

Research Paper: Iranian Brain Imaging Database: A Neuropsychiatric Database of Healthy Brain



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ABSTRACT

Introduction: The Iranian Brain Imaging Database (IBID) was initiated in 2017, with 5 major goals: provide researchers easy access to a neuroimaging database, provide normative quantitative measures of the brain for clinical research purposes, study the aging profile of the brain, examine the association of brain structure and function, and join the ENIGMA consortium. Many prestigious databases with similar goals are available. However, they were not done on an Iranian population, and the battery of their tests (e.g. cognitive tests) is selected based on their specific questions and needs.

Methods: The IBID will include 300 participants (50% female) in the age range of 20 to 70 years old, with an equal number of participants (#60) in each age decade. It comprises a battery of cognitive, lifestyle, medical, and mental health tests, in addition to several Magnetic Resonance Imaging (MRI) protocols. Each participant completes the assessments on two referral days.

Results: The study currently has a cross-sectional design, but longitudinal assessments are considered for the future phases of the study. Here, details of the methodology and the initial results of assessing the first 152 participants of the study are provided.

Conclusion: IBID is established to enable research into human brain function, to aid clinicians in disease diagnosis research, and also to unite the Iranian researchers with interests in the brain.

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Highlights

- An Iranian database of cognitive and MRI data.
- Applicable in studying brain ageing and age-related disorders.
- A tool to provide normative brain measures for the early diagnosis of disorders.
- Useful for the study of the association of brain structure and cognition.

Plain Language Summary

Magnetic Resonance Imaging (MRI) has become an essential part of the Neuroscience researches. These data can answer many questions on the structure and function of the brain. Although Neuroscientists need to have an easy and free access to a huge and standard MRI dataset, such a dataset is not currently available in Iran. This has caused a great waste of resources, as each investigator has to collect his own small-size dataset. The aim of this proposal is to establish a standard MRI dataset of physically and mentally healthy participants in a wide age range, so that the researches in the field of Neuroscience can easily have access to MRI data, in order to investigate their ideas and hypotheses. Establishment of this dataset, as has been shown in other countries, can cause an important progress in the Neuroscience field, the findings of which can help in the development of public health. In this database, called the Iranian Brain Imaging Database (BID), the aim was to develop a database of brain MRI, along with cognitive tests. Multiple MRI protocols, in addition to numerous cognitive tests, mental health, lifestyle, and clinical assessments were performed on more than 300 individuals in the age range of 20 to 70 years old. Each participant was clinically assessed for the physical health by three different general practitioners. Next, our colleagues tested the participant for his/her mental health. After that, the MRI imaging was performed at the National Brain Mapping Lab (NBML), and on a second day, the cognitive tests were performed in a different center. We hope this database boost the quantity and quality of the works studying brain structure and cognition, as well as their associations with ageing.

1. Introduction

The Iranian Brain Imaging Database (IBID) is a cohort of young Iranian adult, middle-aged, and elderly individuals who will undergo 5 categories of assessments, including medical, mental health, cognitive, lifestyle tests, and MRI scanning. This study was sponsored by the Iranian National Institute for Medical Research Development (NIMAD) (Grant No. 962550). It will recruit 300 healthy individuals in the age range of 20 to 70 years old, with an equal number of males and females in each age decade. There are five major goals for this database.

1.1. A standard database

The first goal is to aid researchers, particularly in neuroscience, to access a comprehensive and standard database of neuropsychiatric brain data. Collecting data is expensive and time-consuming. Recruiting mentally- and physically-healthy participants need precise criteria, careful examinations, and routine tests and questionnaires, so

prior experience is a necessity in this process (Batouli & Sisakhti, 2020). Besides, managing diverse data modalities requires a multidisciplinary team, with specific expertise and resources required for the relatively complex Magnetic Resonance Imaging (MRI) data.

Many prestigious and large-scale databases are available. We can mention a few of them: ENIGMA (Enhancing Neuro Imaging Genetics Through Meta-analysis) (Thompson et al., 2014), ABCD (The Adolescent Brain Cognitive Development) (Research & Staff, 2018), MAS (Memory and Ageing Study) (Sachdev et al., 2010), OASIS (Open Access Series of Imaging Studies) (Marcus, Fotenos, Csernansky, Morris, & Buckner, 2010), OATS (Older Australian Twins Study) (Sachdev et al., 2009), SCS (Sydney Centenarian Study) (Theobald et al., 2017), ADNI (Alzheimer's Disease Neuroimaging Initiative) (Mueller et al., 2005), the Human Connectome Project (Van Essen & Glasser, 2016), Brain-Development (Dataset, n.d.), and BRAIN SPAN ('BrainSpan Atlas of the Developing Human,' n.d.). Despite the value of these resources, two issues motivate the need for a specific Iranian database.

The first is the influence of culture and genetics on the structure and function of the brain (Batouli et al., 2012; Batouli, et al., 2014; Park & Huang, 2010). Many previous studies have considered this limitation, which led them to collect data for their population—available cognitive functioning test results were normed for the Portuguese population (Dias et al., 2015). The Montreal Cognitive Assessment (MoCA) was used to build normative data for both older Lebanese (Abou-Mrad, 2017) and Spanish (Pereiro et al., 2017) populations. The battery of standardized cognitive assessments for diagnosing Alzheimer disease in the TOMORROW study, which included episodic memory, language, visuospatial ability, executive function, and attention tests, was normalized for a German population (Romero et al., 2018). These studies illustrate that having access to population-specific data would be more accurate for neuroscientific inferences.

