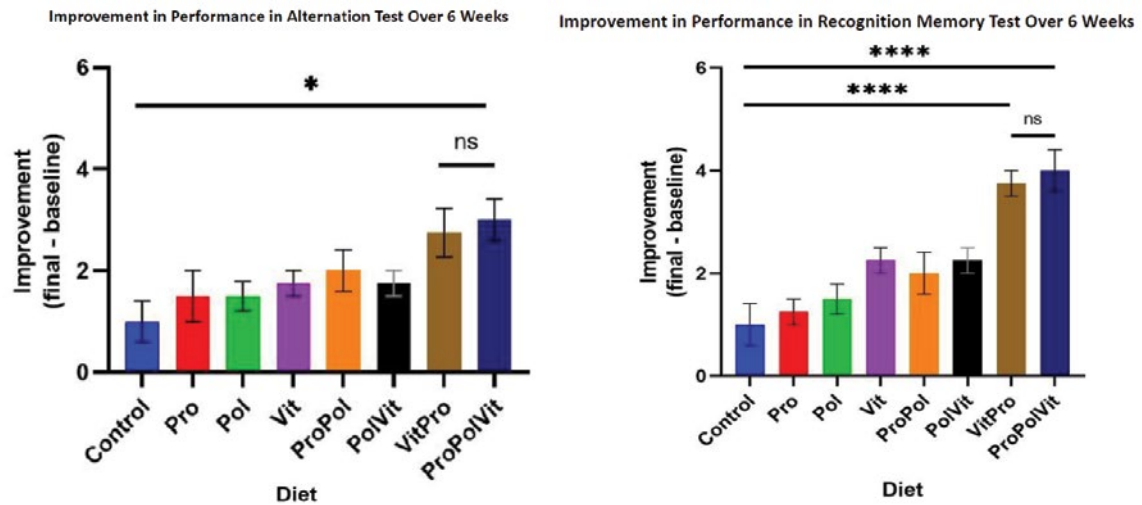


Figure 2 Improvement in performance in alternation test and recognition memory test over 6 weeks

Further, linear regression was run to determine the magnitude of improvement in both tests over time, as represented by the slope. Table 1 shows the ranking of diets in order of slope (trend of improvement) for the Alternation Test and the Recognition Memory Test. Similar to the findings of the ANOVA and Tukey tests, ProPolVit and VitPro ranked highest in measure for the Alternation Test (ProPolVit: slope=2.143, VitPro: slope=1.959) and for the Recognition Memory Test (ProPolVit: slope=2.724, VitPro: slope=2.510). The control ranked the lowest in both tests (slope=0.6735).

Table 1 Ranking of diets in order of slope for alternation test and recognition memory test

Rank	Alternation Test	Rank	Recognition Memory Test
1	Gr 8: ProPolVit (slope=2.143)	1	Gr 8: ProPolVit (slope=2.724)
2	Gr 7: VitPro (slope=1.959)	2	Gr 7: VitPro (slope=2.510)
3	Gr 5: ProPol (slope=1.439)	3	Gr 6: PolVit (slope=1.469)
4	Gr 4: Vit (slope=1.255)	4	Gr 5: ProPol (slope=1.439)
5	Gr 6: PolVit (slope=1.224)	5	Gr 4: Vit (slope=1.439)
6	Gr 2: Pro (slope=0.9490)	6	Gr 3: Pol (slope=0.8878)
7	Gr 3: Pol (slope=0.8878)	7	Gr 2: Pro (slope=0.7959)
8	Gr 1: Control (slope=0.6735)	8	Gr 1: Control (slope=0.6735)

DISCUSSION

Crickets consistently demonstrated more improvement in correct leg choices when fed nutrient-rich diets compared to crickets fed the normal diet, suggesting that these nutrients may indeed play a role in improving memory. While all of the nutrient combinations showed an advantage over the normal diet, the most significant improvement compared to the control was found in groups VitPro and ProPolVit. These two groups were also ranked highest based on the slopes of their improvement, with ProPolVit ranking only slightly higher than VitPro. However, since the post-hoc Tukey test found no significant difference between the performance and improvement of subjects within these two groups (VitPro and ProPolVit), the combination of probiotics and multivitamins may be the most efficient option for supporting memory and cognitive performance among polyphenols, probiotics, and multivitamins. These results do not entirely support the experimental hypothesis because while the group ProPolVit produced significant improvement, this improvement was not significantly higher than that of the group VitPro, making VitPro a potential winning combination as well.

## CONCLUSION

This study investigated the best combination of nutrients for enhanced cognitive performance and is beneficial in developing better strategies for improved memory and cognitive function. In addition, future research could include studying the effect of nutrition on human cognitive performance, particularly in the context of childhood education. This may be examined through natural studies measuring nutrition and performance and finding correlations between these factors and income level. Such studies could illustrate the effect of socioeconomic disparities on nutrition and learning, ultimately pointing to changes that can be made in mass nutrition to better support cognitive performance.

## DECLARATIONS

### Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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