Research Article

Apparent Diffusion Coefficient Value of Normal Brain in Relation to Age and Gender in Adults

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Abstract

Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) is now a powerful tool for functional evaluation of brain tissues. By using Apparent Diffusion Coefficient (ADC) value a sound comparison can be made between different brain parts which otherwise has similar signal characteristics in conventional MRI sequences. The purpose of this study was to investigate the normal ADC values in main cerebral tissues such as grey matter (GM), basal ganglia, white matter (WM), cerebellum and brain stem; we studied changes in ADC with aging. Mean ADC values for 7 different brain structures of 350 normal adult brains were measured, no difference was found according to gender but consistent differences was found between brain structures, and changes with aging found for cerebral white matter and thalamus. This quantitative information may help in better identifying age-related pathology.

Keywords: Magnetic Resonance Imaging (MRI); Apparent Diffusion Coefficient (ADC); Normal brain

Introduction

Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI), as a new functional magnetic resonance imaging sequencing technique, is based on Brownian motion of water molecules in biological tissues, which results from the thermal energy carried by these molecules. [1,2]

Diffusion weighting is expressed with a b value, which is dependent on sequence characteristics. The b value increases with increasing diffusion weighting, and sufficient diffusion weighting is usually achieved with a b value of 1000 s/mm^2. [3] By using at least two data sets with different strengths of diffusion gradient, the apparent diffusion coefficient (ADC, which is the net diffusion of the molecules, measured in mm^2/s) can be calculated to describe diffusion conditions quantitatively. [4] The term "apparent" is used for diffusion coefficient to differentiate from true diffusion coefficient since the measured water diffusion coefficient in the tissue is influenced by a number of other factors such as capillary network orientation and gross motion in addition to random Brownian motion. [5]

ADC is the main tool for a sound comparison between brain tissue features and/or cerebrospinal fluid (CSF), being more useful than the DWI signal intensity analysis, [6] and Therefore offers a unique opportunity to obtain information about morphology and have the potential to visualize subtle structural and functional alterations that are otherwise inaccessible to conventional MR imaging methods. [7]

The clinical usefulness of diffusion-weighted images has been reported in the diagnosis of acute cerebral infarction, tumor and degenerative diseases [8] ADC measurements are useful for the quantitative assessment of pathological states of the brain, such as neurological disorders of the brain, [9] the detection of tumors, the characterization of lesions, and the evaluation of the treatment response. [10] Quantitative measures in normal-appearing white matter are presently being performed in several disease processes (e.g., multiple sclerosis). [11]

Despite many disease processes that alter ADC values, Changes in brain ADC May be due to morphological and tissue composition alterations that occurs with normal aging. ADC in newborns and children is initially very high at term, approximately twice normal adult levels, with slightly higher values observed in white matter. [12] This difference has been ascribed to the lack of or incomplete myelination, with consequent increased water motion relative to the more restrictive environment seen in fully mature, myelinated brain. [13] Normal ADC values drop steeply over the first 2 years of life, and then decrease more gradually to adult values over several years. In normal older patients mild increases in average brain ADC values may be seen with advancing age. [12]. These changes are attributed to fiber degeneration, subcortical infarction, increasing Virchow-Robin spaces, and capillary changes in the blood-brain barrier.

Therefore an accurate characterization of normal human brain by ADC calculation and the knowledge of age-dependent diffusion changes in the human brain can be helpful in the proper interpretation of diffusion-weighted images. Hence, the goal of our work is to investigate microstructural changes using the ADC values of specific structures in normal brains over a wide age range with the b values used in clinical practice.

Patients and Methods

This is a cross sectional study. Patients with normal brain

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MRI confirmed by two radiologists and healthy volunteers that attended Hiwa Hospital in Sulaimaniya city/Iraq were included. The data collection carried out during the period of: first December 2018 to first November 2019. A total of 350 subjects were subjected to standard brain MRI examination, including T1 Weighted Images (T1WI), T2 Weighted Images (T2WI), Fluid Attenuated Inversion Recovery (FLAIR), and Diffusion Weighted Images (DWI). Patients with no significant morphological abnormality observed by two radiologists in conventional MRI examination were considered normal and included in the study.

The MRI studies performed by MAGNETOM Aera 1.5 Tesla Siemens MRI machine. Images acquired using echoplanar DWI. The DW sequence was applied using identical parameters ; FOV: 230 × 230 mm, TR/TE 6000/109.0 ms, slice thickness 5mm, 25 slices.

Variables

- Diffusion was measured in three orthogonal directions with two b values (0 and 1000 s/mm^2), and trace images obtained with averaging of the three (x, y, & z) gradients for each b value, after that ADC values were calculated directly from automatically generated ADC maps, with circular Region of Interests (ROI). This is the average ADC value along the three orthogonal directions, so it is rotationally invariant.
- Data analysis performed after transferring the images to a separate workstation, a total of 9 ROIs were manually placed on different brain regions in each hemisphere, including two different selected regions from cerebral grey matter, two regions from cerebral white matter, cerebellar white matter, caudate, putamen, thalami, and pons bilaterally. The size of marked ROIs was about 10 mm^2 [Figure 1].
- The obtained ADC results were divided into 7 groups against the subject's age. And mean values of each region against age calculated.

