

PQQ boosts brain function in older and younger generations



- Pyrroloquinoline quinone disodium salt (PQQ) is a nutritional component found in trace amounts in normal diet and in breast milk. It can also be obtained artificially by fermentation and purification.
- PQQ has antioxidant properties, promotes energy production in cells, and is known to enhance memory and cognition in older adults.
- Using advanced statistical techniques, Dr Kazuto Ikemoto and fellow researchers at the Niigata Research Laboratory of Mitsubishi Gas Chemical Company, Japan investigated whether PQQ substantially improves brain functions over much wider age ranges than previously known.
- The findings of this research could substantially improve the quality of life for many individuals.

The human brain supports several high-order functions that are essential for life, including perception, memory, attention, and the ability to understand language and interact with other people and with our environment. Brain functionality naturally deteriorates with age, even in healthy people. In addition, specific conditions, such as Alzheimer's and Parkinson's diseases in elderly people and attention-deficit/hyperactivity disorder (ADHD) in younger individuals, can compromise the ability of the brain to function normally. This can have dramatic consequences to the quality of life for people of all ages.

Dr Kazuto Ikemoto and his collaborators at the Niigata Research Laboratory of Mitsubishi Gas Chemical Company, Japan have carried out detailed statistical studies of the effects of a naturally occurring compound, known as pyrroloquinoline quinone disodium salt or PQQ, in maintaining and enhancing brain functions in healthy people.

PQQ: A miracle brain food

PQQ, in its disodium form, is a water-soluble salt of the coenzyme pyrroloquinoline quinone. A coenzyme is a relatively small molecule that interacts with the proteins responsible for regulating physiological processes in living organisms, like producing energy or synthesising new molecules, and helps them carry out their functions. PQQ occurs naturally in soils, in some fruits – like the kiwi fruit, and in human breast milk.

Mitsubishi Gas Chemical Company has developed processes to produce PQQ by proprietary bacterial fermentation at large scale followed by purification, and products have been extensively tested for safety, making it available as a food ingredient. To date, MGCPQQ is the only PQQ ingredient permitted to be sold in the EU by the European Commission. Mitsubishi Gas Chemical Company has also marketed the ingredient under the brand name BioPQQ in USA, Canada, and Japan.

PQQ is recognised as an important nutritional component; it is not currently classified as a vitamin but appears to be beneficial for long-term health.

PQQ's multiple benefits

The effects of PQQ on human metabolism are subtle and diverse. PQQ enhances the biogenesis of mitochondria, the organelles responsible for supplying energy to cells. It also has antioxidant properties, protects nerves from the degradation caused by neurotoxins, and improves skin texture. Experiments on rodents have also shown that PQQ supplementation reduces body fat accumulation, which could lead to obesity, without affecting normal body growth.

Conversely, PQQ deficiency can cause growth impairment, immune system dysfunction, and abnormal reproductive performance. Although the details of the molecular mechanism responsible for the physiological activity of PQQ remain largely unknown, these studies have shown that PQQ plays a crucial role in metabolic processes involving the transfer of electrons within biomolecules as a scavenger of dangerous free radicals in the body, and in the modulation of cell signalling pathways.

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The effects of PQQ at different ages

Most of what is known about the physiological effects of PQQ in humans comes from clinical trials conducted on adults, aged 45 years and older. These studies have shown that PQQ increases attention, improves the identification and processing of information, and benefits language and short-term memory. It also reduces stress and fatigue and promotes sleep.

However, so far, little work has been devoted to the effects of PQQ on younger adults between the ages of 20 and 40. The belief behind this choice is that PQQ does not exert any noticeable impact on younger generations, who are generally not afflicted by brain deterioration.

However, the absence of trials and rigorous analysis for younger people leaves a gap in our understanding of the potential benefits of PQQ in this age group.

