The Effects of Ginseng on Physiological Processes Involved in Mental Function

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As the world population is living to increasingly older ages so there is a greater incidence of age-related disorders. Some of these, such as Alzheimer's disease (AD), are associated with cognitive decline. Current treatments for AD target specific brain neurotransmitter systems, and in particular the cholinergic system. However there are numerous factors involved in the aetiology of AD. These include genetic susceptibility as well as a number of biological processes including free radical exposure, compromised glucose metabolism, neurodegeneration, hormonal status and others. Over the last few years attention has turned to the possibility that treatments which interact with different aspects of the disease process may be more effective then specific drugs from mainstream pharmacology which are often designed to target single neural substrates. Herbal extracts containing many potentially active compounds may show some promise in this respect. As Mantle (2000) recently wrote "...such a polypharmacological approach, with attention to the individual is strikingly similar to philosophy of traditional herbalism".

In our own laboratory we have been examining the effects of herbal extracts upon cognitive function in healthy young adults. The rationale behind this approach is that any treatment which effectively improves mental performance in such individuals is likely to be effective in the treatment of age-related cognitive decline and possibly dementia. Extracts which we have examined include Ginseng, Ginkgo biloba, a Ginseng-Ginkgo combination and several European herb species. The effects of Ginseng suggest that single doses may have a beneficial effect upon cognitive performance (see talk by Dr. Kennedy, this conference). One question arising from this is "what are the physiological mechanisms underlying these effects?" The experiments described in this talk were aimed at addressing this question by examining the effects of ginseng on glucose modulation, on brain activity and how these may relate to cognitive function.

Glucose has been shown to be capable of improving mental function in healthy young adults,

particularly during tasks associated with a particularly high level of mental effort. One such task is Serial Subtractions which is associated with increased heart rate, is rated as highly demanding and can be improved by the administration of glucose (Kennedy and Scholey, 2000). Indeed performing Serial Sevens (repeatedly subtracting seven from a given number) results in a measurable fall in blood glucose (Scholey et al., 2001). It therefore follows that any intervention which improves glucose regulation may modulate performance on this task.

There is some evidence that Ginseng can modulate blood glucose levels in animals, human diabetics and healthy humans. An experiment from our own laboratory confirms these findings. Our results showed that Ginseng can reduce resting blood glucose levels in healthy young volunteers. Specifically 200 mg of Panax Ginseng extract G115 significantly reduced blood glucose one to two hours following administration. Importantly this effect was time- and dose specific and was not evident in the first hour following Ginseng nor for a higher dose of 400 mg. These data suggest that Ginseng can promote uptake of blood glucose in a dose-dependent manner and therefore have implications for cognitive performance.

To assess this possibility experiments were performed using tasks which are known to be sensitive to glucose levels, namely the Serial Subtractions task described above (here we used Serial Threes and Serial Sevens). Twenty healthy young adults took part in a series of randomised, double-blind, balanced crossover studies. In Study 1 they received placebo, 120 mg, 240 mg and 360 mg of Ginkgo biloba (GK501). In study 2 they received placebo, 200 mg, 400 mg and 600 mg of Ginseng (G115). In Study 3 they received placebo, 320mg, 640mg, 960mg of a 60:1000 Ginkgo-Ginseng combination. On each visit participants were tested 1 hr, 2.5 hr, 4 hr and 6 hr following the days treatment and returned every seven days until all treatments had been completed. Following Ginseng there was an improvement in accuracy of performance of Serial Sevens for the 200 mg and 400 mg doses 4 hrs following treatment. Again a higher dose of 600 mg was ineffective in changing performance. This effect was particular striking when Ginkgo was added the Ginseng-Ginkgo combination was associated with dramatically improved performance of Serial Subtractions at all time points following administration. We interpret these data as suggesting that under conditions of high mental demand Ginseng may improve the delivery of glucose to biological mechanisms involved in intense cognitive processing and thus raise the level of mental performance (Scholey and Kennedy, 2001).

The final experiment addressed the issue of whether Ginseng administration directly influences brain function. This was assessed using electroencephalography (EEG), a technique which mea-

sures underlying brain activity via electrodes attached to the scalp. In this study fifteen participants took part in a three period crossover design where they received Single doses of 360 mg Ginkgo, 200 mg Ginseng and placebo. EEG activity was monitored using a full head array (comprising 18 electrodes) and was recorded 4 hours following the days dose. Each treatment was separated by a 7-day washout period. The results showed for the first time that Ginseng can directly modulate brain activity. Specifically there was a trend ($p=0.069$) towards a main effect for reduced P300 latency following Ginseng. An effect which is consistent with the notion that Ginseng improves aspects of memory, in particular the efficiency by which stimuli are assessed. Additionally there was a significant reduction in the theta waveband, which was most pronounced in frontal areas of the brain. There was a similar pattern for alpha brain activity, again with results being most pronounced more frontally. There was also a significant overall reduction in the beta waveform. The frontal lobes of the human brain are involved in so-called executive functioning controlling behaviours involved in planning, attention, decision-making and response organisation. They also play a crucial role in memory.

In conclusion the experiments described here go some way to explaining the potential physiological processes by which Ginseng improves memory function in humans. Ginseng can aid the regulation of blood glucose and this may have effects on cognitive processing (as well as other important health areas). The modulation of brain activity, as measured by EEG, also suggests that Ginseng is capable of direct effects upon neurotransmitter function which may be more pronounced in the frontal areas of the human brain. It seems possible that Ginseng may improve memory due to a complex interaction between metabolic and neurochemical effects (Scholey, 2001). This interpretation is reinforced by the complex dose-time-task interactions observed when measuring mental function. Indeed it is essential that similar experiments should include multi-dose and multi-time testing procedures. In the future it is hoped that these effects may be applicable to situations where cognitive function and in particular memory is fragile.

References

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