



Verifying psychophysiological effects during hydrogen inhalation



Exploring new possibilities in hydrogen intake

Joint research program with the University of Tsukuba since December 2016

— Verifying psychophysiological effects during hydrogen inhalation —

Since December 2016, Aqua Bank has been conducting a study to verify psychophysiological effects during hydrogen inhalation. The research is being conducted under the supervision of Dr. Yukihiro Yada at the University of Tsukuba Graduate School. As part of the study, Aqua Bank has asked CPCC Co., Ltd., a third-party institution with expertise in human clinical trials, to carry out clinical testing with the approval of the University Ethics Committee.

Significant results have been obtained for a variety of verification items over the course of the research. Our work has certainly verified the efficacy of portable hydrogen gas inhalers, while also helping provide evidence for other forms of hydrogen-related research. The psychophysiological effects on healthy subjects in particular was clearly demonstrated through our recent clinical trials—which is great news not only for our company, but for the many people who work with hydrogen as well. We are delighted to be able to confidently offer hydrogen-related projects to our customers.

Aqua Bank used this study as a jumping-off point in our efforts to scientifically verify the effects of hydrogen, and we intend to work even harder to contribute to people's good health in the future. In closing, we would like to take this opportunity to offer our sincerest gratitude to Dr. Yukihiro Yado and everyone who has supported us in our efforts so far.

> Takashi Takehara Aqua Bank Co., Ltd. President and CEO



Aqua Bank CEO Takashi Takehara (left) with Dr. Yukihiro Yada (right) Tests were conducted in a thermostatic and humidistatic room in order to prevent external factors

from influencing the clinical testing lab at the CPCC clinic

Takashi Takehara

Agua Bank Co., Ltd.

Takashi Takehara graduated from the Department of Materials Physics in the School of Engineering Science, Osaka University in 1983. He then went on to establish a research lab to develop freshness preservation techniques using magnetic fields and environmental controls. In 1987, Takehara founded NCA System Services Co., Ltd. and was appointed president and CEO. He first got into the telecommunications business in 1997. founding BAJ Co., Ltd. business in 1997, founding BAJ Co., Ltd. where he served as president and CEO as well. In 2011, Takehara founded Aqua Bank Co., Ltd. with the aim of extending people's healthy years. He currently serves as president and CEO of Aqua Bank.

Yukihiro Yada, MD

School of Integrative and Global Majors (SIGMA) at the University of Tsukuba PhD Program in Human Biology

Yukihiro Yada joined the Kao Soap Company (now Kao Corporation) in 1984, where he worked on basic Kao Corporation) in 1984, where he worked on basic research in the area of skin physiology. His team was one of the first in the world to explain the mechanism for UV-driven melanism in skin and to describe lipid metabolism in skin affected by atopic dermatitis. During that time, he studied overseas and received his Doctor of Medicine degree in 1992. He has been a senior researcher since 2010, while concurrently serving as a professor in the School of Integrative and Global Majors (SIGMA) at the University of Tsukuba. His areas of specialization include integrated physiology (which incorporates central, autonomic, and peripheral nerve function), skin physiology (skin physiology (Winch intor) portates central, autonomic, and peripheral nerve function), skin physiology (skin aging and analyzing the functions of various types of skin cells), and biochemistry (analyzing intracellular information transmission system mechanisms and body composition). Yada has published numerous papers and taught many seminars.





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in the medical field

Note: The data published here from various clinical tests involving hydrogen inhalation were obtained under specific testing conditions. They do not necessarily reflect data associated with Aqua Bank products or guarantee the quality of those products.

What are the revolutionary possibilities in hydrogen inhalation?

Effects of hydrogen inhalation on psychological and physiological functioning

We conducted clinical tests on the effects of hydrogen inhalation using a portable hydrogen gas inhaler. Research was done under the supervision of Dr. Yukihiro Yada at the University of Tsukuba Graduate School.



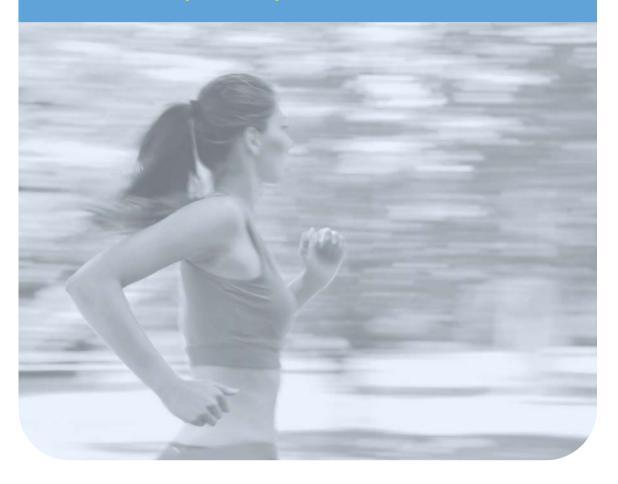
Clinical tests

I

Verifying the effects of hydrogen gas inhalation on psychological and physiological functioning

We conducted public clinical testing through the University Ethics Committee.