PQQ clinical trials

To gain a more comprehensive insight into PQQ's potential effects on cognitive performance at various stages of adulthood, Ikemoto and colleagues examined how PQQ impacts the cognitive functions of adults between the ages of 20 and 65. The primary focus of their investigation

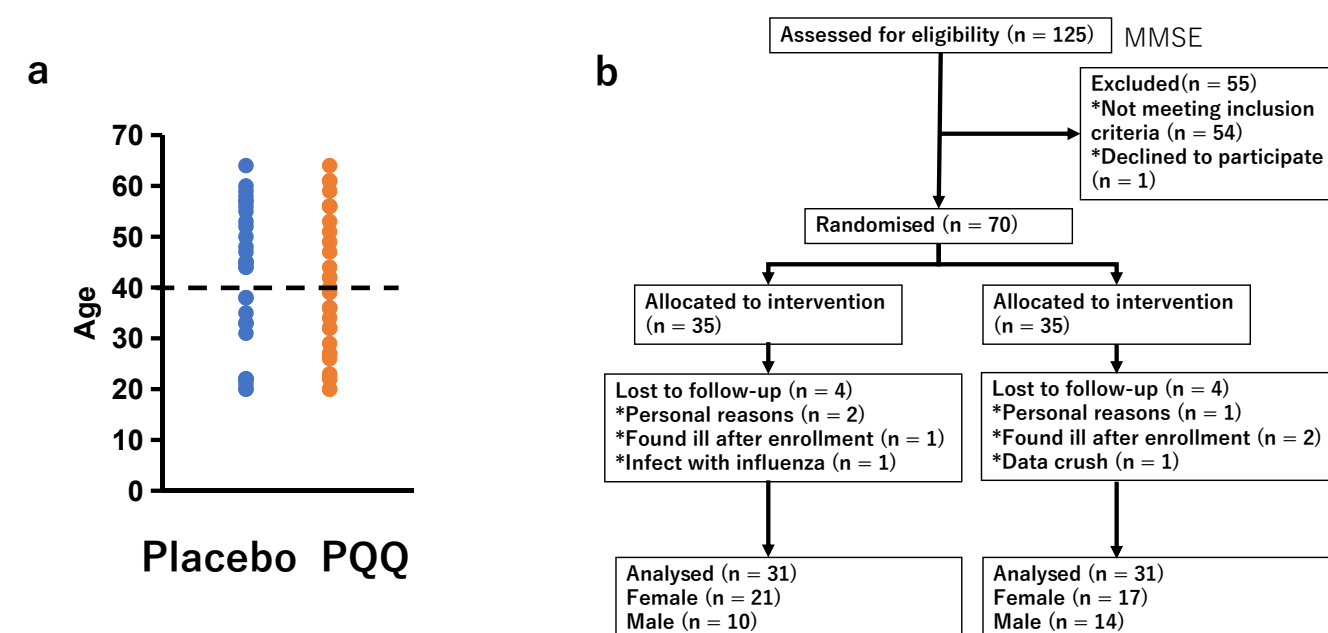


Figure 1. a) Age distribution of participants.

b) Flow diagram of the study.

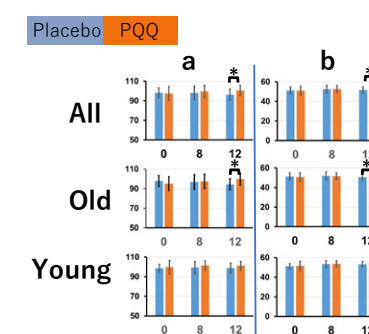


Figure 2a. (a) Composite memory and (b) verbal memory scores of the placebo and pyrroloquinoline quinone groups.

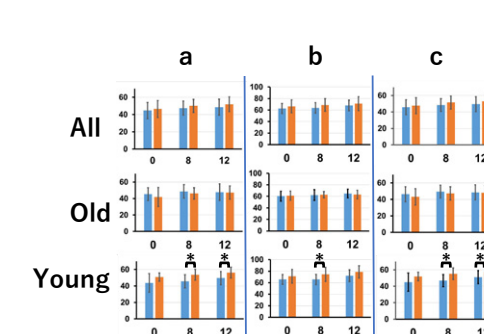


Figure 2b. Characteristic cognitive function scores for the young group - (a) cognitive flexibility, (b) processing speed, and (c) executive speed.

