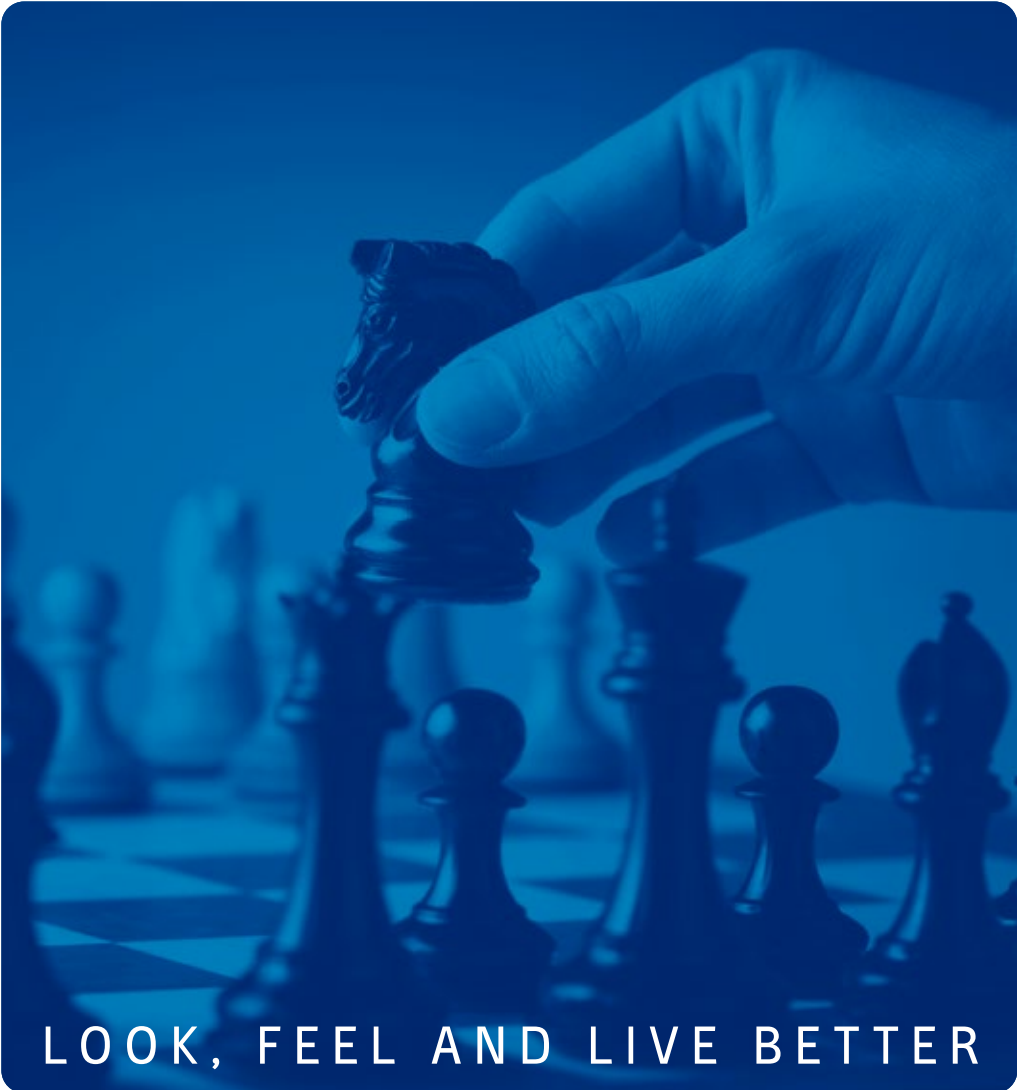


PYCNOGENOL®

Cognitive Health



Introduction

A normal cognitive function is a prerequisite for a healthy life. The brain function may be altered in case of either hyperactivity or hypo-activity of the brain. Hyperactivity is frequently observed in children, commonly referred to as Attention Deficit Hyperactivity Disorder (ADHD), whereas the decline of brain activity is related to the aging process.

