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SERIES H: AUDIOVISUAL AND MULTIMEDIA SYSTEMS

E-health multimedia services and applications –
Multimedia e-health data exchange services

**Requirements on establishing brain healthcare
quotients**

Recommendation ITU-T H.861.1



ITU-T H-SERIES RECOMMENDATIONS
AUDIOVISUAL AND MULTIMEDIA SYSTEMS

CHARACTERISTICS OF VISUAL TELEPHONE SYSTEMS	H.100–H.199
INFRASTRUCTURE OF AUDIOVISUAL SERVICES	
General	H.200–H.219
Transmission multiplexing and synchronization	H.220–H.229
Systems aspects	H.230–H.239
Communication procedures	H.240–H.259
Coding of moving video	H.260–H.279
Related systems aspects	H.280–H.299
Systems and terminal equipment for audiovisual services	H.300–H.349
Directory services architecture for audiovisual and multimedia services	H.350–H.359
Quality of service architecture for audiovisual and multimedia services	H.360–H.369
Telepresence	H.420–H.429
Supplementary services for multimedia	H.450–H.499
MOBILITY AND COLLABORATION PROCEDURES	
Overview of Mobility and Collaboration, definitions, protocols and procedures	H.500–H.509
Mobility for H-Series multimedia systems and services	H.510–H.519
Mobile multimedia collaboration applications and services	H.520–H.529
Security for mobile multimedia systems and services	H.530–H.539
Security for mobile multimedia collaboration applications and services	H.540–H.549
VEHICULAR GATEWAYS AND INTELLIGENT TRANSPORTATION SYSTEMS (ITS)	
Architecture for vehicular gateways	H.550–H.559
Vehicular gateway interfaces	H.560–H.569
BROADBAND, TRIPLE-PLAY AND ADVANCED MULTIMEDIA SERVICES	
Broadband multimedia services over VDSL	H.610–H.619
Advanced multimedia services and applications	H.620–H.629
Ubiquitous sensor network applications and Internet of Things	H.640–H.649
IPTV MULTIMEDIA SERVICES AND APPLICATIONS FOR IPTV	
General aspects	H.700–H.719
IPTV terminal devices	H.720–H.729
IPTV middleware	H.730–H.739
IPTV application event handling	H.740–H.749
IPTV metadata	H.750–H.759
IPTV multimedia application frameworks	H.760–H.769
IPTV service discovery up to consumption	H.770–H.779
Digital Signage	H.780–H.789
E-HEALTH MULTIMEDIA SERVICES AND APPLICATIONS	
Personal health systems	H.810–H.819
Interoperability compliance testing of personal health systems (HRN, PAN, LAN, TAN and WAN)	H.820–H.859
Multimedia e-health data exchange services	H.860–H.869

For further details, please refer to the list of ITU-T Recommendations.

Recommendation ITU-T H.861.1

Requirements on establishing brain healthcare quotients

Summary

Recommendation ITU-T H.861.1 describes healthcare indices derived from neuroimaging analysis that are called brain healthcare quotients (BHQs), intended to be used for facilitating the communication of information about brain status. It describes the requirements on how such an index is created and also how some concrete BHQs can be defined and calculated. This Recommendation also includes examples of services using BHQs to better monitor health for supporting active and alert living. By its defining requirements, BHQs are linked to various healthcare aspects of human life and can be used to improve lifestyles. It gives standardized measurements and indices of brain conditions for specialists and non-specialists.

History

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Table of Contents

	Page
1 Scope.....	1
2 References.....	1
3 Definitions	1
3.1 Terms defined elsewhere	1
3.2 Terms defined in this Recommendation.....	1
4 Abbreviations and acronyms	2
5 Conventions	3
6 Background.....	3
7 Brain healthcare quotients	4
7.1 Types of MRI images	4
7.2 Types of BHQs	5
7.3 Uses of BHQ.....	5
7.4 Requirements for creating a brain healthcare quotient.....	5
Annex A – The GM-BHQ grey matter volume index	7
A.1 Definition.....	7
A.2 GM-BHQ and health aspect: ageing.....	7
Annex B – The FA-BHQ fractional anisotropy index	9
B.1 Definition.....	9
B.2 FA-BHQ and health aspect: ageing.....	10
Appendix I – Example method for obtaining GM-BHQ and FA-BHQ.....	11
Appendix II – An example of reproducibility tests at different facilities	12
Appendix III – A practical use case: BHQ for citizens.....	13
Bibliography.....	14