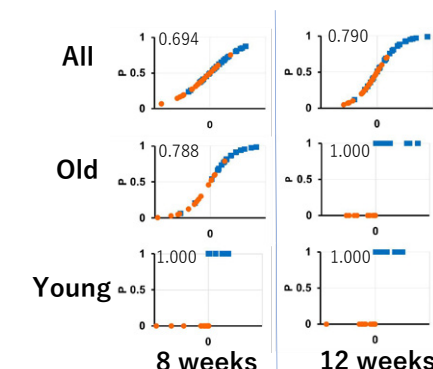


Figure 2c. Logical function scores where each dot represents an individual participant. The score indicates the probability of being able to determine placebo or PQQ intake. A score of 1 can be completely determined from the Cognitrix score.

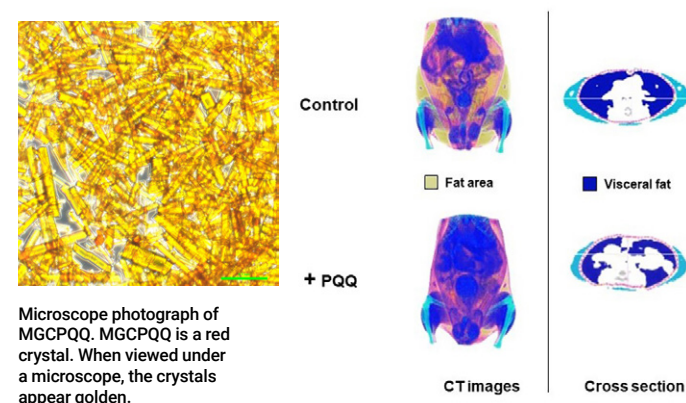
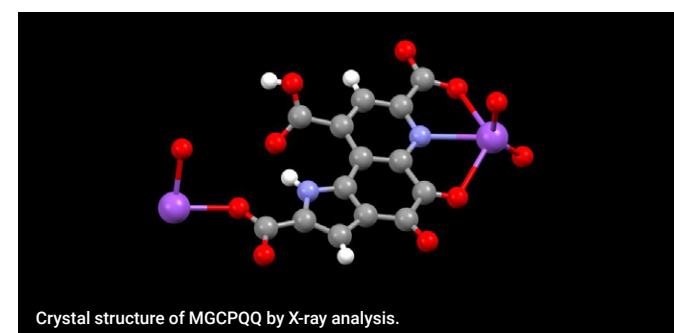


Figure 3. Microphotograph of PQQ and CT image of obesity mice.



was to explore PQQ's influence on cognitive abilities across different age groups within the adult population. The trials were conducted on 70 participants, whose ages were roughly equally distributed within two groups, aged 20–40 years and 41–65 years, respectively. To analyse the results of the trials, the team used a powerful statistical method known as 'logistic regression.' This technique can be used to classify groups with widely variable data, such as brain test scores over large age ranges.

PQQ improves brain function at all ages

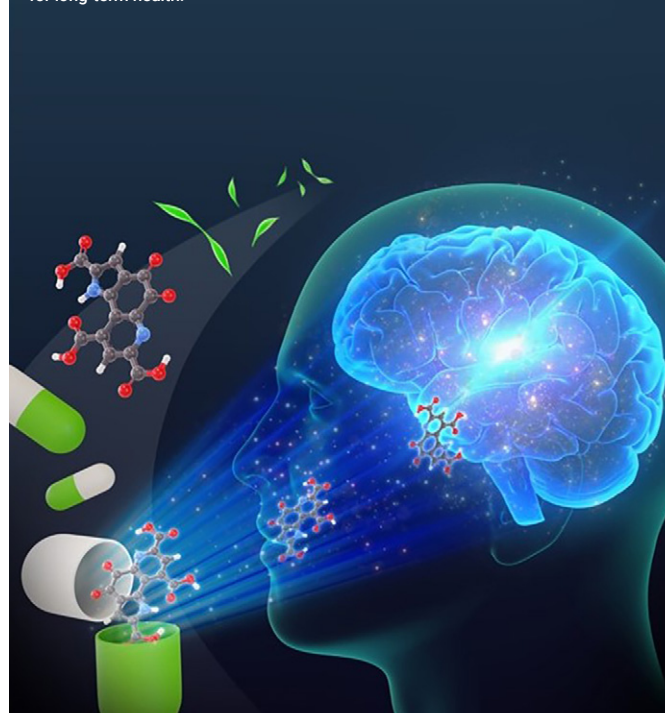
The team used logistic regression to assess whether statistically significant changes in cognitive abilities occurred between participants of the trial who were given a placebo and those who were administered PQQ in daily doses of 20 mg for a period of 12 weeks. After 12 weeks,

The results of the research confirm that PQQ acts as a powerful 'brain food' at all ages.

an improvement in cognitive functions, including cognitive flexibility and executive speed, along with memory, were observed in individuals administered with PQQ across both age groups. In younger adults, these improvements were observed within eight weeks.