Test subjects: Healthy women in their 20s and 30s

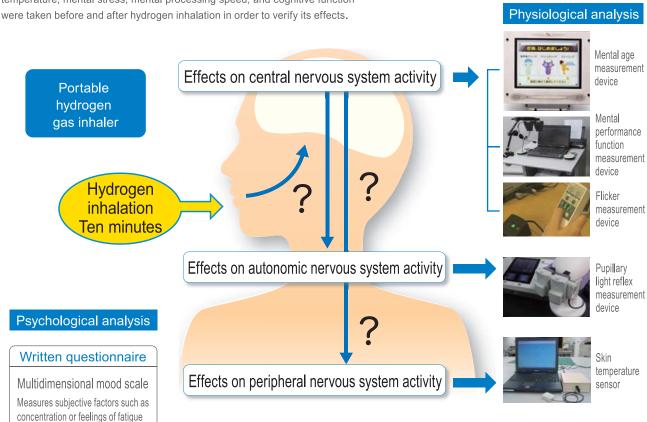




We hoped to confirm physiological activity resulting from the direct inhalation of hydrogen...

These clinical tests sought to demonstrate the effects of hydrogen inhalation via a portable hydrogen inhaler. The study was conducted on twenty healthy women in their 20s and 30s living in the Tokyo area. Participants were given a written questionnaire and physiological measurements were taken. The tests were conducted over the course of two days. Measurements such as skin temperature, mental stress, mental processing speed, and cognitive function

Pupil contraction rate Skin temperature Mental processing speed Mental stress Cognitive function



What mental and physical changes are caused by hydrogen inhalation?

We used a variety of instruments to measure psychological and physical changes in healthy women (age 20-39) as a result of hydrogen inhalation.

Test subjects: Healthy women in their 20s and 30s living in Tokyo and the surrounding area (n =17)

Skin temperature sensor



of tension, the sympathetic nervous system takes over, contracting blood vessels and reducing body temperature in the fingertips. The parasympathetic nervous system is dominant when we're in a relaxed state, and this raises skin temperature in the fingertips. These differences in skin temperature can be measured.

Measuring skin temperature

Pupillary light reflex measurement device



The pupils' reflexive reaction to light can be used to measure the status of the autonomic nervous system. This is because when the parasympathetic nervous system is dominant, the eye that experiences a light stimulus gets smaller than the other eye (has a higher contraction rate).



Measuring pupil contraction rate

Flicker measurement



Flicker measurements are a way to study eye fatigue and optic nerve sensitivity by looking at whether the eves are able to distinguish between bursts of light when it is flashed at high speed.



Measurements taken using numerical indicators from various devices able to measure psychological and physiological changes due to hydrogen inhalation

Measuring mental processing speed

Mental age measurement device



A mental age measurement device uses a screen that users tap to select answers to various questions, including fill-in-the blank equations or remembering colors or numbers. The results are used to determine things like mental age, mental stress, and brain health.



Mental performance function measurement device



Mental performance measurement devices measure a variety of performance indicators for the brain, which controls cognition and behavior. They work by having subjects engage in complex tasks, follow rules, perform mental switching, update information, and so on.



Measures short-term memory, left-right perception, hearing function, visual function, finger movement function, and knee movement function

Relaxation effects

The relaxation effects of hydrogen inhalation are already known, but we conducted clinical tests in order to verify these conclusions through the collection of detailed measurement values. Changes due to hydrogen inhalation were confirmed in the form of mood changes, an increase in skin temperature, pupil contraction rate, and measurements of pupil diameter.

What are relaxation effects?

Two different nervous systems operate in humans in a balanced way in order to maintain health. They are the sympathetic nervous system and the parasympathetic nervous system.

Sympathetic nervous system

Functions when the body is active, stressed, or tense

Parasympathetic nervous system

Functions when the body is resting, recovering, or relaxed

In order to maintain a state of relaxation, the parasympathetic nervous system must take a dominant position over the sympathetic nervous system. We conducted clinical tests in order to find out how those changes show up as a result of hydrogen inhalation. Verification tests were conducted in order to collect detailed measurement values.