Recommendation ITU-T H.861.1

Requirements on establishing brain healthcare quotients

1 Scope

This Recommendation describes the requirements of a brain healthcare quotient (BHQ), a healthcare index derived from neuroimaging analysis intended to be used for facilitating the communication of information on brain status. It describes the requirements on how such an index is created and also how some concrete BHQs can be defined and calculated.

2 References

The following ITU-T Recommendations and other references contain provisions which, through reference in this text, constitute provisions of this Recommendation. At the time of publication, the editions indicated were valid. All Recommendations and other references are subject to revision; users of this Recommendation are therefore encouraged to investigate the possibility of applying the most recent edition of the Recommendations and other references listed below. A list of the currently valid ITU-T Recommendations is regularly published. The reference to a document within this Recommendation does not give it, as a stand-alone document, the status of a Recommendation.

[ITU-T H.861.0] Recommendation ITU-T H.861.0 (2017), *Requirements on communication platform for multimedia brain information*.

[ISO 12052] ISO 12052:2006 (2017), *Health informatics – Digital imaging and communication in medicine (DICOM) including workflow and data management*.

3 Definitions

3.1 Terms defined elsewhere

This Recommendation uses the following terms defined elsewhere:

3.1.1 brain healthcare quotient [ITU-T H.861.0]: A numerical indicator representing physical characteristics of the brain that are purported to be indicative of some state of a health related condition.

3.1.2 magnetic resonance imaging [ITU-T H.861.0]: A medical imaging technique used in radiology to investigate the anatomy and physiology of the body in both health and disease.

3.1.3 multimedia brain information platform [ITU-T H.861.0]: A platform for exchange information and data concerning the brain such as MRI data.

3.2 Terms defined in this Recommendation

This Recommendation defines the following terms:

3.2.1 brain dry dock examination: A form of preventive medicine, coined after "human dry-dock", where examinations with typical MRIs are conducted to check for brain-related problems.

3.2.2 diffusion tensor imaging (DTI): A magnetic resonance imaging technique that enables the measurement of the restricted diffusion of water in tissue, in order to produce neural tract images instead of using this data solely for the purpose of assigning contrast or colours to pixels in a cross-sectional image.

3.2.3 fractional anisotropy: A scalar value between zero and one that describes the degree of anisotropy of a diffusion process. It is a measure often used in diffusion imaging where it is thought to reflect fibre density, axonal diameter and myelination in white matter. It is taken as a useful measure of connectivity in the brain that can be derived from the diffusion tensor imaging (DTI) dataset.

3.2.4 grey matter: A major component of the central nervous system, consisting of neuronal cell bodies, neuropil (dendrites and myelinated, as well as unmyelinated axons), glial cells (astroglia and oligodendrocytes), synapses and capillaries.

3.2.5 human dry-dock: A system of general medical check-up or health appraisal, where a voluntary (supposedly healthy) client undergoes a series of medical examinations, such as blood tests, urine and faecal tests, X-rays and ultrasonography, over the course of one or two days, after which the results of the tests are explained to the client in a consultation with a doctor, with some advice on how the client can maintain his/her health.

3.2.6 (brain) morphometry: The measurement of brain structures and changes thereof during development, ageing, learning, disease and evolution. Since autopsy-like dissection is generally impossible on living brains, brain morphometry starts with non-invasive neuroimaging data, typically obtained from magnetic resonance imaging (MRI).

3.2.7 voxel-based morphometry: A neuroimaging analysis technique that allows the investigation of focal differences in brain anatomy using a statistical approach.

3.2.8 white matter: Areas of the central nervous system that are mainly made up of myelinated axons (also called tracts).