The second limitation is relevant to the collected data types; the available databases are either mostly concentrated on the MRI data or have selected the battery of their tests and questionnaires based on their research questions and clinical needs. This condition limits the applicability of those databases to answer specific questions about a different population

1.2. Clinical applications

The tests and assessments of IBID are selected for being applicable for disease diagnosis research. Examples for the cognitive domain are the Rey auditory verbal learning test in the diagnosis of dementia (Ricci, Graef, Blundo, & Miller, 2012), ADHD (Pollak, Kahana-Vax, & Hoofien, 2007), and verbal learning and memory impairments (Batouli & Sisakhti, 2019; Rosenberg, Ryan, & Prifitera, 1984), forward and backward digit span tasks in learning disorders (Giofrè, Stoppa, Ferioli, Pezzuti, & Cornoldi, 2016), Wechsler adult intelligence in cognitive complaints (Ruchinskas, 2019), the n-back task in depression (Delaveau et al., 2017) and schizophrenia (Li et al., 2019), the trail making test in identifying executive dysfunction (Chan et al., 2015), chronic diseases (Ihle et al., 2018), or brain damage (Gordon, 1972), and tests of the cognitive domains such as executive functions, language, memory, and visuospatial skills for diagnosing Parkinson disease (Pal et al., 2018).

Lifestyle tests to assess factors such as education, occupation, and engagement in cognitive activities are also illustrated to have clinical applications, such as evaluating the treatment of Huntington disease (Garcia-Gorro et al., 2019). Another example is using the health-promoting lifestyle profile questionnaire for examining the condi-

tions of patients with heart disease (Dehkordi, 2018), hypertension (Li, Yu, Chen, Quan, & Zhou, 2018), or after a coronary intervention (Xiao, Wang, Fang, & Zhao, 2018).

Neuroimaging data are also primarily used for disease diagnosis research: as a few examples, fMRI is used for the diagnosis of depression (Neufeld et al., 2018), bipolar disorder (Li, Liu, Andari, Zhang, & Zhang, 2018), Alzheimer disease (Oghabian, Batouli, Norouzzian, Ziaei, & Sikaroodi, 2010), aging (Batouli et al., 2009), autism (He et al., 2018), epilepsy (Klugah-Brown et al., 2018), and coma (Tomaiuolo et al., 2016). The analyses for functional connectivity between brain areas are also helpful in diagnosing mild cognitive impairment (Lin, Xing, & Han, 2018), lateral sclerosis (Clark et al., 2018), addiction (Zare Sadeghi et al., 2017), and many other conditions (Du, Fu, & Calhoun, 2018). Structural MRI such as diffusion tensor imaging helps assess Parkinson disease (Schwarz et al., 2014), Alzheimer disease (Kantarci et al., 2017), mesial temporal sclerosis (Corrêa et al., 2018), brain injury (Shenton, Price, Levin, & Edersheim, 2018), and for differentiating tumors and demyelinating diseases from normal tissues (Giussani et al., 2010). Similarly, volumetric MRI can help in distinguishing the addiction-related (Keihani et al., 2017) and sedentary lifestyle-related (Batouli & Saba, 2020) abnormalities of the brain, as well as in imaging genetics (Batouli, et al., 2014), schizophrenia (de Moura et al., 2018), migraine (Coppola et al., 2017), and epilepsy (Quan et al., 2017). The normative quantitative measures of the brain would act as the foundation for abnormality diagnosis purposes.

The machine learning tools trained with a large sample size could be easily implemented for clinical purposes. Examples are using data mining models for dementia diagnosis (Moreira & Namen, 2018) or deep learning methods for predicting Alzheimer disease (Basaia et al., 2018). Other applications are for identifying abnormalities in the brain (Pinaya, Mechelli, & Sato, 2019), to examine brain aging (Eavani et al., 2018), and for building normative rules in the brain (Sato, Rondina, & Mourão-Miranda, 2012).

1.3. Brain aging

Increasing age changes the human brain in weight, size, Grey Matter (GM), and White Matter (WM) density and integrity (Batouli, et al., 2014; Batouli & Saba, 2017). Brain volume also declines with age, observed in both cross-sectional (Raz et al., 2004) and longitudinal approaches (RI et al., 2003), and this decline accelerates in adulthood (Sowell et al., 2003). Similarly, the cognitive abilities of the human decline in aging (Dause

& Kirby, 2019), such as the speed of processing, executive function, attention, working, and episodic memory (Alemi, Batouli, Behzad, Ebrahimipoor, & Oghabian, 2018; Chee et al., 2009; Mattay, Goldberg, Sambataro, & Weinberger, 2008).

Studying brain aging trajectory is significant in terms of evaluating environmental influences on it. Twin studies have illustrated that the influence of genes on brain structure declines with age (Batouli, Trollor, Wen, & Sachdev, 2014). This condition allows us to maintain brain health during aging by providing a healthy lifestyle. The association of enriched environments with a healthy brain is illustrated previously, such as by Physical Activity (PA) (Batouli & Saba, 2017) or by appropriate nutrition (Rutjes et al., 2018). To further elaborate, studies have shown that PA changes WM structure (Scholz, Klein, Behrens, & Johansen-Berg, 2009), causes myelination of unmyelinated axons (Zatorre, Fields, & Johansen-Berg, 2012), and alters myelin thickness and axon diameter (Canu, Carnaud, Picquet, & Goutebroze, 2009). In terms of cognitive improvements, there are reports on the positive associations of PA with learning and memory (Cotman & Berchtold, 2002), processing speed, attention and executive functions (Smith et al., 2010), reaction time and language (Snowden et al., 2011), and visuospatial ability (Åberg et al., 2009). Using the cross-sectional design of the IBID, brain alterations during aging, as well as the influence of environmental factors on this process, could be studied.

