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Double blind placebo and active (Caffeine) controlled study to examine the effects of "Wake up" herbal drink on vigilance and function following lunch.

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Background:

Post lunch dip is a very well established phenomenon which results in substantial deterioration of function and productivity following lunch, between noontime and 16:00. Indeed, in several places around the world it is common to take a nap ("siesta") between 13:00-15:00 or 14:00-16:00. The reason for this mid-day post lunch sleep propensity is complex, and consists of hormonal, circadian, and nutritional/gastrointestinal mechanisms. Temperature changes, decreased cortisone levels, and re-distribution of blood following lunch contribute to this sleepiness following lunch. It has been shown that this post-lunch dip during these 2-3 hours following lunch has a substantial impact on work performance. There is a reduced productivity and decreased quality of work during these hours, as well as increase in errors and work accidents. A recent study which sampled 28902 adults aged 18 to 65 found that fatigue results in lost productive time that can cost the employers 136.4 billion dollars annually, an excess of 101 billion dollars annually compared with workers without fatigue.

A wake promoting drink may reduce this phenomenon and result in significant improvement of vigilance, productivity and work achievements. One potential way to achieve this wake promotion is by drinking coffee. Caffeine containing drinks may improve vigilance and function by blocking adenosine receptors and by inhibiting phospho-di-esterase (PDE) which results in increased cAMP and adrenergic activity. However, caffeine has a short half-life and potential side effects (such as increased pulse rate and blood pressure). In addition, regular coffee drinking results in tolerance and substantial reduction of the effect of caffeine.

The newly developed "Wake-up" drink (C.O.L. group, Ltd, Tel Aviv, Israel) is a wake promoting drink based on herbal ingredients consisting of extracts of Ginkgo Biloba, guarna, and fruit-up.

Guaraná (Paullinia cupana) seeds have a long history of usage as a stimulant by Amazonian tribes. The putative stimulant properties were generally assumed to reflect the presence of caffeine, although it comprises only 2.5–5% of the extract's dry weight. However the psychoactive properties of guaraná may also

be attributable to relatively high content of other potentially psychoactive components, including both saponins and tannins, which may also account for antioxidant properties of the plant. It has been previously shown that Guarana improves memory performance and mood, and increases alertness, even in relatively low doses. The Ginkgo Biloba is a unique tree which can be found predominantly in China. Extract of Ginkgo Biloba are believed to have some important healing properties, and are used in herbal medicine for asthma, bronchitis, fatigue, and tinnitus. On top of its' vigilance promoting, it has been shown to have favorable effects on memory. It is currently being used predominantly in Asia as a preventive treatment for Alzheimer's disease and other types of dementia. It also has been shown to reduce vertigo. The fruit-up adds to the "Wake up" drink predominantly taste, although its' glucose content may also improve alertness. It has a relatively low glycemic index which stabilizes the blood glucose levels and may have implications in reducing morbidity. In addition, unrelated to alertness, the "Wake up" drink includes also elderberry extract, which has been shown to have efficient anti-viral activity, effective especially against influenza. Thus, this drink has the potential to improve vigilance and performance, and alleviate the undesired effects of the post-lunch dip.

Aim:

We sought to examine whether "Wake up" may improve vigilance and function following lunch, and to compare it to caffeine and placebo in the short term (30min) and longer term (2h) after lunch. We hypothesized that drinking "Wake-up" following lunch will improve short term memory and function similarly to caffeine, but better than placebo, and better than both caffeine and placebo in the longer term. We expected that it will affect blood pressure and pulse rate to a lesser extent compared to caffeine.

Methods:

The study was proved by the institutional review board (IRB, Helsinki committee) of Rambam Medical Center and all participants have signed an informed consent prior to participation. 30 healthy volunteers were studied in 3 different days, 6 ± 3 days between each 2 study days. In each visit they had a standard lunch between 12:00 - 13:00, following which they drank either "Wake up", 50mg caffeine or placebo in a cross over double blind regimen. All three drinks had a similar look and taste, and were in a similar bottle containing 100ml volume. 30min and 120min following drinking, they underwent a battery of tests including measurement of vital signs, blood pressure, and validated commonly used standard function and vigilance tests such as an immediate word recall test (short term memory), digit symbol substitution test (concentration), and subjective rating (on a visual analogue scale - VAS) of their vigilance, ability to focus, and effectiveness at work. The results of the 3 visits were compared utilizing one way analysis of variance, with $p < 0.05$ considered statistically significant.