4 Abbreviations and acronyms

This Recommendation uses the following abbreviations and acronyms:

AAL	Automated Anatomical Labelling
AHI	Apnoea–Hypopnoea index
BDE	Brain dry Dock Examination
BHQ	Brain Healthcare Quotient
DTI	Diffusion Tensor Imaging
FA	Fractional Anisotropy
FA-BHQ	Fractional Anisotropy – BHQ
FMRI	Functional Magnetic Resonance Imaging
GM	Grey Matter
GM-BHQ	Grey Matter-BHQ
GMV	Grey Matter Volume
KPIs	Key Performance Indicators
MBI-PF	Multimedia Brain Information Platform
MRI	Magnetic Resonance Imaging
VBM	Voxel-Based Morphometry
WM	White Matter

5 Conventions

The following conventions are used in this Recommendation:

- The keywords "is required to" indicate a requirement which must be strictly followed and from which no deviation is permitted, if conformance to this Recommendation is to be claimed.
- The keywords "is recommended" indicate a requirement which is recommended but which is not absolutely required. Thus, this requirement need not be present to claim conformance.
- The keywords "can optionally" indicate an optional requirement which is permissible, without implying any sense of being recommended. This term is not intended to imply that the vendor's implementation must provide the option and the feature can be optionally enabled by the network operator/service provider. Rather, it means the vendor may optionally provide the feature and still claim conformance with this Recommendation.

6 Background

It is understood that the multimedia brain information platform (MBI-PF) should be able to exchange not only imaging data (e.g., MRI data which experts only can use) but metadata about brain functions, including indicators of brain health level, which is useful for various application services for e-health (e.g., monitoring one's health status of the brain, evaluating lifestyles from the point of brain health).

Such indicators are important in practice as MRI data sometimes cannot so easily be interpreted. Even when continuous monitoring of the brain is possible, some minute differences and changes over time can be overlooked, resulting in a grave situation when the change is clearly visible to the human eye.

Brain images contain a variety of information, but the conventional medical model often failed to provide useful information for cases other than clear cases of brain disorders. For example, in a typical brain dry dock examination (BDE), a patient would often ask the doctor about the health status of his brain, but often all the doctor can say is "it is normal for your age". In fact, whether the patient is really "normal for his age" is the subjective opinion of the doctor.

On the other hand, studies based on brain imaging have shown that the brain can change due to various factors, such as:

- ageing shrinks brain size;
- some diseases shrink the brain;
- some activities such as learning can enlarge the brain.

It is also to be noted that various "indicators" are used in many healthcare and medical areas. Examples are the atherogenic index for cardiovascular disease and the apnoea–hypopnoea index (AHI) for sleep apnoea syndrome. Considering the fact that these indices are used successfully to raise awareness of a patient's heart condition and sleep quality, there is a possibility that citizens can have a better understanding of his or her own brain if brain information can be represented by an indicator using the images ordinarily obtained by general brain health screening using MRI. Moreover, such an index may help citizens to reconsider how they manage their brain healthcare.

This point becomes more salient when data is exchanged among different organizations, because these organizations may have different equipment, with different makes and features. The resulting data may be readily interpreted by the experts who are accustomed to the equipment, but not by other equally qualified experts.

Therefore, it is necessary to describe the well-managed criteria for creating and using such indicators of brain health for sustainable growth of e-health services of the brain.

7 Brain healthcare quotients

This clause describes the background rationale for a BHQ and the types of BHQ derived from, specifically the grey matter-BHQ (GM-BHQ) and the fractional anisotropy – BHQ (FA-BHQ).

The definition of other quotients is for further study.

7.1 Types of MRI images

There are several MRI techniques generally used in BDE. For example:

- T1 weighted image: this is one of the basic pulse sequences in MRI and demonstrates differences in the T1 relaxation times of tissues. This is appropriate for seeing the "shape" of the brain.
- T2 weighted image: this is appropriate for seeing "diseases" such as cerebral infarction and encephalitis.
- Diffusion-weighted image: this is appropriate for observing acute strokes.

In practice, these images are evaluated by "visual inspection". This means that considerable amount of training is necessary to correctly "see" or gather information from these images.

There are other MRI techniques that are expected to be used more often in BDE, such as:

- Diffused tensor image: this can help evaluate the "nerve fibres" of the brain.
- Resting-state functional MRI (fMRI): this can evaluate the network (connectivity) of brain.