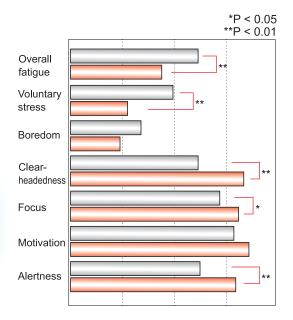
Mood changes before and after hydrogen inhalation using a visual analog scale (VAS)

Visual analog scale (VAS)

Psychological analysis using a written questionnaire

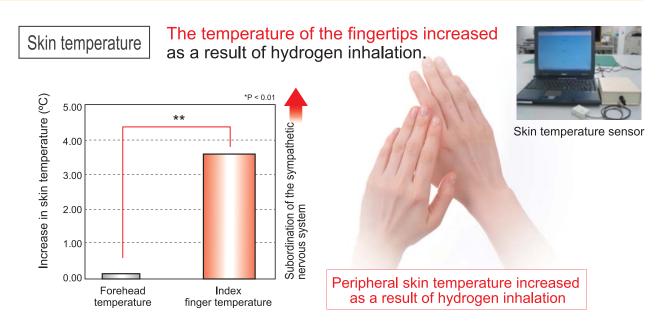
Multidimensional mood scale to measure subjective factors such as concentration or feelings of fatigue

Changes in mood were observed before and after hydrogen inhalation. (Individual results varied)



Feelings of fatigue and voluntary stress were reduced, while clear-headedness, focus, and alertness increased as a result of hydrogen inhalation.

Effects of inhaling hydrogen on sympathetic nervous system activity (peripheral skin temperature)

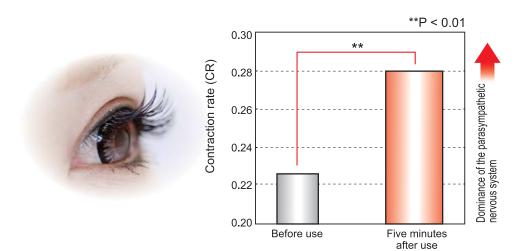


The study confirmed inhibition of the sympathetic nervous system and dominance of parasympathetic nervous system activity.

Effects on autonomic nervous system activity as a result of hydrogen inhalation (pupil contraction rate)

Pupil contraction rate

Pupil contraction rate increased significantly as a result of inhaling hydrogen.





Pupillary light reflex measurement device

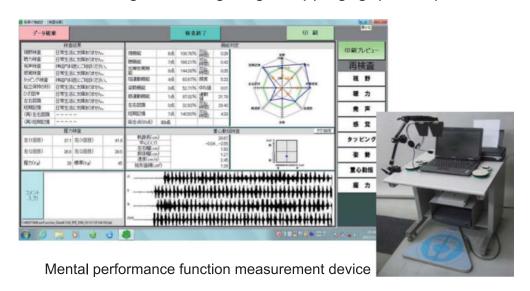
Parasympathetic nervous system activity is dominant (sedative effects confirmed)

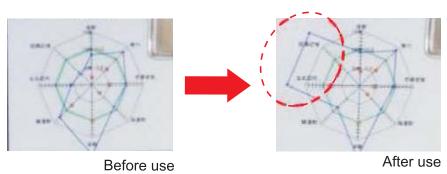
We measured the effects of hydrogen inhalation on mental performance and brain stimulation as well as on various kinds of brain activity, including short-term memory, left-right perception, hearing function, visual function, finger movement function, and knee movement function.

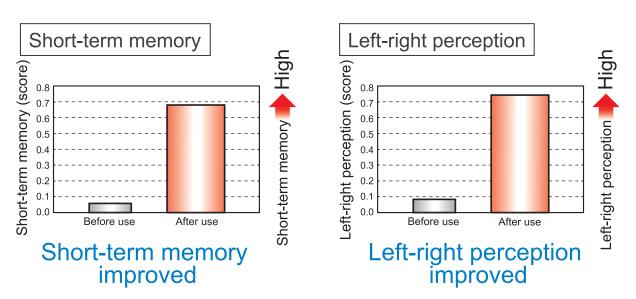
Effects of hydrogen inhalation on mental performance

Mental performance functions:

We comprehensively measured cognitive function by looking at functions like sight, hearing, finger-tapping, grip, and postural sway.