The results of the research confirm that PQQ not only acts as a powerful 'brain food' at all ages, but also surprisingly indicates that cognitive function, memory improvement, and the response time to PQQ administration vary significantly among different age groups. 'We were surprised', says Ikemoto, 'to find that PQQ improves brain function at all ages. This effect was unexpected for younger generations, which are not affected by brain function decline.' The researchers suggest that the findings may have important implications for the use of PQQ as a supplement in learning and in physical training. Determined by the groundbreaking research findings, the team is now studying how PQQ affects human metabolism in addition to brain function; for instance, how it helps prevent fat accumulation and muscle decay with age. Ultimately, Ikemoto hopes that the extensive research on PQQ can help people live longer and healthier lives.

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Personal response

What prompted you to examine the effects of PQQ on brain function across wider age groups?

Young adults aged 20–40 play an important role in society. However, to date, the research has been limited to older adults. It is also important that functional foods are effective for active businessmen. Therefore, I decided to investigate a wide range of age groups, including the younger generation.

According to your research, PQQ holds promise not only as an exceptional 'brain food', but also to influence human metabolism, for instance in suppressing fat accumulation. What are the most promising future applications of PQQ in this context?

PQQ increases and activates mitochondria, which are responsible for producing cellular energy. Therefore, PQQ has beneficial effects on mitochondria-related functions in various parts of the body. Additionally, PQQ can be expected to suppress ageing. We believe that mitochondrial function is most easily manifested in muscles. We aim to enhance the sports-related effects of PQQ intake. We hope that exercise and PQQ will work more effectively in maintaining proper weight and preventing metabolic syndrome and frailty. Studies have reported that diseases are caused

by deterioration of body functions due to ageing, metabolic syndrome, deterioration of brain function and metabolism. PQQ may be a functional food that enables the realisation of healthy and long life.

What are the most pressing questions that we need to address to develop a holistic understanding of how PQQ interacts with enzymes and other biomolecules in physiological conditions?

The function of PQQ in the body is still unclear. At this stage, we believe that the interaction between the ageing-related gene, *sirtuin* and mitochondria-related gene, *PGC-1α* with PQQ is important. Ingestion of PQQ enhances PGC-1 expression. PGC-1 is a transcription factor that plays a key role in mitochondrial generation and function. Exercise promotes PGC-1 expression and improves mitochondrial formation and function. Exercise thus improves the efficiency of energy metabolism, promotes muscle growth and recovery, and promotes fat burning. Exercise also helps reduce the risk of lifestyle diseases such as heart disease and diabetes. Therefore, we believe that the relationship with the function of this gene is important. In addition to this interaction, it is necessary to comprehensively investigate interactions with various enzymes.

Details



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Competing interest statement

RIKEN's joint research is sponsored by Mitsubishi Gas Chemical Company, Inc.

Bio

Dr Kazuto Ikemoto received his PhD in chemistry from Nagasaki University, Japan in 1995. Since then, Ikemoto has been working for Mitsubishi Gas Chemical Company, Inc, Niigata. He received the JSBBA Award for Corporate Researchers in 2023.

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Collaborators

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Further reading

Tamakoshi, M, Suzuki, T, Nishihara, E, et al, (2023) Pyrroloquinoline quinone disodium salt improves brain function in both younger and older adults, *Food & Function*, 14, 2496–2501.

Mohamad Ishak, NS, Ikemoto, K, Kikuchi, M, et al, (2021) Pyrroloquinoline quinone attenuates fat accumulation in obese mice fed with a high-fat diet. *Daphnia magna* supplied with a high amount of food, and 3T3-L1 adipocytes, *ACS Food Science & Technology*, 1(10), 1979–1989.

Akagawa, M, Nakano, M, Ikemoto, K, (2016) Recent progress in studies on the health benefits of pyrroloquinoline quinone, *Bioscience, Biotechnology and Biochemistry*, 80(1), 13–22.

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