In any of these methods, the original raw image cannot be directly evaluated but has to be processed with imaging processes to provide useful information.

Neuroscientific findings have shown that several well-known quantitative features of the brain can be associated with the characteristics of brain functions. For example, the volume of grey matter (GM) is associated with various learning possibilities, whereas the complexity in white matter (WM) is associated with the efficiency of information transmission. There already exists systematic means to measure and quantify these characteristics in a scientifically viable way.

These quantitative characteristics in turn are sometime linked to some human properties related to health, such as age or gender. If these quantitative features of the brain can be universally obtainable in statistically significant ways, these quantities can be interpreted as indicating aspects of health-related properties and thus can be used as "indices" for these aspects of the brain.

These indices are defined here as brain healthcare quotients (BHQs). Once established, it is expected that BHQs can be used not only by experts but also by non-experts.

The purpose here is to represent the information about (healthy) the brain in a simple format (i.e., as a number), taking into account the following factors:

- the brain has diversity, as with individuals;
- the biggest factor for shrinking the brain is "ageing";
- the level of shrinking can change depending on the region of the brain;
- in a disease model, "localized/regional" information is sought after, from the "healthcare" point of view; it is more understandable with a simple value.

Thus the requirement on such an index (BHQ) is that although analysing each region of brain, the final result is represented as an integrated value, which will provide a value which is easily understood by, e.g., a subject in BDE.

7.2 Types of BHQs

Two types of BHQ are described in annexes A and B: GM-BHQ based on the volume of GM, as assessed by voxel-based morphometry (VBM), and FA-BHQ based on the FA value of WM, as assessed by Diffusion tensor imaging (DTI) analysis.

Methods that are well established and proven to have high reproducibility are chosen to represent these physical features. Thus:

- Grey matter: voxel-based morphometry (VBM) is adopted;
- White matter: voxel-based analysis using FA image is adopted.

BHQs other than GM-BHQ and FA-BHQ are also plausible. For example, quantification of hyper-intensities reflecting ischemic changes of the brain can be the white-matter hyper-intensity BHQ (WMH-BHQ). Though both GM-BHQ and FA-BHQ are based on measurements of the whole brain, it is plausible to think of a BHQ based on measurements of a specific area of the brain. Also there can be a BHQ related to a health aspect other than age. For example, a certain type of BHQ may be found to be correlated to some blood components. These other potential BHQs are for future study.

The following figure shows the relationship between these BHQs.

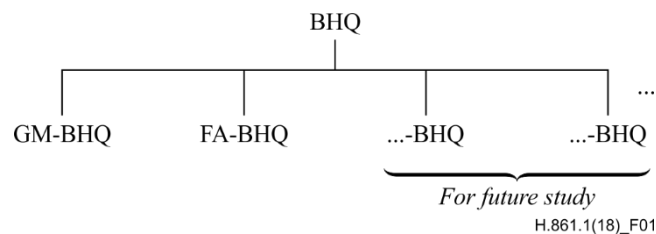


Figure 1 – Relationship between different BHQs

7.3 Uses of BHQ

BHQ can be used for several purposes:

- It will allow the exchange of information about the brain in a standardized way.
As BHQ is a standardized index about a physical characteristic of the brain, it will allow the information, e.g., the size of GM, to be exchanged and utilized in different organizations and comparison can be made possible.
- It can be used to detect minute changes in the brain of a person in the course of time.
Since BHQ is numerical and easily calculated with an algorithm, it is easy to detect a very small change in the physical makeup of the brain of a person. Such a small change may not be easily detected by looking at the actual image from MRI. This feature of BHQ can be utilized to monitor temporal changes of the brain of a person, leading to early detection of any significant features that may affect that person.
- It can be used in combination with other health indices.
Since BHQ is a numerical index it can be combined with other indices, for example, AHI, to see if there is a correlation between the state of the brain and other symptoms of that person.

7.4 Requirements for creating a brain healthcare quotient

Depending on the type of brain data or metadata exchanged on the MBI-PF, or on services or applications utilizing such data, there could be various types of BHQ. It is sought to define KPIs in the creation of the BHQ itself, and also in service operation.