It is very remarkable that Pycnogenol®, French maritime pine bark extract is able to both reduce hyperactivity in children and improve memory and cognitive function in adults.

Pycnogenol® is able to regulate the endothelial function. The active metabolites of Pycnogenol® build up inside the endothelial blood cells and have been proven to pass the blood-brain barrier (4). Pycnogenol® helps endothelial cells produce more nitric oxide (NO) which has multiple effects on brain function. Initially, NO increases blood flow (1), which improves oxygenation and the transport of nutrients to brain cells. Furthermore, NO regulates neuronal functions and thus contributes to processing signals inside the brain (2). In addition, NO helps modulate key neurotransmitters such as dopamine, serotonin and norepinephrine (3).

Pycnogenol® regulates NO production in two ways: it stimulates normal synthesis of NO from the endothelial NO synthase, and it inhibits the overproduction of NO which is toxic in high concentration in brain cells by blocking inducible NO synthase (4). Cognitive health requires a well-balanced release of NO in the brain.

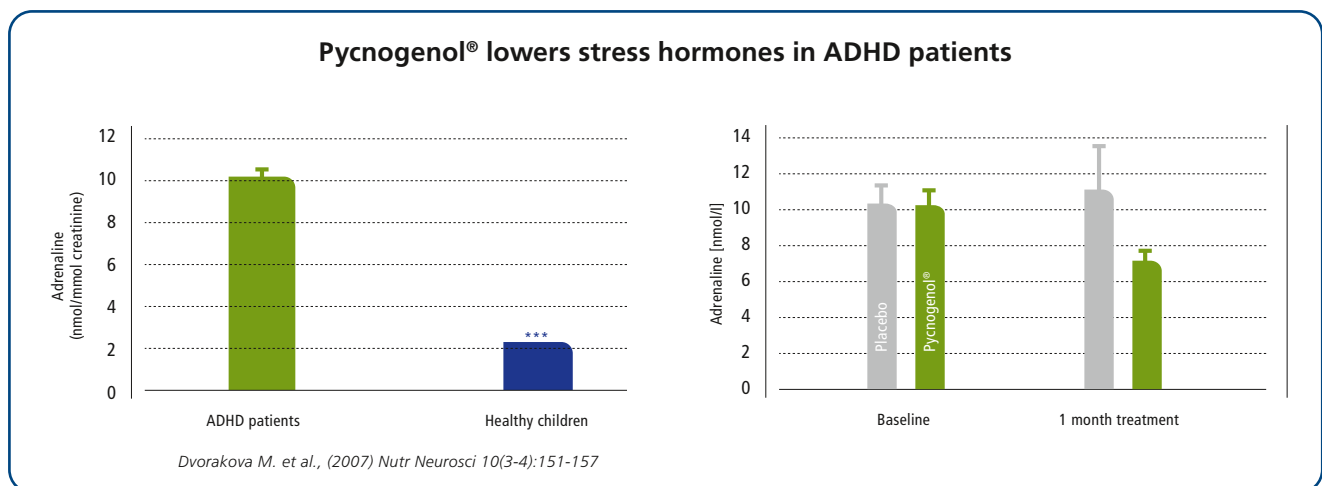
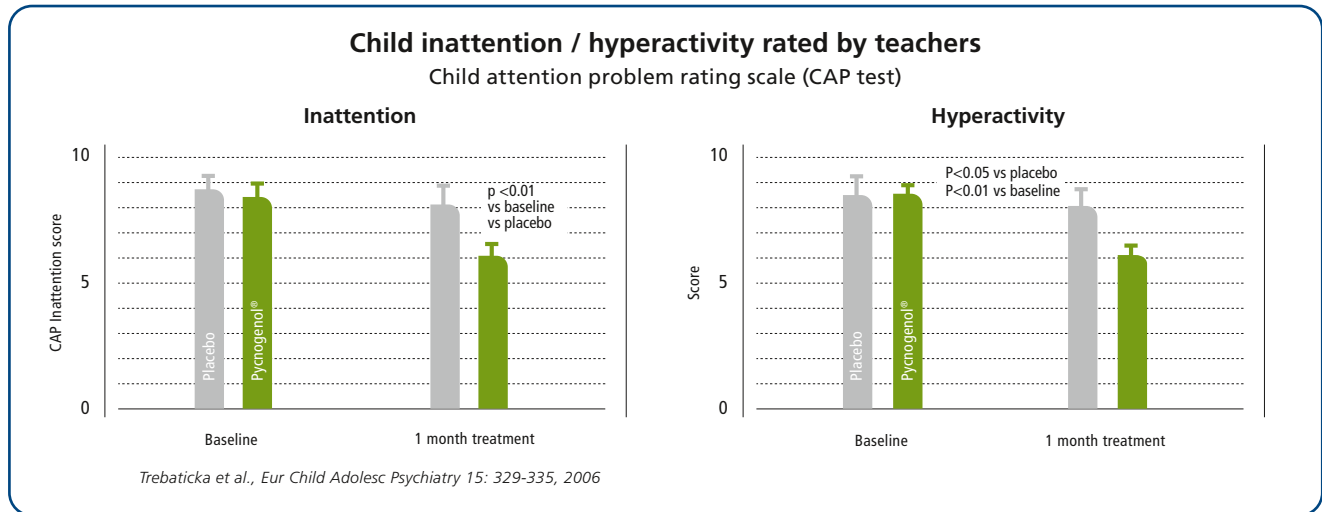
A number of animal experiments have demonstrated that learning increases NO production inside the brain (5). Therefore, the improvement of memory and learning in mice taking Pycnogenol® (6) is most likely the result of the enhancement of NO production inside the brain.