1.4. Association of brain structure and function

There is an association between brain structure and function. A few examples are the association of total and regional volumes of the brain with intelligence, skill acquisition performance, working, verbal and spatial memory, executive function, and processing speed (Chee et al., 2009; Plomin & Kosslyn, 2001; Posthuma et al., 2002). The connections between brain function and structure is due to the neural information processing being dependent on the size, arrangement, and configuration of the neurons, the number, and type of the synaptic connections of the neurons, on the quality of their relationship with distant neurons, and the properties of non-neuronal cells such as glia (Zatorre et al., 2012). Studying the degree of this association could be a valuable approach in revealing the operational mechanisms of the brain in handling different cognitive functions. IBID provides the basis for such studies by providing MRI data of brain structure and a battery of cognitive and mental health tests.

1.5. Joining ENIGMA

This database aimed to join the ENIGMA consortium, and the “Life Span” working group of ENIGMA seems to fit the IBID data best. The request for joining this consortium is submitted, and the application is in progress.

2. Materials and Methods

2.1. Advertisement

For recruiting participants, we prepared posters and flyers, which provided general information about the project. These were spread on online social networks such as Instagram, Telegram, and Facebook. They were also printed and handed to the people working in places such as schools, universities, banks, public transport, and hospitals. The instruction to participate in the study was to fill the online form on the project’s website (www.brainee.ir/ibid) to contact us by text message or call.

2.2. Participants

The age range of the included participants was from 20 to 70 years. This range comprises five age decades, with 30 males and 30 females in each decade, resulting in a total number of 300 participants. The demographic data recorded from each participant included full name, national ID number; date of birth, phone number and address, marital status, the number of siblings and children, years and field of education, type of job and the amount of income, and the mother tongue and the degree of fluency in a second language (if any). Because of the broad ethnicity of the people living in Iran, their race and city of birth were also recorded.

2.3. Telephone screening

After registration, the first contact with the participant was from the general practitioner of the study, to have a telephone interview and to check the necessary inclusion criteria. The criteria were weight below 110 kg; Iranian nationality, Persian as the first or second mother tongue, ability to read, minimum 12 years of education, not being pregnant or breastfeeding, not using drugs or alcohol (only based on the subjective report), consent to participate in all steps of the study, and not being claustrophobic. In the early stages of the project, our alcohol consumption criteria changed to “not being addicted to alcohol”.

Several other essential criteria were also checked: any diagnosed internal or neurologic diseases, such as asthma, high blood pressure, diabetics, cardiovascular diseases

es, high cholesterol, migraine, head trauma, encephalitis, epilepsy, meningitis, multiple sclerosis, liver disease, hepatitis, HIV⁺, anemia, stroke, or cancer; past or current medications used for neurologic disorders; a long-term history of medicine consumption (with exceptions on aspirin, vitamins, antibiotics, pain killers, hypnotics, anti-nausea drugs, and vaccinations); any history of chronic headache, tinnitus, dizziness, seizure, nausea, or memory impairments; family history of any disease; any surgery with anesthesia (with exceptions on tonsillectomy/adenoidectomy, pulling wisdom tooth, cesarean delivery, and vasectomy); a history of losing consciousness; and any metal objects in the body, such as a pacemaker, dental brace, coronary stent, any type of implant, tattoo, etc. The participant signed his/her telephone interview form and the given information on his/her first referral day.

2.4. Ethical issues

The ethical approval code for this study was IR.NIMAD.REC.1396.319, issued by NIMAD and in agreement with the Declaration of Helsinki. A unique code was devoted to each participant, and therefore there was no name written on the forms. Nobody accessed the completed forms and questionnaires of the study except the manager and the medical doctor of the research. The documents were kept in a secured and locked office closet. A two-page consent form was prepared in which all details of the study and the relevant ethical issues were written, and one copy (signed by both parties) was handed to the participant, and the second was kept in our documents.

2.5. Research design

Each participant was initially informed that the tests were performed on two referral days: the first day was devoted to medical and mental assessments, the cognitive tests, and the second day to the MRI scanning and the lifestyle questionnaires. An executive member of the study contacted the participants to schedule an appropriate date and time for their referral. Despite signing the consent form to perform all the assessments, a few participants refused to attend their second day's tests, and therefore they were excluded from the study. Any excluded participant was replaced with a new participant to ensure collecting enough data. A book on healthy aging and an envelope, including cash (equal to 4 times of taking a taxi), were gifted to each participant on completing the tests on the second day.

2.6. Assessments

The five categories of assessments in this study included medical, mental health, cognitive, lifestyle tests, and MRI scanning.

2.6.1. Medical examination

The medical tests of IBID were designed based on consultations with a group of experienced medical doctors. These tests examined the weight and height of the participants, as well as the blood pressure, heart and breathing rates; the ability of sight and hearing; examining pupils such as their size, symmetry, and response to light; examining middle ear and tympanum; and further general examinations, including a history of alcohol consumption or drug abuse; symptoms of chronic or acute diseases; any surgery scar; and a few of neural examinations, such as cranial nerves, motor, and sensory exams, and reflexes. Finally, handedness was assessed using the Edinburgh handedness inventory (Oldfield, 1971).