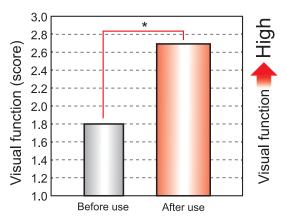




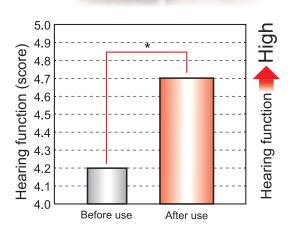


Effects of hydrogen inhalation on brain activity level





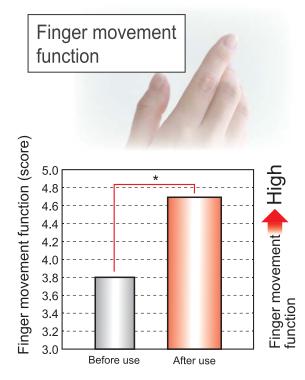
Hearing function



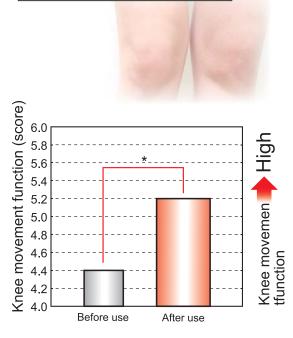
Visual function improved

Hearing function improved

Knee movement function



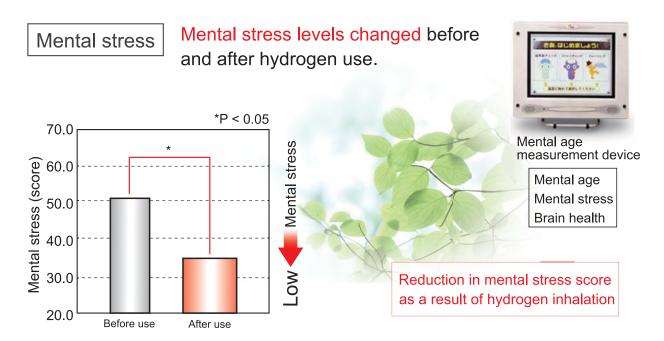




Knee movement function improved

We also scientifically measured mental stress effects along with relaxation effects. We found that hydrogen inhalation not only lowered mental stress, but also stimulated the brain.

Effects of hydrogen inhalation on mental stress



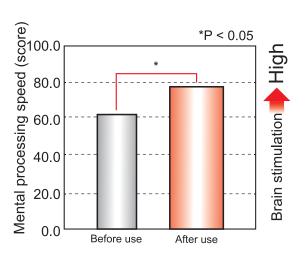
Reduction in mental stress was confirmed

Effects of hydrogen inhalation on brain stimulation

Mental processing speed

Hydrogen inhalation was shown to have a brain-stimulating effect.

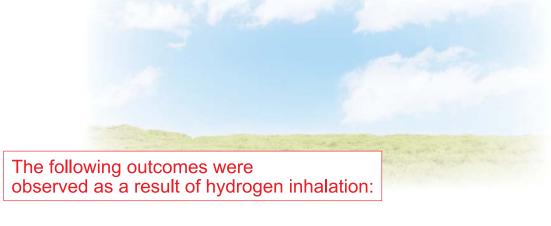






Stimulation of brain function was confirmed

Discussion and summary



Subjects reported a reduction in fatigue and voluntary stress along with a significant increase in clear-headedness, focus, and alertness

Significant increase in pupil contraction rate along with a significant increase in peripheral skin temperature

Suggestion of inhibited sympathetic nervous system activity and increased parasympathetic nervous system activity

Significant increase in blood flow,

particularly in the center of the prefrontal cortex of the brain

Suggestion of possible effects on cognition, emotion, and other brain functions

Reduction in mental stress scores and better mental processing speed

Suggestion that hydrogen inhalation may lower stress and increase brain activity

Improved mental performance according to functional measurements in sight, hearing, finger movement, and other indicators

Suggestion that hydrogen may enhance left-right perception and short-term memory

Potential effects confirmed not only on autonomic nervous system functioning, but on central nervous system functions as well.

We will continue to study effects on central nervous system functioning in the hopes that we might verify hydrogen's ability to alleviate fatigue and stress, improve sleep, and enhance athletic performance.

Analysis of brain function using near-infrared spectroscopy (NIRS)

Why did we get these results?

Study of blood flow in the brain during hydrogen inhalation

Analysis of brain activity (changes in blood flow in the prefrontal cortex) as a result of hydrogen inhalation

Measurement principle

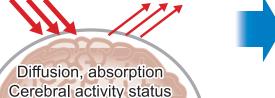
Near-infrared light (700-950 nm) is projected into the head (frontal region).