The selection of indicators for creating a BHQ is based inter alia on the following principles:

- The BHQ is required to be built on the basis of neuroscience.

- The BHQ is required to be derived from neuroimaging analysis.
- The BHQ is required to consider the regional differences of the brain.
- The BHQ is required to be linked to healthcare aspects.
- The BHQ is required to represent the state of health-related conditions.
- The BHQ is required to employ a standardized score (e.g., mean of population is 100 and 1 standard deviation is 15, so that 95% of population falls within the range of 70-130.).
- The BHQ is recommended to be built upon an established method to assure its validity.
- The BHQ is recommended to be tested for reproducibility at different facilities.

Annex A

The GM-BHQ grey matter volume index

(This annex forms an integral part of this Recommendation.)

A.1 Definition

GM-BHQ is an index that represents "brain volume" considering regional differences of the brain. Grey matter is a major component of the central nervous system and it consists of neuronal cell bodies, neuropil (dendrites and myelinated, as well as unmyelinated axons), glial cells (astroglia and oligodendrocytes), synapses and capillaries.

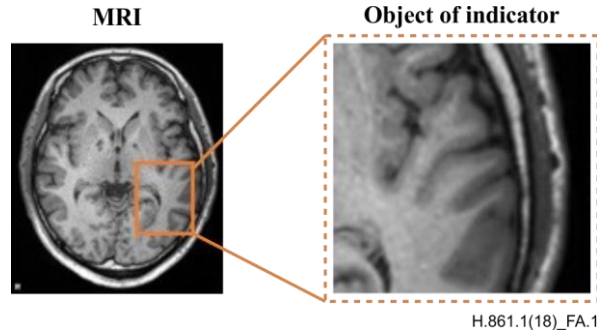


Figure A.1 – MRI image of GM

In GM, an appropriate amount of expanse of dendrites and a reasonable increase in synapses of the neural cells are thought to be signs of a good state of health [b-Erickson]. This good health induces high plasticity in synapses and can be interpreted as indicating flexibility of learning in the future [b-Kandel]. This brain state is reflected in the GM volume [b-Ashburner]. GM-BHQ is the indicator that quantifies the volume of GM.

Voxel-based morphometry (VBM) is one of the well-known neuroimaging analysis techniques that allows investigation of focal differences in brain anatomy. It uses a statistical approach of statistical parametric mapping. GM-BHQ is defined by the volume of GM, as assessed by VBM.

GM-BHQ is obtained with a two-step procedure. First, local GM-BHQs is calculated for 116 regions of the brain. Then, the (Global) GM-BHQ is defined as the sum of the local GM-BHQs. The formula for GM-BHQ is as follows;

$$(\text{Global}) \text{ GM_BHQ} = \frac{1}{n} \sum_{j=1}^n \left(100 + 15 \times \frac{\text{SubGMV}_j - C_{\text{mean}j}}{C_{\text{sd}j}} \right)$$

where:

- j : region of brain based on certain atlases
- SubGMV_j : grey matter volume (GMV) of a subject in region j
- $C_{\text{mean}j}$: average of GMV of control subjects
- $C_{\text{sd}j}$: standard deviation of GMV of control subjects

A.2 GM-BHQ and health aspect: ageing

Figure A.2 shows that the value of GM-BHQ significantly declines as people become older. This indicates that ageing decreases the volume of GM.