2.6.2. Mental health

For mental health assessments, we selected the Symptom Checklist-90-Revised (SCL-90-R) (Derogatis & Unger, 2010) and the depression anxiety stress scales (DASS-21) (Henry & Crawford, 2005) questionnaires. These tests are normalized for the Persian language and population (Modabernia, Shojaie Tehranie, Falahi, & Faghripour, 2010; Sahebi, Asghari, & Salari, 2005).

SCL-90-R is appropriate for assessing psychiatric disorders and includes items to measure the general psychological factor, as well as psychiatric symptoms in 9 subscales of somatization, hostility, obsessive-compulsive disorder, anxiety, depression, interpersonal sensitivity, paranoid ideation, phobic anxiety, and psychoticism, based on DSM-IV categories (Ardakani et al., 2016). Furthermore, DASS-21 is the short version of the 42-item Depression Anxiety Stress Scales (DASS) test, introduced by Lovibond and Lovibond (1995). This test is also a self-report test, which includes three 7-item scales to measure depression, anxiety, and stress (Henry & Crawford, 2005).

2.6.3. Cognitive tests

The cognitive tests of the study were in 8 categories, each including 1 or 2 tests, resulting in a total number of 13 cognitive tests. For those tests which were language-based, the Persian-normalized versions of the tests were used. Three tests were computerized, and the rest were in paper and pencil format. The participant was once taking

rest in the middle of his/her cognitive tests, and drinks and biscuits were provided in the meanwhile. Similar settings and timing were applied to all participants.

2.6.4. Episodic memory

Rey Auditory Verbal Learning Test (RAVLT) (Mitrushina, Satz, Chervinsky, & D'Elia, 1991) was selected here. It measures the abilities in attention and learning, and specifically several aspects of the memory. Useful information could also be obtained using this test about the type of difficulty of a participant in memory, attention, and learning processes (Ferreira Correia & Campagna Osorio, 2013). The RAVLT test is normed for the Persian population and language (Rezvanfard et al., 2011) "men delay": {"formattedCitation": "(Rezvanfard et al., 2011).

The second test in this category was the Benson complex figure (copy, delayed recall, and recognition) (Posin, Laluz, Alcantar, Miller, & Kramer, 2011). This test is a simplified version of the Rey-Osterrieth figure test, assessing visuoconstructional and visual memory functions, including copying, a delayed reconstruction (after 10-15 minutes), and a recognition phase (Rosselli et al., 2019).

2.6.5. Working memory

The forward and backward digit span task, a subtest of the Wechsler memory scale revised test, was used (Wechsler, 1987). In this test, the subject is asked to recall the items just after the examiner read them aloud, in the right order (Forward) or the reverse order (Backward). The forward digit span test relies on the phonological loop capacity, and the backward test needs the ability to manipulate while maintaining the information. Therefore it depends on the central executive function (Hester, Kinsella, & Ong, 2004).

The second test in this category was the one-back version of the n-back task (Kane, Conway, Miura, & Colflesh, 2007). In this test, several digits were randomly presented to the participant only once, and the participant was asked to indicate if the currently presented number matched the previously presented one. We used a Persian-normed version of this test (Mirdehghan, Nejati, & Ganjian, 2016).

2.6.6. Visuospatial domain

For the block design task, a subtest of the Wechsler Adult Intelligence Test (WAIS-III) was used. This test was initially designed by Kohs (1920) is an appropri-

ate measure for the visuospatial ability (Fenouillet & Rozenchwajg, 2015) and is independent of the language function (Kohs, 1920).

2.6.7. Executive functioning

The trail making test A and B was performed (Lezak, Howieson, Loring, & Fischer, 2004). This test is a well-known assessment included in most batteries. It gives information on the executive function and mental flexibility, processing speed, and visual search and scanning (Tombaugh, 2004).

2.6.8. Processing speed

Symbol digit modality task (Smith, 1979), as a representation for the speed of information processing, was chosen. In this test, 9 pairs of symbol-digit are given to the participant as the key. The participant is asked to write the correct number associated with each written symbol according to the given key in 90 seconds.

A simple and complex reaction time test (Zajdel & Nowak, 2007) was also used here. This test is a computerized assessment of information processing speed, and we performed the test in three modes. In the simple mode, only one stimulus is presented, and the subject is asked to press the key as soon as possible. In the discriminative mode, two kinds of stimuli are presented, and the key is pressed only for one of them, and the second is ignored. In the selective mode, again, two kinds of stimuli are presented, but specific keys are pressed for each stimulus

2.6.9. Decision making

The automatic balloon analog risk task (Automatic BART) (Fukunaga, Brown, & Bogg, 2012) but accounts of how these regions contribute to decision making under risk remain contested. To help clarify the roles of these and other related regions, we used a modified version of the Balloon Analogue Risk Task (Fukunaga et al., 2012). Journal of Experimental Psychology: Applied, 8, 75-84, 2002 is a common computerized task for studying risk-taking behavior. In this test, the participant is asked to indicate a number for pumping a balloon and will gain a score if the balloon does not pop.

2.6.10. Inhibition

The Stroop task (Stroop, 1935) represents a measure of resistance to interference. The Stroop effect is caused by the fact that when the name of a written color does

not match the color in which the word is printed, it takes longer to name the printing color and causes more errors.