Pycnogenol® and Attention Deficit Hyperactivity Disorder

First reports about positive effects of ADHD patients taking Pycnogenol® were reported by Japanese neurologists who tested Pycnogenol® on 40 children with ADHD. The study reported a success rate of 40 % (7).

Another double-blind, randomized, placebo-controlled clinical study in the Department of Child Psychiatry at the University Hospital in Bratislava demonstrated that 1mg per kg of bodyweight a day of Pycnogenol® relieved hyperactivity and improved attention of children with ADHD compared to placebo (8).





No side effects were reported.

Judgements were made by both teachers and parents. Children who took Pycnogenol® produced less stress hormones (9), suffered less from oxidative stress and DNA damage was reduced (10).

The results of that clinical study show that Pycnogenol® helps to manage the symptoms of ADHD. Pycnogenol® may also act by reducing the production of stress hormones and reducing interference with the

system of neurotransmitters via modulation of the NO production.

Parents are sometimes reluctant to give prescription drugs such as methylphenidate, a stimulant sold under the trademark Ritalin®, to their children.

Altogether, Pycnogenol® offers a natural alternative to prescription drugs.



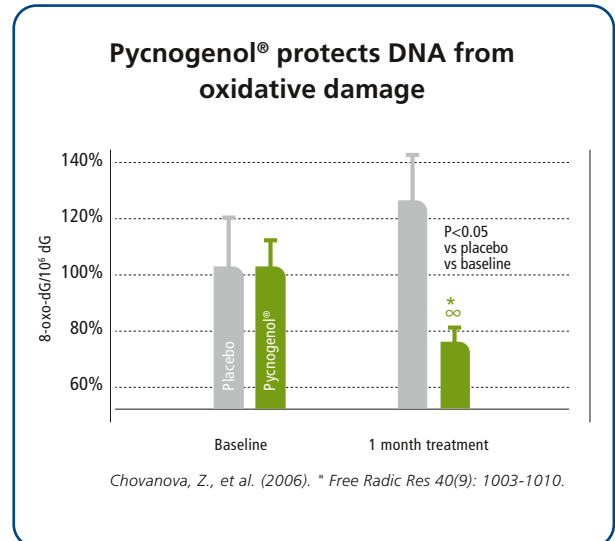
Improvement of the cognitive function in adults

A well-functioning vascular and nervous system is one of the very basic preconditions for a healthy life at all ages. The ability to learn and memorize is of the utmost importance for a healthy and productive lifestyle. From children to students, from professionals to baby boomers, learning is a continuous process.