The absorption properties of light that bounces back are changed.

Oxy-Hb concentration reflects hemodynamics,



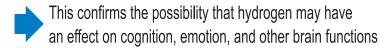
allowing us to study brain activity

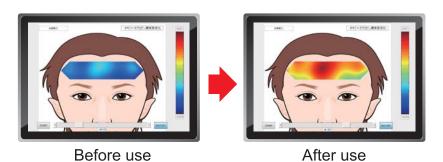


NIRS equipment



Hydrogen inhalation produced significant increase in blood flow, particularly in the center of the prefrontal cortex of the brain





Blood flow rapidly improved, confirming stimulation of the brain

Clinical tests

Effects of ongoing hydrogen gas inhalation on mental performance functions in the elderly

We conducted public clinical testing through the University Ethics Committee.

Test subjects: Healthy men and women in their 60s and 70s





We hoped to confirm immediate and lasting correlations with the inhalation of hydrogen...

These measurement tests were conducted on healthy elderly men and women in their 60s and 70s. The tests measured both temporary, immediate effects as well as lasting effects resulting from two weeks of consecutive use. We also measured the effects of ongoing hydrogen inhalation.

Short-term memory Left-right perception Mental processing speed Mental stress Brain health **Blood tests**

Physiological analysis

Portable hydrogen gas inhaler



Used to measure skin temperature



Used to measure pupil contraction rate



Used to measure mental processing speed

isual function



Before inhalation

Measurement

Hydrogen inhalation

After inhalation

Measurement

Two weeks

Measurement

Before

inhalation

Hydrogen inhalation

After inhalation

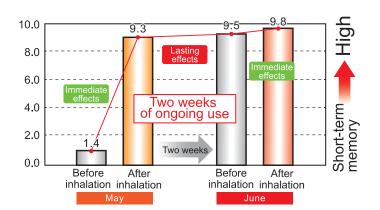
Measurement

Hydrogen inhalation was carried out five times a day for two weeks, each inhalation lasting for five minutes

Effects of hydrogen inhalation on brain activity level

Short-term memory

After two weeks of ongoing hydrogen inhalation, participants maintained their high performance. This confirms both the immediate effects of hydrogen and the maintaining of high performance with regular (ongoing) use.





Mental performance function measurement device

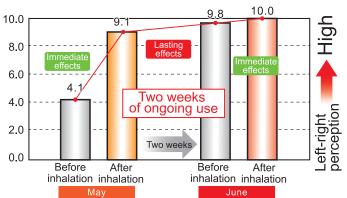
Short-term memory improved and stayed there

Effects of hydrogen inhalation on brain activity level

Left-right perception

Participants maintained their high performance after two weeks of ongoing inhalation, and two weeks after that as well.

This confirms both the immediate effects of hydrogen and the maintaining of high performance with regular (ongoing) use.





Mental performance function measurement device

Left-right perception improved and stayed there

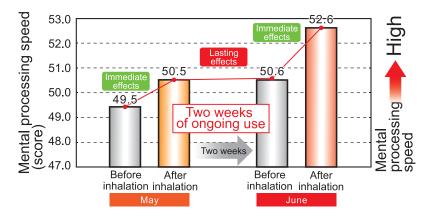
In order to measure the effects of hydrogen inhalation on mental performance functions, values were taken for mental processing speed, mental stress, and brain health before and after inhalation, and then two weeks after ongoing use. The results were then graphed. Effects were seen across all measures as a result of ongoing use. We also analyzed the effects of hydrogen inhalation on components related to mild cognitive impairment (MCI).

Effects of hydrogen inhalation on brain activity level

Mental processing speed

Mental processing speed scores improved as a result of hydrogen inhalation.

High scores were maintained after two weeks of ongoing inhalation, and two weeks after that as well.





Flicker measurement device

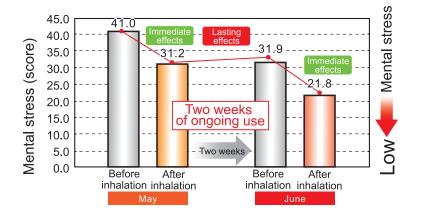
Mental function activity level improved and stayed there

Effects of hydrogen inhalation on mental stress

Mental stress

Mental stress scores fell as a result of hydrogen inhalation.

Low scores were maintained after two weeks of ongoing inhalation, and two weeks after that as well.