2.6.11. Language ability

Verbal fluency is measured by the number of words a person can produce in 60 seconds. Both semantic Verbal Fluency Tests (VFT) and phonemic VFT were chosen here (Lezak et al., 2004). For the Persian phonemic VFT, the three letters of “P,” “M,” and “K” were used due to their highest frequency in the Persian language (Ghasemian-Shirvan, Shirazi, Aminikhoo, Zareaan, & Ekhtiari, 2018). In the Persian version of the semantic VFT test, the same original categories (animals, grocery store, and fruits) (Ghasemian-Shirvan et al., 2018) were used.

2.6.12. Lifestyle tests

Among the many questionnaires regarding lifestyle, two had been normalized for the Persian language. The first was the Health-Promoting Lifestyle Profile II (HPLP II) questionnaire (Walker, Sechrist, & Pender, 1995). In the Persian version of this test, the 52 items were reduced to 49, and some items were changed to fit the Iranian habits (Mohamadian, Eftekhar, Taghdisi, Mousavi, & Sabahi, 2013; Mohammadi Zeidi, Pakpour Hajiagha, & Mohammadi Zeidi, 2012).

The second test was the Internet addiction test for adults by Young (1999), normed and validated for the Persian population (Bahri, Sadegh Moghadam, Khodadošt, Mohammadzadeh, & Banafsheh, 2011; Ghassemzadeh, Shahraray, & Moradi, 2008). This test helps the diagnosis of Internet addiction. It examines symptoms such as internet preoccupation, hiding the amount of internet usage, the capability of internet usage control, and keeping on using the internet regardless of its costs.

2.6.13. MRI protocols

The MRI machine used in this study was a Siemens 3.0 Tesla scanner (Prisma, 2016), devoted to research, at the Iranian National Brain Mapping Lab (www.nbml.ir). A few characteristics of this machine included 50-cm FOV with the industry best homogeneity; whole-body; superconductive zero helium oil-off 3T magnet; and head/neck 20 direct connect. We used the 64-channel head coil in our study. The MRI protocols were selected to match the international projects, such as the UK Biobank or the ENIGMA consortium. Accordingly, this study included 6 MRI protocols.

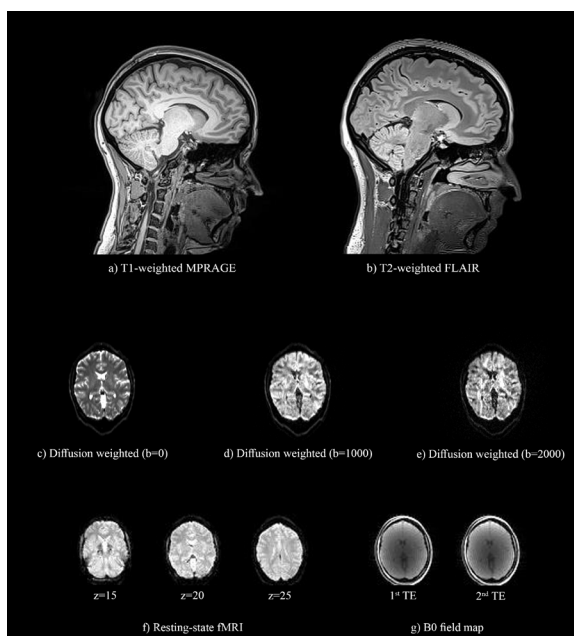
Resting-state fMRI: TA= 6 min; TR= 2500 ms; TE= 30 ms; flip angle = 90 degrees; voxel size = 3.0×3.0×3.0 mm; #slices = 40; matrix size = 64×64×40; distance factor = 0%; phase encoding direction = anterior >> posterior; averages = 1; delay in TR = 0 s; measurement = 144; multi-slice mode = Interleaved.

B0 field mapping: TA= 1:28 min; TR= 444 ms; TE-1= 5.19 ms; TE-2 = 7.65 ms; flip angle = 60 degrees; voxel size = 3.0×3.0×3.0 mm; distance factor = 0%; #slices = 40; phase encoding direction = anterior >> posterior; averages = 1; matrix size = 64×64×40.

T1-weighted MP-RAGE. TA = 4:12 min; TR = 1800 ms; TE = 3.53 ms; TI = 1100 ms; flip angle = 7 degrees; voxel size = 1.0×1.0×1.0 mm; multi-slice mode = sequential; FOV read = 256 mm; #slices = 160; phase encoding direction = anterior >> posterior; matrix size = 256×256×160; averages = 1.

T2-Weighted FLAIR: TA = 5:37 min; TR = 5000 ms; TE = 386 ms; TI = 1800 ms; voxel size = 0.9×0.9×0.9 mm; Matrix size = 256×256×176; #slices = 176; phase encoding direction = anterior >> posterior; averages = 1.

Diffusion weighted_1: Diffusion weighting = 2; b-value_1= 0 s/mm²; b-value_2= 1000 s/mm². #B0= 2; diffusion directions = 64; TA= 11:05 min; TR = 9900 ms; TE = 90 ms; voxel size = 2.0×2.0×2.0 mm; FOV read = 256mm; #slices= 65; distance factor = 0; phase encoding direction= anterior >> posterior; measurement = 1;



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Figure 1. Sample screenshots of the MRI data collected in IBID

delay in TR= 0 ms; matrix size = 128×128×65; multi-slice mode = interleaved. Diffusion weighted_2: Similar settings with the first diffusion protocol, but b-value_2 = 2000 s/mm². Sample screenshots of the collected MRI data are provided in [Figure 1](#).

