Ginkgo biloba: specificity of neuropsychological improvement; a selective review in search of
differential effects

Kaschel R

CRD summary
The author concluded that chronic administration of Ginkgo biloba improved selective attention, some executive processes and long-term memory for verbal and non-verbal material. Although the conclusions reflected the evidence presented, the reliability of the conclusions is unclear given multiple limitations in the review processes.

Authors’ objectives
To assess the specific effects of chronic administration of Ginkgo biloba on neuropsychological outcomes in healthy and cognitively impaired participants of any age.

Searching
MEDLINE was searched from inception to May 2008 without language limitations. A previous Cochrane review of randomised controlled trials published between 1976 and 2005 was also searched for relevant included papers. Search terms were reported.

Study selection
Randomised double-blind placebo controlled trials (RCTs) that evaluated the effects of chronic administration (greater than four weeks) of Ginkgo biloba (at any concentration and over any period of time) on objective function-specific cognitive performance were eligible for inclusion. Studies of treatments of less than one month and those that reported global cognitive and pure sensory measures were excluded. All participants were considered irrespective of age and diagnosis (if any).

The included studies included participants with dementia, mild cognitive impairment (MCI), depression and multiple sclerosis. Healthy participants were included. Mean age of participants ranged from 21 to 83 years. Preparations, doses and treatment durations of Ginkgo were varied and included: EGB 761 (120mg to 240mg, four to 24 weeks), Lichtwer’s LI 1370 (120mg to 150mg, six to 12 weeks), ethanolic extract (1.14mg, 24 weeks), Blackmore’s extract (120mg, 30 days to 12 weeks), standardised Ginkoba extract (80mg to 184.5mg, six to 13 weeks) and Maze productos (80mg, eight months). Most trials evaluated EGB 761 extract. Cognitive outcomes considered included: memory (short-term, long-term), attention (intensity, selectivity), executive functions (working memory, concept formation, planning, flexibility) and intelligence (crystallised, fluid).

The authors stated neither how the studies were selected for the review nor how many reviewers performed the study selection.

Assessment of study quality
The authors did not state that they assessed validity. However, methodological aspects (sample selection, blinding, randomisation and so on) of included studies were discussed.

Data extraction
Data on cognitive function outcomes were extracted to calculate ratios and percentages of significant effects per cognitive function. Data on the highest dose and longest treatment duration were extracted where studies reported multiple comparisons and different treatment durations.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Ratios (significant versus non-significant) and percentages of cognitive functions per test with significant outcomes (in
Results of the review
Twenty nine RCTs (n=2,414 participants, 209 comparisons) were included in the review. Sample sizes ranged from 24 to 240 participants.

Ginkgo was associated with significant effects in memory functions in 20.7% to 32.6% of comparisons. Significant effects were more common in the long-term recall of verbal (23.0% short-term versus 26.5% long-term) and visual (20.7% short-term versus 32.6% long-term) material.

Ginkgo was associated with significant effects in the following proportions of cognitive functions: attention intensity aspect (33.0%), attention selectivity aspect (46.1%), executive working memory functions (15.3% to 20.7%), flexibility executive functions (23.4% to 24.4%), planning executive functions (9.5% to 33.2%) and fluid intelligence (37.8%).

Authors’ conclusions
Chronic administration of Ginkgo biloba improved selective attention, some executive processes and long-term memory for verbal and non-verbal material.

CRD commentary
The review question was clearly stated. Relevant papers may have been missed as only one database was searched and no attempts were made to search for unpublished papers. No measures were taken to minimise the risk of reviewer error and bias in the review processes. Aspects of study quality were discussed, but no formal validity assessment was done. No statistical tests of heterogeneity were performed. The decision to combine results statistically may not have been justified given significant study differences. The author acknowledged the limitations of small sample sizes and potential reporting bias. The author’s cautious conclusions reflected the evidence presented. The reliability of the conclusions is unclear given multiple limitations in the review processes.

Implications of the review for practice and research
Practice: The author did not state any implications for practice.

Research: The author stated that future RCTs of the effects of chronic administration of Ginkgo biloba on cognitive functions should use validated psychometric tests.

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