Mental age measurement device

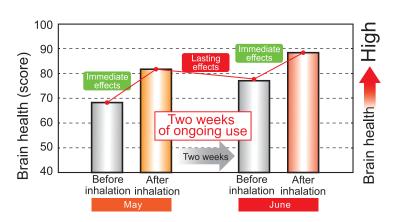
Mental age Mental stress Brain health

Mental stress was reduced and stayed there

Effects of hydrogen inhalation on brain health

Brain health Brain health scores improved as a result of hydrogen inhalation.

High scores were maintained after two weeks of ongoing inhalation, and two weeks after that as well.





Brain health was stimulated and stayed there

Effect of hydrogen inhalation on MCI-related components in the elderly

Results of blood tests measuring three components considered risk factors for MCI

検査項目	単位	摂取前			摂取2週後			
ApoA1	mg/dL	193. 9	±	23. 6	183. 7	±	21. 1	**
TTR	mg/dL	30. 85	±	6. 67	29. 60	±	5. 26	*
C3	unit	0.809	±	0. 330	1.035	±	0. 367	**
MCIリスク	-	0.652	±	0.070	0.645	±	0.072	
n=20								
平均値±標準偏差								

Note: Hydrogen inhalation was carried out five times a day for two weeks

It is likely that ApoA1 and TTR (components that inhibit inflammation) were reduced as a result of hydrogen inhalation. This conclusion was reached because (1) tests revealed a significant decrease in ApoA1 and TTR, but also showed a significant increase in C3; and (2) C3, which is produced in the liver, increased significantly and inflammation was inhibited.

Discussion on the results of hydrogen inhalation in the elderly (after two weeks of ongoing use)

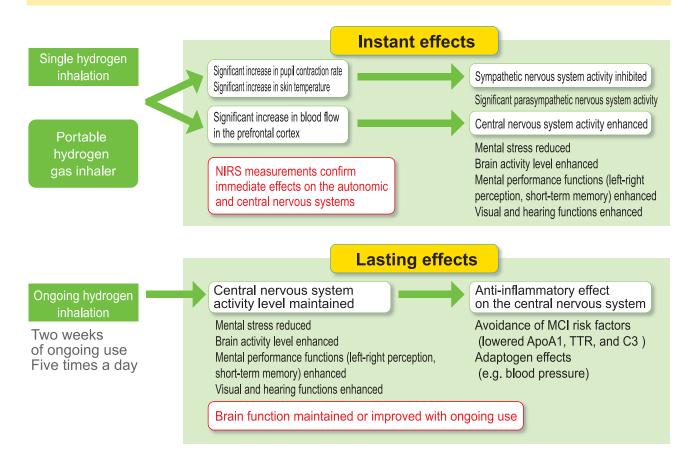
Compared to measurements taken prior to hydrogen inhalation, post-inhalation revealed significant decreases in MCI screen components ApoA1 and TTR, while C3 showed a significant increase. Other blood test results revealed a significant decrease in AST and a tendency for ALT values to decrease, findings that could be explained by hydrogen's antioxidant effects. In other words, inhaling hydrogen reduces oxidative stress on the body, improving liver function, increasing the production of C3 in the liver, and inhibiting inflammation. This in turn is what may lead to reductions in ApoA1 and TTR, components with are produced for the purpose of reducing oxidative stress and inflammation.

Other test results (blood pressure and LDL cholesterol) revealed that an adaptogen (a substance that enhances an organism's ability to adapt to the environment and stress) effect may lower test values when they are above the standard level or maintain them if they are not.

Loss of brain function (dementia) may be caused by Alzheimer's, Lewy bodies, or cerebrovascular issues (cerebral arteriosclerosis). Our MCI screening results showed significant changes in component factors associated with MCI risk, but only slight effects were seen in terms of MCI risk values. On the other hand, our mental stress test, flicker measurements, and mental performance function tests did show improved brain function, making it possible that hydrogen inhalation may, via a mechanism that improves brain function, help inhibit cerebrovascular issues (cerebral arteriosclerosis) if not Alzheimer's or Lewy bodies. It may also have a direct positive effect on nerve tissue.



Hydrogen inhalation summary (single use/ongoing use)



Clinical tests

Results of mental performance function tests on Kashima Antlers youth (18 and under) soccer players

Test subjects: Soccer players age eighteen and younger



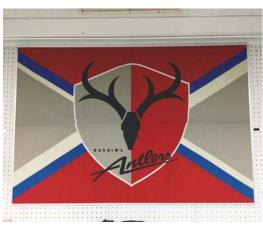


Changes in brain function as a result of hydrogen inhalation

After conducting a variety of performance tests on eighteen-and-under members of the Kashima Antlers youth soccer team, subjects inhaled hydrogen for five minutes in order to measure changes in their condition.