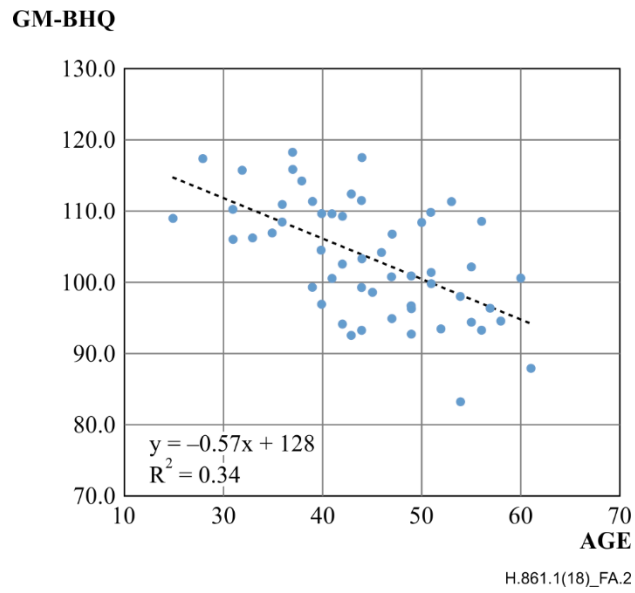


Figure A.2 – Correlation between GM-BHQ and ageing

Annex B

The FA-BHQ fractional anisotropy index

(This annex forms an integral part of this Recommendation.)

B.1 Definition

White matter refers to the areas of the central nervous system that are mainly made up of myelinated axons. Healthy WM is reflected by dense axonal packing [b-Tromp], as well as the expanse of glial cells, which support nerve cells.

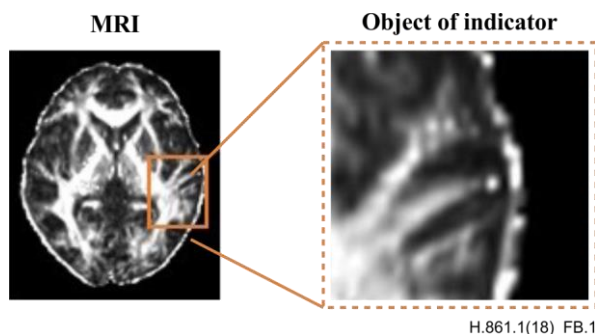


Figure B.1 – FA image derived from DTI

The fibre density, axonal diameter and myelination in WM is typically associated with the value of fractional anisotropy. This value is taken as a useful measure of connectivity in the brain that can be derived from the DTI dataset. The transmission efficiency of the network between brain regions is thus supported by WM integrity, which is reflected in the FA of axons [b-Johansen-Berg], as measured by DTI.

This is the basis of the FA-BHQ, based on the FA value of WM, as assessed by DTI.

DTI has the following characteristics:

- can be used to observe the microstructure of brain tissue and nerve fibres;
- used primarily for:
 - visualizing neural fibres (tractography)
 - evaluating the integrity of neural fibres.
- Primary parameters for evaluating the integrity: mean diffusivity (MD) and fractional anisotropy (FA):
 - MD: index expressing how easy diffusion occurs (mean diffusivity (MD) describes the rotationally invariant magnitude of water diffusion within brain tissue);
 - FA: index representing the degree of anisotropy the diffusion has.

Similar to GM-BHQ, FA-BHQ is defined by the following equation:

$$(Global) FA_BHQ = \frac{1}{n} \sum_{j=1}^n \left(100 + 15 \times \frac{SubFA_j - C_{mean_j}}{C_{sd_j}} \right)$$

where:

- j : region of brain based on certain atlases
- $SubFA_j$: fractional anisotropy (FA) of a subject in region j
- C_{meanj} : average of FA of control subjects
- C_{sdj} : standard deviation of FA of control subjects

B.2 FA-BHQ and health aspect: ageing

Figure B.2 shows that the value of FA-BHQ significantly declines as people become older. This may reflect brain deterioration as people age, which suggests that BHQ is an appropriate indicator for brain health status.

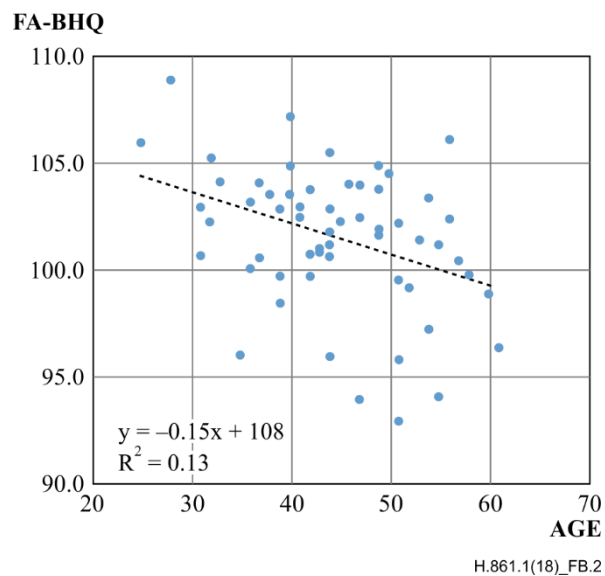


Figure B.2 – Correlation between FA-BHQ and ageing

FA-BHQ evaluates the integrity of fibre tract, and it builds on white matter, i.e., fibres that are connecting brain areas.