Results:

All 30 (13m, 17f) volunteers completed the study. Their age and BMI were 36.6 ± 12.4 years (range 18-61) and 24.3 ± 3.5 Kg/m² (range 17.0-31.8). Two participants have complained in dizziness after drinking the 50mg caffeine. No side effects or complaints have observed following drinking "Wake up" or placebo. In all performance tests and subjective vigilance and effectiveness assessment both "Wake up" and caffeine were significantly superior to placebo 30 min following lunch. However, 2hours following lunch performance following caffeine containing drink deteriorated, and "Wake up" was superior to both caffeine and placebo. The VAS rating of vigilance, ability to focus and performance (effectiveness) at work are presented in figures 1-3, respectively. As can be seen, in all three dimensions 30min following drink both caffeine and "Wake up" resulted in significant improvement. However, 2 hours following drink there was a deterioration of the self rating following caffeine (in all 3 dimensions),

and only following "Wake up" vigilance and performance remained high. The number of correct words recalled 30 min after drinking was 12.6 ± 4.1 with "Wake up", compared to 11.6 ± 4.8 and 9.7 ± 3.8 with caffeine and placebo, respectively, $p < 0.05$ for both caffeine and "Wake up" compared to placebo. However, 2 hours following drinks the number of words recalled were 12.1 ± 4.3 with "Wake up", compared to 9.8 ± 4.9 and 9.4 ± 3.5 with caffeine and placebo, respectively, $p < 0.05$ for "Wake up" compared to both caffeine and placebo (fig 4). The number of correct symbols 30min and 120min following various drinks is presented in fig 5. As can be seen, both 30min following the drink and 120 min following the drink the best performance was after drinking "Wake up" ($p < 0.05$ between "Wake up" and placebo 30min following the drink and 120min following the drink). Pulse rate and blood pressure were significantly higher 30 min following caffeine drink than following "Wake up" drink: $77.4 \pm 1.9/\text{min}$ vs $71.9 \pm 1.8/\text{min}$ and $119/75$ vs $113/71\text{mmHg}$, $p < 0.05$ for both. Two hours following drinks pulse rate and blood pressure were similar in the three experiments. These numbers are presented in Table 1:

	30 min following drink			120 min following drink		
	Pulse	Systolic BP	Diastolic BP	Pulse	Systolic BP	Diastolic BP
Wake up	72 ± 10	113 ± 13	71 ± 9	73 ± 8	112 ± 13	71 ± 7
Caffeine	77 ± 10 *	119 ± 13 *	75 ± 9 **	73 ± 8	117 ± 14	74 ± 9
Placebo	74 ± 13	115 ± 13	71 ± 7	73 ± 10	112 ± 15	70 ± 7

Table 1: Hemodynamic measures with the various drinks 30 and 120 min following the drink.

* $p < 0.05$ (caffeine vs Wake up); ** $p < 0.05$ caffeine vs both wake up and placebo.

Conclusions: drinking "Wake up" after lunch improves vigilance and performance 30 min following the drink, similarly to caffeine and significantly better than placebo. 120min following the drink, performance and vigilance with "Wake up" remains high, significantly superior to both placebo and caffeine. While Caffeine was associated with increasing pulse and blood pressure in the short term, with "Wake up" there were no hemodynamic differences compared with placebo, both 30min and 120min following drinking. Thus, "Wake up" seems as a good and effective drink to counteract the somnolence and reduced performance during the post lunch hours.

Figures:

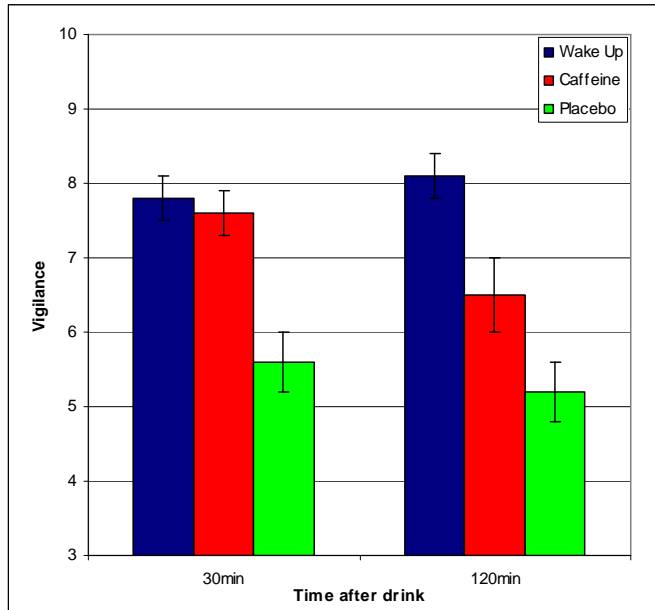


Fig 1: The effect of drink content and time after drink on participants' rating of their vigilance (VAS)