2.7. Quality check

The quality check in this study was both during and after data collection. A one-page form was prepared to check the completion of all tests for each participant, as well as the performance of telephone screening and clinical examination, signing the consent form by the participant, completion of the cognitive, mental health, and lifestyle tests, the performance of all MRI protocols and collection of the data, the gift being handed out to the participant, all data is archived, and the forms being anonymized.

All MRI data were visually checked for good quality. This step included checking the total number of protocols, image information such as matrix and voxel sizes, the number of directions (for diffusion-weighted sequence), and the number of time-points (for resting-state fMRI) checking the images to be right-to-left oriented. Besides, the visual check was performed to spot possible macroscopic artifacts and vibration/motion evidence in images and to check head tilt and head positioning, signal loss, ghosting, or other possible artifacts in the data. No quality check of the post-processed data was considered at this stage of the study.

2.8. Databasing

There are three simple steps for an applicant to use the IBID data. 1) Filling the form on the IBID website (www.brainee.ir/IBID/data-sharing) to inform us of the number and types of the requested data; 2) a unique code is created for each application, used as the “IBID data access code”; and 3) the link for downloading the requested anonymized data is sent to the applicant. To inform the applicants on the contents of the database, the demographics of the study participants and the methodological details of the collected data will be available on the IBID website upon completion of data collection.

3. Result

3.1. Aims and ideas

As explained before, the initial aim of establishing IBID was to provide a dataset by which the researchers test their hypotheses on the healthy brain and cognition. This dataset could also have significant clinical research applications, for example, by providing the normative MRI and cogni-

tive measures for our population. In addition to these applications, there are several particular questions which we will test using these data. A few of them include the effect of handedness on the localization and not laterality of brain functions observable in resting-state fMRI. The association of brain structure with the different domains of the memory function, as well as other cognitive abilities, and identifying the brain structures or the cognitive processes which show the earliest signs of aging.

3.2. The included participants

At the time of preparing this manuscript (7 months after the start of data collection), 387 individuals did register to participate in the study, of which 235 were excluded based on our criteria. Then, 152 participants (of the total number of 300) completed all their MRI and cognitive tests, and 33 participants are in the middle of their examinations. Also, 152 participants with completed data (69 M) include 51 participants in the first group (20-30 years old), 50 in the second (30-40), 34 in the third (40-50), 15 in the fourth (50-60), and 2 in the fifth group (60-70 years old).

3.3. Power analysis

The power of the dataset in response to a few of the leading research questions was estimated. For this aim, we evaluated the power in identifying the possible differences between the young (20-30 years old) and middle-aged (50-60 years old) groups in three measures: 1. A cognitive domain in the processing speed: simple reaction time; 2. A test in the visuospatial domain: the block design task; and 3. Total brain volume. Comparing the young group with an older group (60-70 years old) would lead to a better power measure. However, we selected a stricter approach.

The Mean±SD reaction time in the young group was 458.4±90.08 ms, and it was 537.2±134.6 ms in the middle-aged group. The two groups were statistically different in this measure ($P=0.048$), and the effect size of the difference was 0.688. The Mean±SD block design score of the young group was 32.94±8.59, and it was 26.15±10.34 in the older group, with the effect size of their significant difference ($P=0.014$) being 0.712. Finally, the Mean±SD total cerebral volumes were 1173536±112333 mm³ and 1099007±94902 mm³ in the young and middle-aged groups, respectively. The difference here did not reach the statistical significance level ($P=0.09$), but there was a sound effect size (0.716). According to Cohen's *d* formula ([Sullivan & Feinn, 2012](#)), the three effect sizes obtained here are categorized as “large”.

Using the power analysis package (Package ‘pwr’; V.1.2-2; <https://github.com/heliosdrm/pwr>) in the R-GUI software (v.3.5.3), we estimated the power of IBID in the above three research questions. The inputs for the calculation of energy (using the “power.t” command) were the effect size of the difference, the number of observations (60), significance level (0.01), and the type of the analysis (two-sided 2-sample t test). Based on these values, the power for identifying the difference of the two groups in the reaction time was 0.872, it was 0.897 for the block design results, and the power was 0.901 for the total cerebral volumes. The estimated power measures showed the strength of IBID in answering the research questions.

3.4. Current findings

We performed preliminary analyses on the collected MRI and cognitive data. As the first question, we examined the association of brain structure with the cognitive capacity of the human. For this aim, we selected the same two cognitive functions: the block design task

and the software-based complex reaction time test. The first test was under the visuospatial domain. It included 10 increasing-complexity designs, with a varying time limit of 1 to 2 minutes to complete each design and a maximum score of 51. The second test measured the processing speed.

There were 64 data (30F) included in this examination, with a mean age of 32.8 years for the participants (20 to 59 years old). Voxel-Based Morphometry (VBM) using the SPM12 software package (Wellcome Department of Imaging Neuroscience: <http://www.fil.ion.ucl.ac.uk/spm>) was performed in MATLAB (version 9.0), with the total brain volume, age, and sex imported as the controlling variables. The scores of the block design task, the reaction time of the participants, and the Standard Deviation (SD) of the reaction times were the three covariates of interest, investigated in three separate VBM tests. The hypotheses were a higher brain volume being associated with a higher block design score, with slower reaction time, and with a lower SD of the reaction time.