Appendix I

Example method for obtaining GM-BHQ and FA-BHQ

(This appendix does not form an integral part of this Recommendation.)

Figures I.1 and I.2 describe how GM-BHQ and FA-BHQ, respectively, can be obtained.

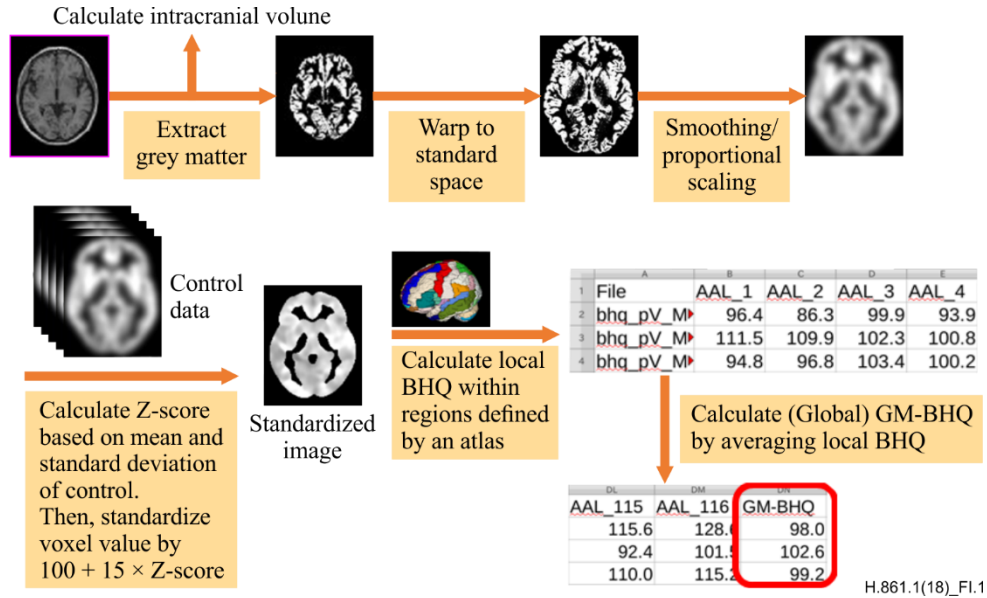


Figure I.1 – Example of how GM-BHQ can be obtained

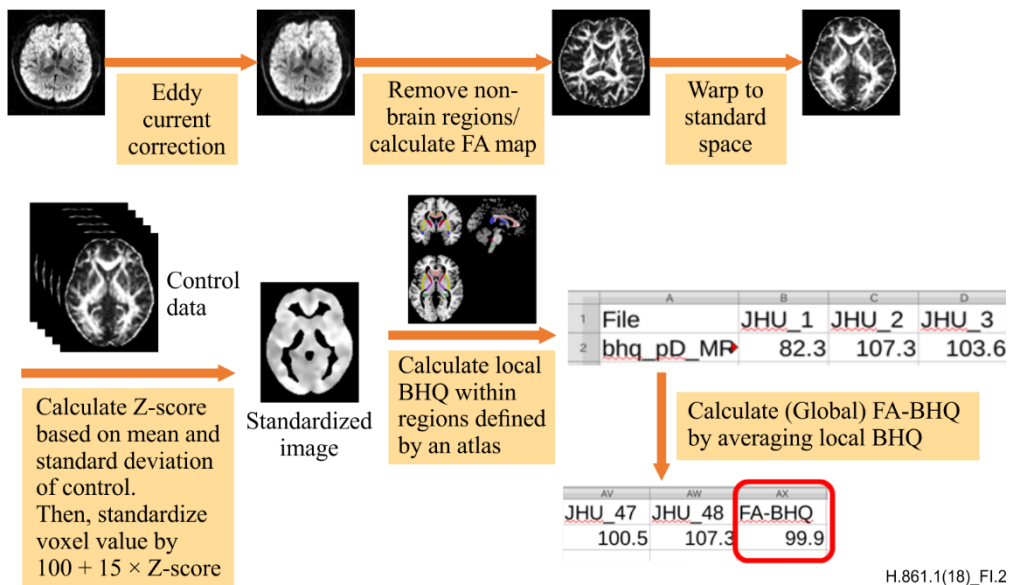


Figure I.2 – Illustration of how FA-BHQ can be obtained

Appendix II

An example of reproducibility tests at different facilities

(This appendix does not form an integral part of this Recommendation.)

In the case of GM-BHQ and FA-BHQ, the data acquired at different MRI facilities are tested. Data is acquired at the Kyoto University (N=58) and the University of Tokyo (N=54), respectively. The relationship between age and BHQ showed the same trend with the brain data scanned at both facilities (GM-BHQ: The Pearson correlation coefficient R , $R=0.57$, $b=-0.56$, $p<.001$ at Kyoto University, $R=0.55$, $b=-0.51$, $p<.001$ at Tokyo University, FA-BHQ: $R=0.36$, $b=-0.14$, $p<.01$ at Kyoto University, $R=0.36$, $b=-0.19$, $p<.01$ at Tokyo University). Therefore, GM-BHQ and FA-BHQ have reproducibility as health indicators.