The proven benefits of Pycnogenol® helping improve memory and ability to learn has been demonstrated in four clinical studies with various age groups across three generations.

First clinical trial with students

53 healthy students (aged between 18–27 years) received Pycnogenol® 50mg/twice daily for a period of eight weeks. A comparable group of 55 students was monitored as control. The statistically significant results showed Pycnogenol® improved attention, memory, executive functions and mood ratings



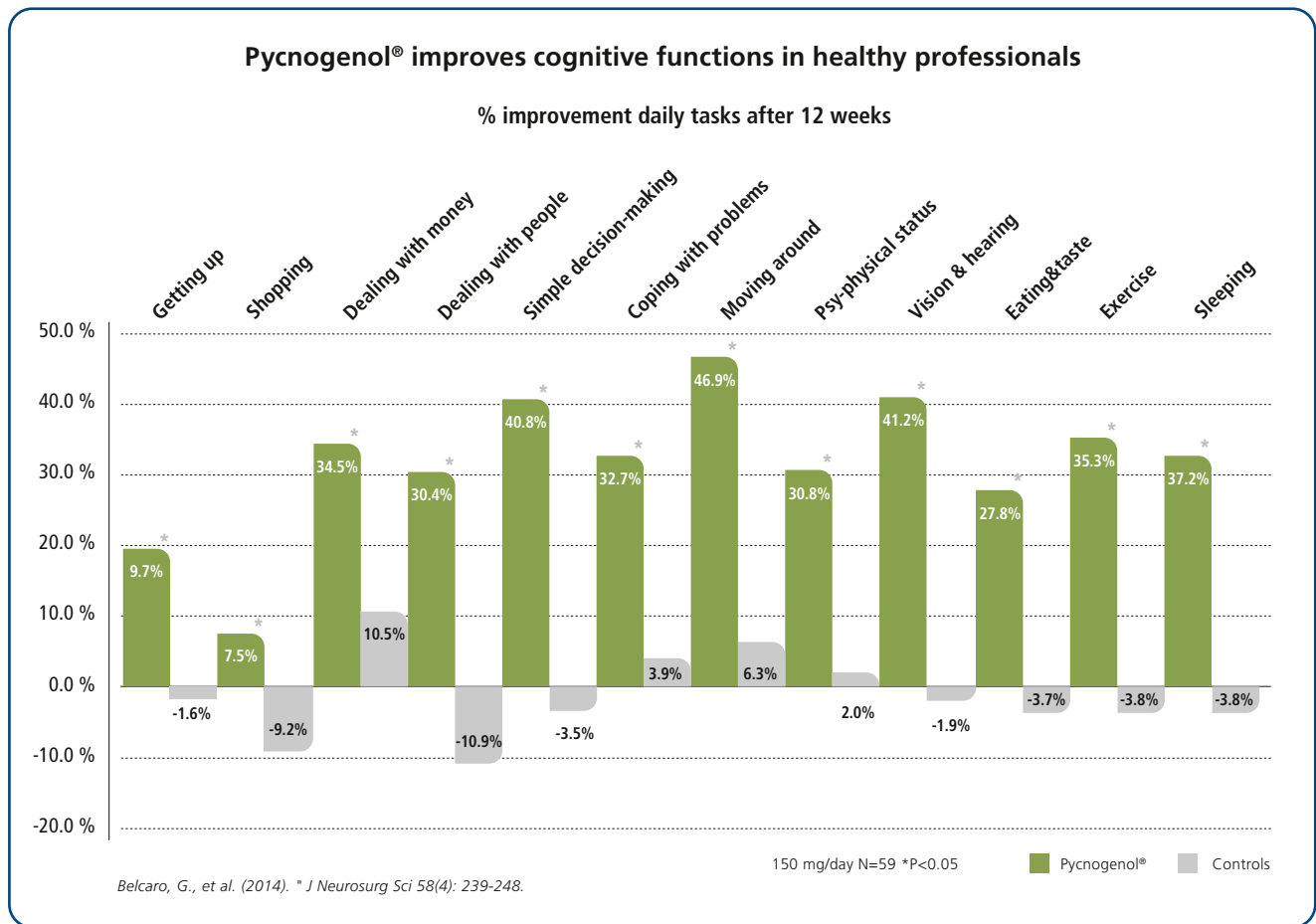
versus control. As a result, students performed better than controls in exams. This study has provided evidence that Pycnogenol® increases mental performance in normal, healthy, young subjects (11).

