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Herbal extracts and memory enhancement: response to Scholey et al.

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This communication is a response to the “letter to the editor” authored by Scholey and colleagues in which they criticized the work previously reported by Persson et al. (2004). Their letter contains several accounts of criticism and, for the sake of brevity, this response will comment on the major issues raised by Scholey et al. regarding our original publication. The principal claim that they make is that, although negative findings of cognition-enhancing effects have been found in several studies, this is not enough evidence to conclude that these products do not improve cognitive performance. The authors emphasize that the methods used in these studies need careful examination and they identify a number of criteria that, preferably, should be met for these studies to be “adequately powered”. The problem is—and this is also discussed by Scholey et al.—that even if these criteria are met, there are still negative findings. The authors themselves refer to the results found in the study by Solomon and colleagues (2002) as representing a negative finding. They point out, however, that there are also other well-controlled studies that support the memory-enhancing effect of Ginko biloba. One example is the study by Mix and Crews (2002). We do not, however, agree with the authors that the findings of Mix and Crews (2002) are indicative of the cognitive-enhancing effects of Ginko biloba. There are several reasons for this. The significant effects of Ginko biloba reported in the study were found in only 3 of the 13 cognitive tests that were used. Also, even if the age difference between the groups was accounted for using difference scores, there was a significant difference in pretreatment performance (in favor of the Ginko biloba group) between the two groups on one of the tests, and it is quite possible that pretreatment differences may have led to differential effects on improvement over time. The finding of an effect of Ginko biloba on only one or a few of the cognitive tests used is by no means unique, and there is no study, to my

knowledge, that shows effects on all or the majority of the cognitive tests used. The negative findings together with the lack of dose effects, and the fact that effects are often only found at one or a few time points following administration certainly do not support the claims often made by manufacturers of these products that daily use will “improve short- and long-term memory, increase reaction time, and improve mental clarity”.

We would also like to take the opportunity to respond to some of the comments that were made on the recent report by Persson et al. (2004). The measurement of long-term effects of herbal remedies on memory performance makes it difficult to apply the same criteria as used in previous studies. For example, it is not possible to monitor the intake of a certain dose of Ginko biloba or ginseng for each participant over months and years. Therefore—and this was pointed out by the authors—some methodological problems are evident. One problem, and this is in many ways the primary concern, is the lack of control over the frequency and level of dosing. As was pointed out in the paper, one can only assume that the participants in the study used the product as recommended. At best, one can argue that this reflects a valid measurement of how the product is used in a large population. Duration of intake should not be an issue since the effects of these herbal remedies are not related to whether it has been used for a week, a month, or a year. Another problem that was raised by the authors was the lack of pre-treatment performance. Instead of using difference scores (which have proven statistically unreliable) direct group comparisons were made. The groups were carefully matched with regard to a number of important criteria that have been shown to effect memory performance, including age, education, gender, and basic cognitive status (as measured by the MMSE). The Ginko biloba/ginseng groups were also compared with a second well-matched group in an attempt to control for effects based on general health awareness. If herbal remedies have such a pronounced effect on memory performance, as suggested by the manufacturers, a difference in performance between the groups should have been found. Another comment regarded the participants’ awareness of the study (with

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this pertaining to the aspect of the use of herbal remedies), and the tester's awareness of the participants' conditions. It is highly unlikely that the participants even reflected on the relationship between the use of herbal products and memory performance, since these analyses were not a primary goal of the study (see also Nilsson et al. 1997). The statistical analyses were carried out on existing data that was collected during the second wave of the longitudinal study referred to in the paper. The questions regarding use of herbal products were included in one of several questionnaires given to the participants on issues such as life-style factors, health, and social variables. The questionnaire was filled out under the supervision of a trained nurse and carried out on a separate day from the psychological testing. Psychological testing was carried out by trained psychometricians who were unaware of the participant's responses to questions regarding Ginkgo biloba and ginseng.

The tests that were used have proven sensitive to a number of factors affecting memory performance including age, genetic background, gender, and birth order, and these tests have been used for assessing memory performance in several published studies (for more information, see <http://www.psy.umu.se/memory/Betula/Prespub.html>). We are fully confident that the tests have the sensitivity to pick up possible effects on memory related to herbal remedies. Also, verbal fluency has been widely used as a neuropsychological test, and the claim that the tests "have been generated solely for the purpose of the study" (implying that this may have biased the results) is not accurate.

Taken together, the positive memory effects in normal healthy individuals following herbal treatments remain elusive. The number of experiments is small and many experiments are of uneven quality. Ginkgo may have a more pronounced effect in slowing decline in dementia, and since neither Ginkgo biloba nor ginseng appears to be associated with health risks it is hard to recommend to people not to use it. Our data and the data of others also suggest that the positive results found in many studies may act on acute cognitive processes and not on chronic problems. None of the possible effects of Ginkgo biloba and ginseng on memory to date is specifically attributable to direct effects on memory processes. It is more likely that the effects are indirectly related to memory performance via direct effects on other processes such as attention and arousal.

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