Appendix III

A practical use case: BHQ for citizens

(This appendix does not form an integral part of this Recommendation.)

Appendix III describes BHQ-School as a use case of BHQ, in which the general public uses BHQ. BHQ-School aims to find solutions that might potentially contribute to brain health by having BHQ widely used by not only researchers or companies but also the general public.

For the general public to participate in BHQ-School, a person leverages "one's own BHQ" or "brain age" inferred from the BHQ to find solutions to maintain or improve brain health including diet and exercise matched to the brain health status, appropriate sleep duration to protect brain health, and hobbies or lifestyle environments to improve brain health. By sharing such activities of citizen scientists and researchers, it will enable the scientific discovery of the lifestyles that are good for brain health.

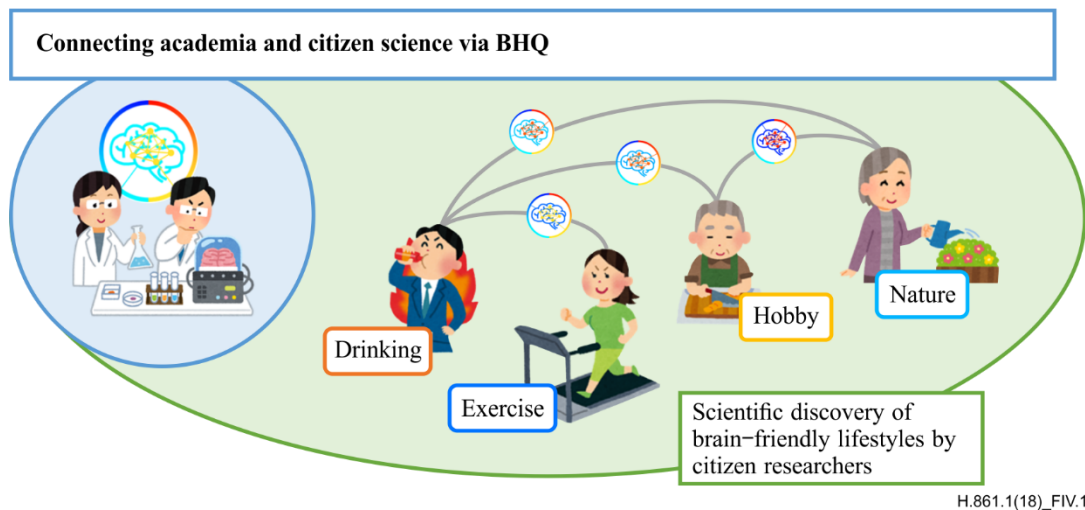


Figure III.1 – Citizen science by BHQ

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