Cognitive test rating results Pycnogenol® vs control in healthy students

	Improvement after 8 weeks treatment Pycnogenol® N=55	Control N=52
Paced Auditory Serial Addition [connect numbers]	+ 52.9 %	+ 4.7 %
Picture recall [number of items]	+ 35.8 %	+ 11.6 %
Stockings of Cambridge [decreased # of moves required]	+ 21.8 %	0 %
Special recognition memory [correct responses]	+ 6.7 % (n.s.)	+ 2.6 %
Mental flexibility (ID/ED) [#shifting task stages completed]	+ 12.5 % (n.s.)	+ 1.1 %
Pattern recognition memory [correct responses]	+ 4.4 % (n.s.)	+ 3.5 %

Luzzi et al., Panminerva Med; 53: 75-82, 2011 100mg N=107





Second clinical trial with healthy professionals between 35–55 years

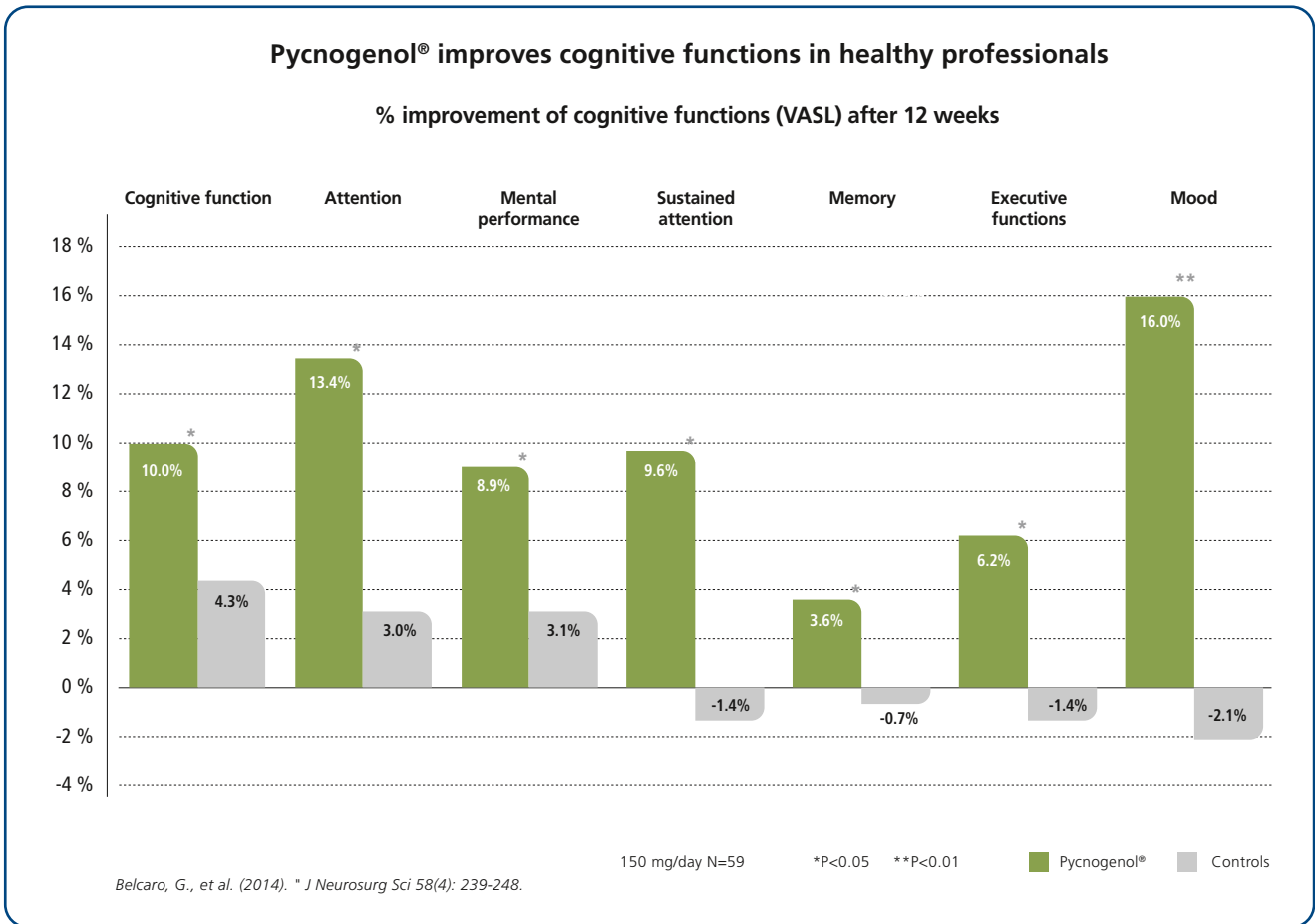
In a controlled study with 60 subjects under high oxidative stress, supplementation of 150mg/day of Pycnogenol® during a 12-week period significantly improved daily tasks of 30 professionals versus controls. Improvements of mental performance, alertness and contentedness were reported, together with a reduction of anxiety.