Static vision Dynamic vision **Cutaneous sensation** Mental stress Hearing function









What mental and physical changes are caused by hydrogen inhalation?

We used a variety of instruments to measure psychological and physical changes in eighteen-and-under members of the Kashima Antlers youth soccer team after five minutes of hydrogen inhalation.

Test subjects: Soccer players age eighteen and under

Dynamic vision measurement device



Dynamic vision is the ability to keep a moving object in the line of sight without losing track of it. This device measures the subject's ability to accurately track a moving object.

Measures static and dynamic vision







Mental age measurement device



A mental age measurement device uses a screen that users tap to select answers to various questions, including fill-in-the blank equations or remembering colors or numbers. The results are used to determine things like mental age, mental stress, and brain health.

Measures mental stress

Mental performance function measurement device



Mental performance measurement devices measure a variety of performance indicators for the brain, which controls cognition and behavior. They work by having subjects engage in complex tasks, follow rules, perform switching, update information, and so on.

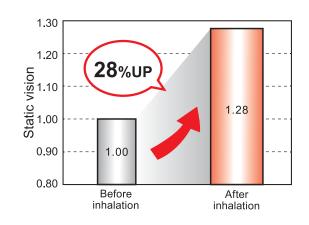
Measures cutaneous sensation and hearing function

After conducting a variety of performance tests on eighteen-and-under members of the Kashima Antlers youth soccer team, subjects inhaled hydrogen for five minutes in order to measure changes in their condition.

The relationship between sports and hydrogen inhalation

What effects can we expect hydrogen inhalation to have on athletic performance?

Static vision



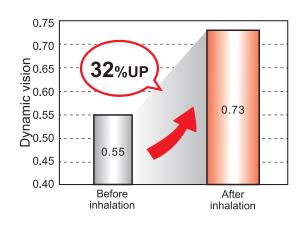


Dynamic vision improved by 28%

Dynamic vision measurement device

Static vision tests found that performance improved by 28% after hydrogen inhalation compared to pre-inhalation levels.

Dynamic vision





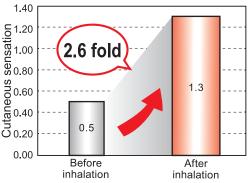
Dynamic vision improved by 32%

Dynamic vision tests found that performance improved by 32% after hydrogen inhalation compared to pre-inhalation levels.

Cutaneous sensation



Cutaneous sensation improved by 2.6 fold



Cutaneous sensation tests found that performance improved by 160% after hydrogen inhalation compared to pre-inhalation levels.

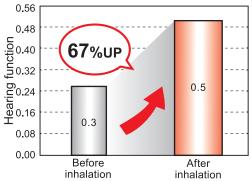
Hearing function



Hearing function improved by 67%

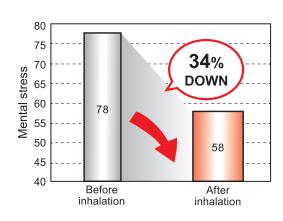


Mental performance function measurement device



Hearing function tests found that performance improved by 67% after hydrogen inhalation compared to pre-inhalation levels.

Mental stress





Mental stress was reduced by 34%

Specialty measurement devices found that stress was reduced by 34% after hydrogen inhalation.



Mental age measurement device Tests:

Mental age Mental stress Brain health

Tests:

Changes in brain function as a result of hydrogen inhalation show that hydrogen appears to be a promising way to boost athletic performance!

*Graphic data from in-house tests

Mental performance function tests on soccer players

Discussion of findings

We can infer that visual function improved due to the observed increases in dynamic vision, visual function, and left-right perception.

We can infer that athletic function and physical sensitivity improved due to the observed enhancement in skin sensitivity, finger tapping function, and posture function.

We can infer changes in mood and awareness, as participants reported reduced fatigue and stress as well as improved motivation and focus.



Overall assessment and next steps

One of the most notable results from the study was the reduced fatigue and stress plus increased motivation and focus seen in both healthy women and young soccer players.

As the results suggest that hydrogen inhalation improves dynamic vision and left-right perception while boosting athletic function and physical sensitivity, we can expect that it would help to maintain or improve key physical and psychological functions in soccer players.