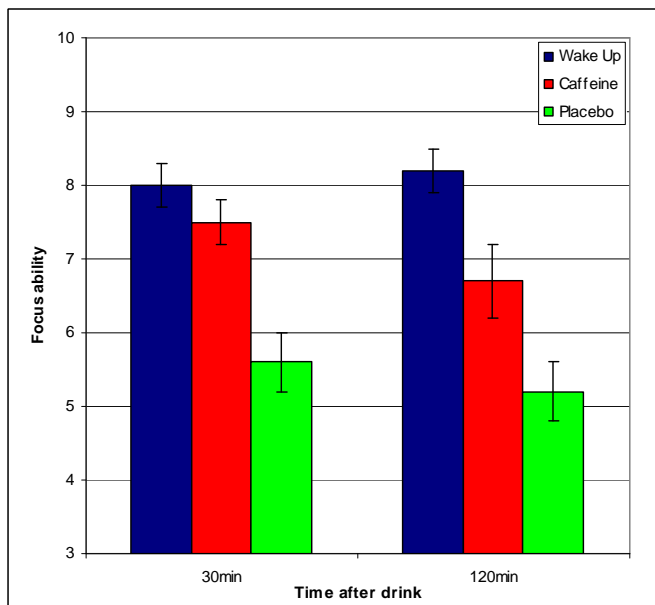


Fig 2: The effect of drink content and time after drink on participants' rating of their ability to focus (VAS)

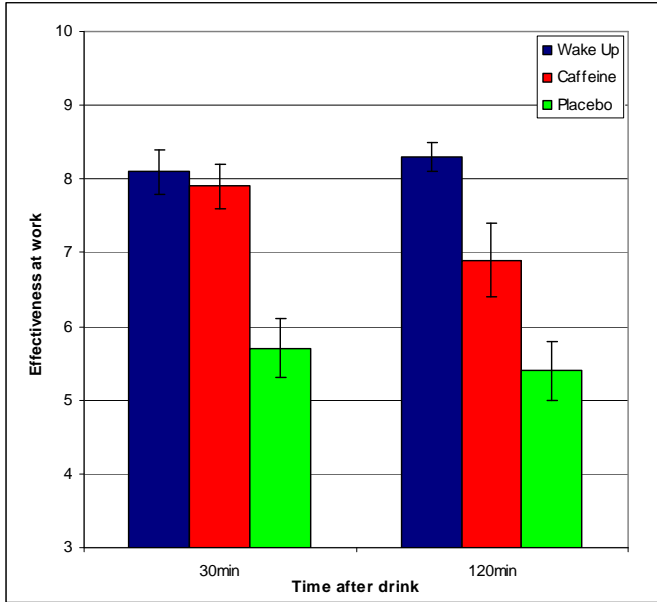


Fig 3: The effect of drink content and time after drink on participants' rating of their effectiveness at work (VAS).

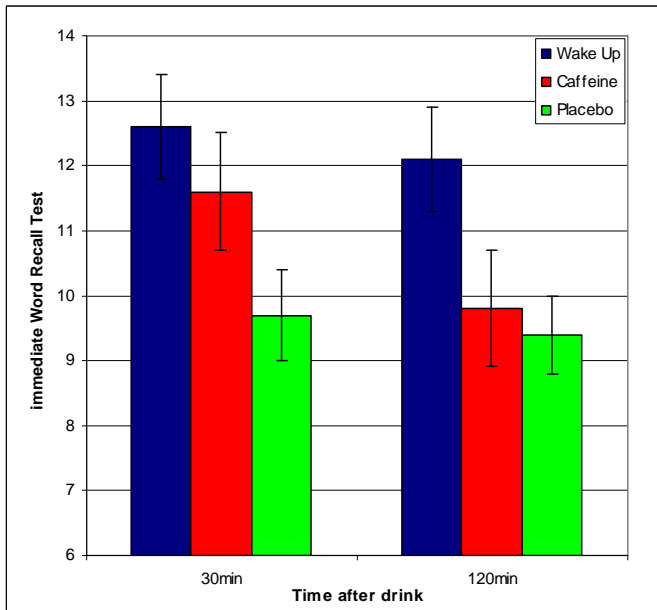


Fig 4: Number of correct words recalled in the immediate word recall test 30min and 120min following various drinks.

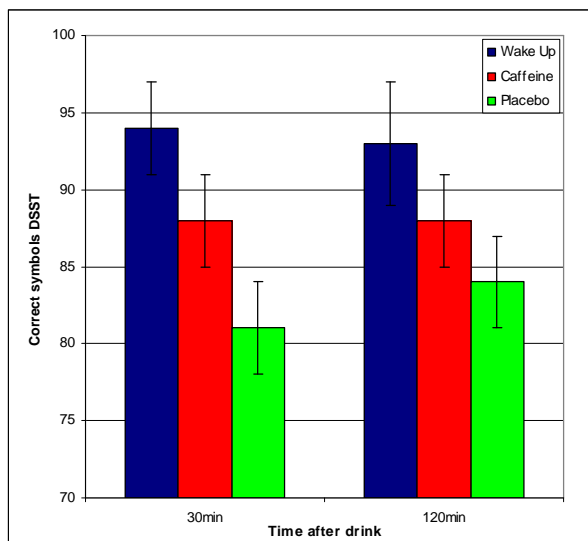


Fig 5: Number of correct symbols in the DSST (Digit Symbol Substitution Test) 30min and 120min following various drinks.

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