Cognitive tests revealed a significant improvement of memory in the Pycnogenol® group. Improvement of attention was measured in the Pycnogenol® group, whereas no significant changes were found in the control group.

In addition, the elevated oxidative stress measured at inclusion dropped down to normal levels in the Pycnogenol® group (-30 %), but remained high in controls (12).

Data suggests Pycnogenol® can be recommended to subjects with elevated oxidative stress, whether it is caused by negative daily stress or diseases.





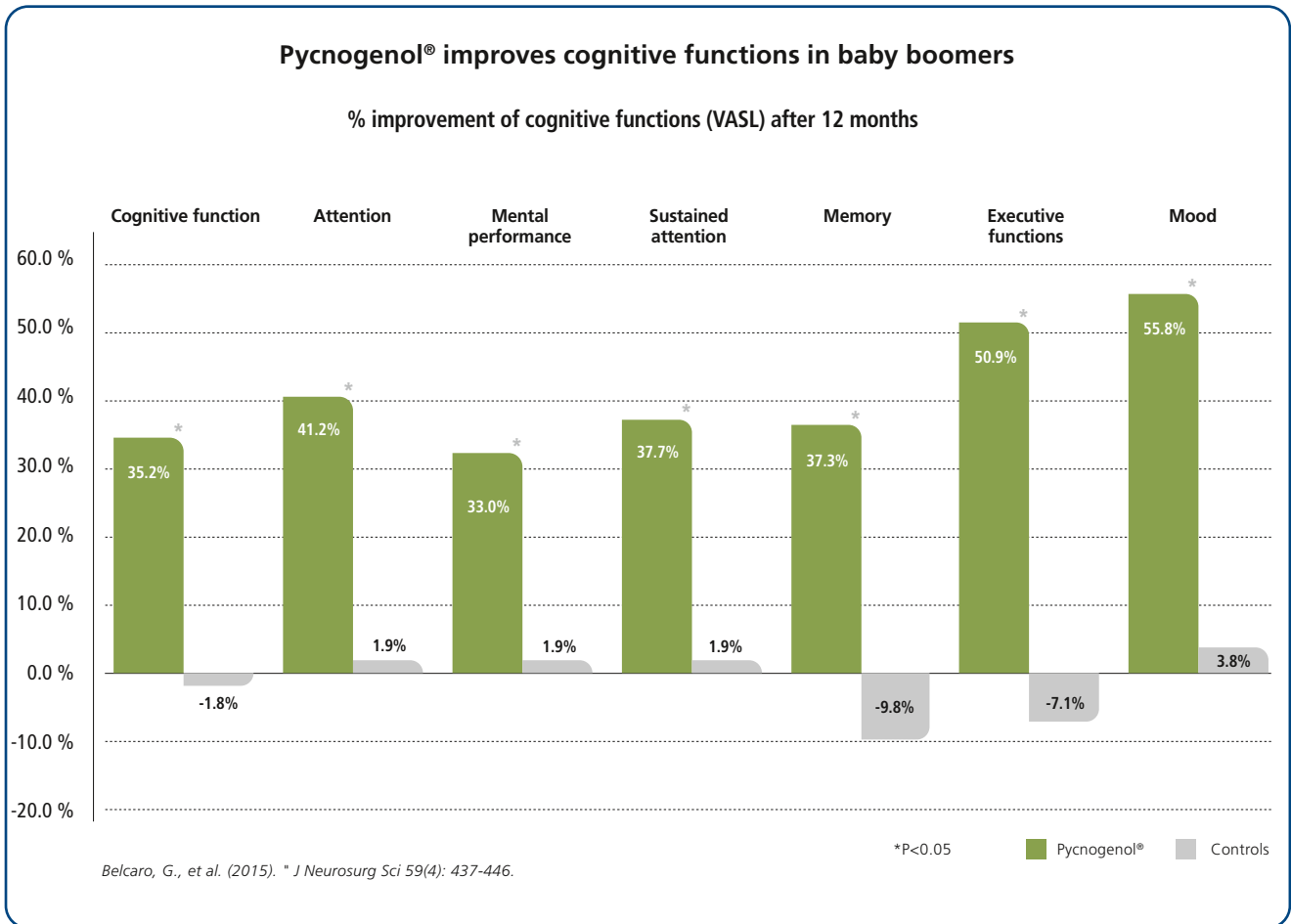
Third clinical study with baby boomers

Two groups of baby boomers aged around 65 years were tested 12 months after inclusion. Researchers investigate possible changes in their cognitive function and oxidative stress levels (13). Forty-five baby boomers received 150mg Pycnogenol® daily, 44 baby boomers remained without supplements as control. The control group showed a slight deterioration of memory, executive functions and daily tasks.

Cognitive impairment – measured by the short blessed test was reduced. In contrast, participants in the Pycnogenol® group showed a significant improvement in all tested parameters including not only attention,

mental performance and memory but also daily tasks like dealing with people, with money or just making decisions. This supports the benefits of taking Pycnogenol® for healthy aging and to help maintain a healthy cognitive function.