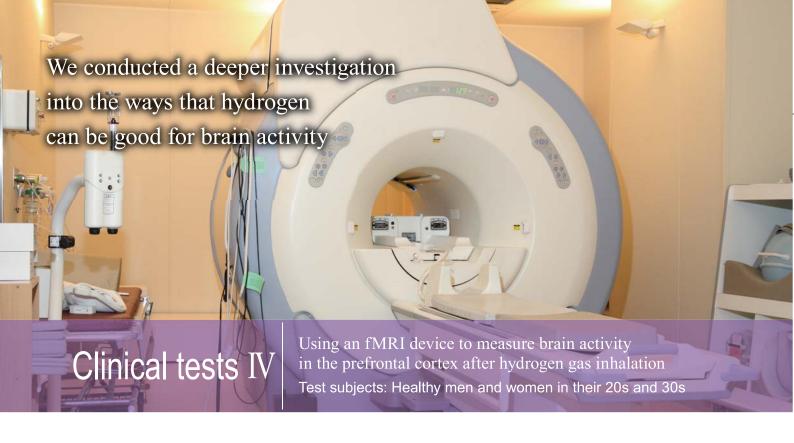
Going forward, we will need to study the effects of hydrogen on factors like performance and mood when it is inhaled before practice or games. We also need further tests to assess the ability of hydrogen to reduce fatigue and aid in physiological recovery when inhaled after practice or games.

Clinical tests IV

Using an fMRI device to measure brain activity in the prefrontal cortex after hydrogen gas inhalation

Test subjects: Healthy men and women in their 20s and 30s





Tracking changes in brain activity resulting from hydrogen inhalation

This test targeted healthy men and women in their 20s and 30s with the aim of tracking changes in brain activity resulting from hydrogen inhalation. An fMRI device was used to measure post-inhalation activity in the prefrontal cortex of the brain.

Activity in the prefrontal cortext

fMRI

The abbreviation fMRI stands for functional magnetic resonance imaging. This technology uses an MRI device to create cross-section images of the body, which can then be used to study brain activity.





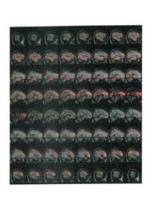


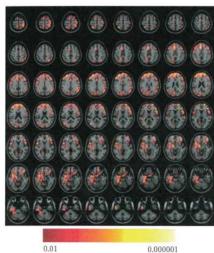
We used an fMRI device to study activity in the prefrontal cortex of the brain resulting from hydrogen inhalation.

Subjects rested for five minutes while inside the fMRI device, and then inhaled hydrogen gas using a portable hydrogen gas inhaler for five minutes. Images showing brain activity were taken under both conditions and compared with one another.

Test subjects: Healthy men and women in their 20s and 30s

Brain stimulation map during hydrogen inhalation P<0.01

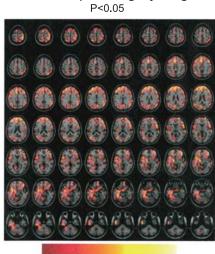


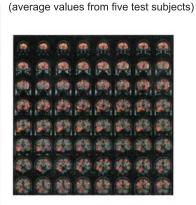




Brain stimulation map during hydrogen inhalation







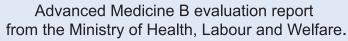
fMRI test results:
Hydrogen inhalation was shown to have an effect on brain activity.

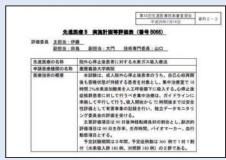
0.00001

Further potentials in the medical field

Hydrogen has been approved under the Advanced Medicine B category by the Ministry of Health, Labour and Welfare.

Hydrogen gas was given to a patient after they were resuscitated from cardiopulmonary arrest. The hydrogen helped save their life and protect brain function, making it an important rehabilitative treatment method.





Note: Advanced Medicine certification is given by the Certification Committee for Advanced Medical Technologies after a rigorous evaluation process to evaluate the treatment's efficacy, safety, and necessity.





Advanced Medicine B, Item #3 (66 types) No. 68: Hydrogen gas inhalation treatment December 9



Posted on the official **MHLW** website

On December 9, 2016, the Ministry of Health, Labour and Welfare approved hydrogen gas inhalation for Advanced Medicine B certification. Japan (the MLHW) is the first country in the world to demonstrate the effectiveness and safety of hydrogen gas.



Providing evidence-based solutions

Our mission is to conduct research aimed at finding the best way to create hydrogen, the best intake method, and the best intake timing so that people receive maximum benefits, meanwhile producing evidence to support these findings.

By tapping into the synergy of industrial-academic cooperation, Aqua Bank offers hydrogen as one of its core solutions as it strives to find more ways to make people happier and healthier.



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