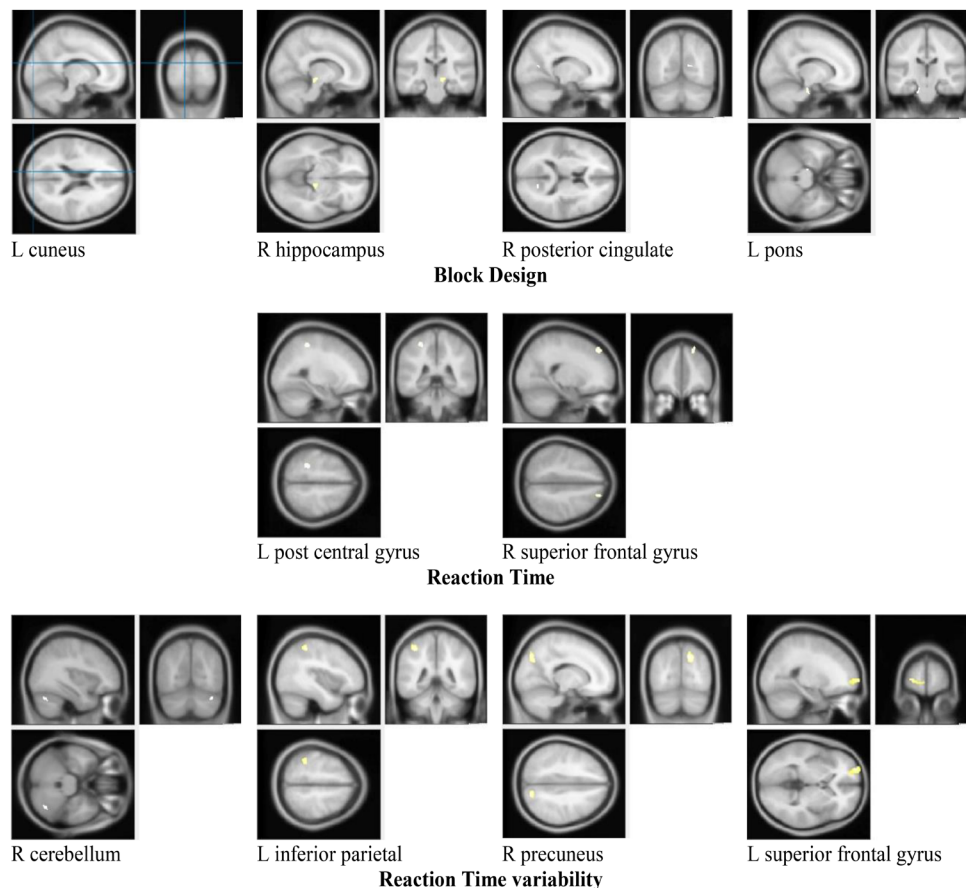


Figure 2. The results of the VBM study, testing the association of grey matter of the brain with the measures of the block design test, as well as the reaction time and the variability of the reaction time test results

Our results showed the association of brain grey matter with the score of the block design test in 4 brain areas: left cuneus (30 voxels; $x, y, z = -12, -90, 19.5$; and z value = 3.55), right brain stem and hippocampus (102 voxels; $x, y, z = 12, -24, -7.5$; and z value = 3.93), right posterior cingulate (37 voxels; $x, y, z = 16.5, -64.5, 13.5$; and z value = 3.43), and left pons (33 voxels; $x, y, z = -13.5, -22.5, -27$; and z value = 3.29). In addition, the results showed the association of grey matter volume with lower reaction times of the participants in 2 brain areas: left post central gyrus (129 voxels; $x, y, z = -25, -38, 56$; and z value = 3.23), and the right Superior Frontal Gyrus (SFG) (81 voxels; $x, y, z = 21, 42, 46$; and z value = 3.64). Finally, lower standard deviation of the reaction times of the participants was in association with the structure of 4 regions: both right and left cerebellum (62 voxels; $x, y, z = 36, -67, -28$; and z value = 3.37; 35 voxels; $x, y, z = -36, -69, -28$; z value = 3.35, respectively), inferior parietal (171 voxels; $x, y, z = -39, -42, 55$; z value = 3.87), precuneus (348 voxels; $x, y, z = 15, -75, 39$; z value = 3.94), and superior frontal gyrus (326 voxels; $x, y, z = -22, 63, 0$; z value = 4.1). All these results were obtained with a P value < 0.001 (FWE-corrected), and by correcting the analyses for the total cerebrum volume, age, and sex of the participants (Figure 2).

4. Discussion

4.1. Association of brain structure and function

The association of brain structure and its cognitive abilities has been documented (Moessnang et al., 2017; Weinstein et al., 2012). Our preliminary analyses tested the association of Reaction Time (RT), its variance (RT-SD), and the executive performance with the GM volume of the brain.

4.1.1. Reaction time

A lower RT showed associations with the GM of two brain areas: the left postcentral gyrus and the right Superior Frontal Gyrus (SFG). The postcentral gyrus is well known to be the location of the primary somatosensory cortex and is considered to be responsible for integrating somatic and visual information (Iwamura, 1998). This area receives data based on the texture from the Brodmann area 3b. As succeeding in this task (RT) needs dissociation between the two colors (red and green), it is suggested that a larger postcentral gyrus is associated with better integrating the visual and tactile information.