Fourth clinical study with baby-boomers

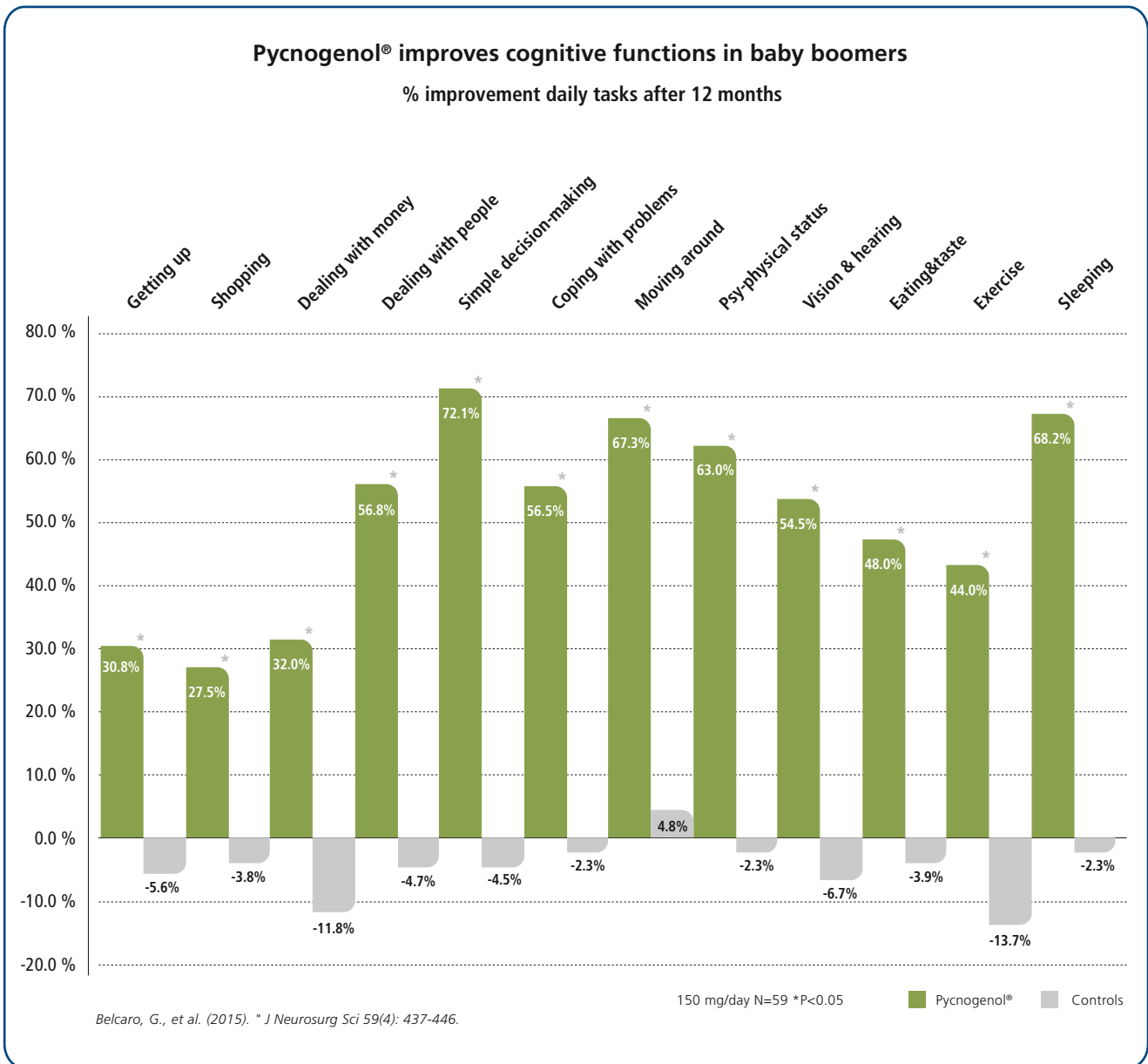
In a double-blind, placebo-controlled trial with 101 Australian baby boomers with moderate decline of their cognitive function, 150mg/day Pycnogenol® was prescribed for a period of three months. Cognitive function was tested with a computerized assessment system. The quality of working memory was significantly improved after treatment with Pycnogenol® versus placebo (14).

In all four clinical studies no side effects were reported.

Reduced oxidative stress

In all three investigations with adults and baby boomers, the level of oxidative stress in blood was reduced by 20–30% versus inclusion. Whether there is a causal relationship between the strong anti-oxidative effect and the improvement of cognitive function remains open for discussion. It is known that oxidative stress is a critical factor in the aging process. However, there are growing evidences that suggest NO also plays a role in the aging process of the brain.





Conclusion

Population aging generates a number of health concerns and maintaining a healthy cognitive function is of the utmost importance.

Research shows Pycnogenol® and its unique properties can help improve cognitive health at all ages.



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