The R SFG also showed association here. In conflicting tasks, the medial SFG is the region involved in task control and selecting action sets (Rushworth, Walton,

Kennerley, & Bannerman, 2004). We used the complex RT test, and in this test, each hand is responsible for a different color. It is previously reported that when contradicting anticipation is demanded (similar to our task), the activation of the right SFG is correlated with the inhibitory control capacity (Hu, Ide, Zhang, & Chiang-shan, 2016), which could be an explanation for the structure of this area being associated with RT.

4.1.2. Reaction time variability

RT-SD is a measure of inconsistency (Wickett, Vernon, & Lee, 2000) and predicts the performance intelligence stronger than the mean RT (Walhovd & Fjell, 2007). A significant negative correlation between RT-SD and brain volume is previously reported, which indicated that the subjects with more processing errors had smaller regional brain volumes (Wickett et al., 2000). Four brain structures in our results were correlated with this measure: both right and left cerebellum, inferior parietal, precuneus, and superior frontal gyrus.

GM of precuneus, a region known as a part of the Default Mode Network (DMN), showed a negative correlation with the RT-SD. DMN is activated during rest and is a task-negative network. A positive correlation has been demonstrated between the DMN activation and the RT inconsistency, evidenced by the performance fluctuation observed in individuals incapable of adequately suppressing the DMN (Tamm et al., 2012). A study suggested that the correlation between the precuneus structure and the Intra-Individual Variability (IIV) is due to the failure in attentional control, suggesting this region be involved in self-referential processing (Jackson, Balota, Duchek, & Head, 2012).

A larger cerebellum was also associated with steadier reaction time. Studies have reported that damage to the cerebellum is correlated with the variability in responses to the go signals in a go/no go task (Brunamonti et al., 2014). Timing is a crucial aspect of motor control, as controlling the onset of each muscle contraction is needed for a sequential action. The cerebellum is thought to be responsible for coordinating eye and hand movements and is also involved in planning, initiation, and timing of voluntary movements (Salman, 2002).

The Inferior Parietal Lobule (IPL) receives afferents from two or more sensory channels and is generally involved in movement control. The eye, hand, and arm motor fields are located in parts of the IPL. Most of the IPL neurons were associated with the monkey's active movement (Chadwick, Diamond, & Goode, 2006). Assmus

et al. showed that IPL is a critical region in space-time integration in complex actions, and collision judgments (relative to size judgments) caused increased activation in the left IPL (Assmus et al., 2003). In another fMRI study, decreased IIV was associated with higher activation in IPL (MacDonald, Nyberg, Sandblom, Fischer, & Bäckman, 2008). Similar to these fMRI studies, in our finding, this area's volume, which is proven to play a crucial role in precise hand movement, was correlated with a slower reaction time variability.

The SFG structure was associated with both lower RT and RT-SD. Parts of the SFG, including pre-supplementary and supplementary motor areas, are involved in task-switching. In the Wisconsin card sorting test, it is seen that lesion in this area leads to an inability to switch between different task rules (Cutini et al., 2008). In an fMRI study, more activation in the SFG was seen in switching trials than in repetition ones (Rushworth, Hadland, Paus, & Sipila, 2002). Our test required switching between the two reactions, and this could be an explanation for observing the association of SFG volume with the RT-SD.

4.1.3. Block design

The structure of 4 brain areas showed associations with the scores of the block design test: left cuneus, right brain stem, hippocampus, right posterior cingulate, and left pons. The block design test requires skills such as executive functioning, spatial visualization, organizational processing, nonverbal problem-solving, and fine motor skills (Johansson & Wahlin, 1998; Soto & Kraper, 2013). The Posterior Cingulate Cortex (PCC) is an important region involved in internally directed cognition (Leech & Sharp, 2014) required for mental imagery (Dixon, Fox, & Christoff, 2014). This area is also reported to be active in planning for the future. It is suggested to play a significant role in regulating attention, based on the reports on the PCC impairment predicting attentional deficits (Leech & Sharp, 2014). Hippocampus is also well known to be responsible for spatial representation and navigation (Burgess, Recce, & O'Keefe, 1995; Kjølstrup et al., 2008). Dorsal and intermediate parts of the hippocampus, connected to the visual and somatosensory cortices, are more critical in spatial behaviors (Kjølstrup et al., 2008). Impairments in spatial learning are seen with lesions in these hippocampal regions. The pyramidal neurons of the hippocampus were initially thought to be only responsible for spatial navigation, but they turned out to be involved in other spatial domains (Behrens et al., 2018).

5. Conclusion

Precise criteria were selected to include mentally- and physically-healthy participants in the study and a wide age range of cognitive tests and the major MRI protocols. However, there are several limitations with the IBID. Despite having 300 participants, this number is not adequate compared to the available databases. The battery of cognitive tests could be larger, although we were limited by the amount of time we could visit each participant. Besides, monetary compensation could cause people from lower socioeconomic status to participate more in the study. Single and married individuals may have different performance tests, but this was not a criterion here. Finally, due to the diverse ethnicity of the Iranian population, the IBID could not be declared to be the representative of the whole population, and this is mostly a community sample. However, collecting data in the capital city of the country was in favor of including people from nearly all cultures and ethnicities, and this information was recorded from each participant.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of the National Institute for Medical Research Development (NIMAD) (Code: IR.NIMAD.REC.1396.319). Also, the study is in agreement with the Declaration of Helsinki.

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Authors' contributions

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Conflict of interest

The authors declared no conflict of interest.

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