SPSS program version 20 was used for data entry and analysis. T-test and ANOVA test was used to identify differences between group means. A p-value of <0.05 was considered to be statistically significant.

Results

The study sample is composed of 350 adults; 190 (54.3%) were females and 160 (45.7%) were males. The female to male ratio is (1.19:1). The age range was between 20 and 87 years, mean ± SD 53 ± 16 years. The largest group was 60-69 years 77 (22%) and 50-59 years 67 (19.1%) [Table 1].

The mean ADC value was significantly greater in grey matter (888 ± 24) × 10^{-6} mm^2/s than cerebral white matter (750 ± 13.4) × 10^{-6} mm^2/s (p-value <0.0001), cerebellar white matter (600 ± 11.3) × 10^{-6} mm^2/s(p-value<0.0001), caudate (776 ± 37.2) × 10^{-6} mm^2/s(p-value <0.0001), putamen (740 ± 10.4) × 10^{-6} mm^2/s (p-value<0.0001), thalamus (754 ± 22.6) × 10^{-6} mm^2/s (p-value <0.0001) and pons (632 ± 52.4) × 10^{-6} mm^2/s(p-value<0.0001).

There was no significant difference in the mean ADC values between males and females, [Table 2] and also between right and left hemispheres in all ROIs.

Regarding mean ADC values between age groups; significant variation found between age groups for all cerebral white matter regions (p-value<0.0001) Figure 2, and thalamus

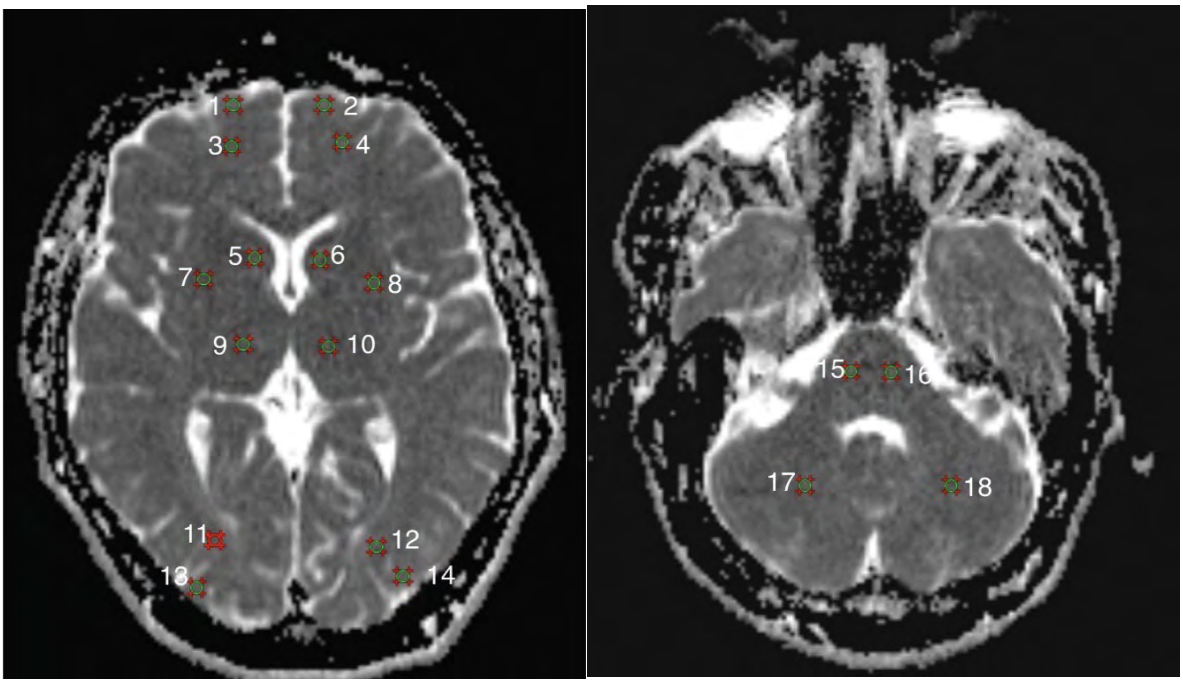

Figure 1: An example of Region of Interest (ROI) for selected structures on the ADC map: (1) Right frontal gray matter, (2) Left frontal gray matter, (3) Right frontal white matter, (4) Left frontal white matter, (5) Right caudate, (6) Left caudate, (7) Right putamen, (8) Left putamen, (9) Right thalamus, (10) Left thalamus, (11) Right occipital white matter, (12) Left occipital white matter, (13) Right occipital gray matter, (14) Left occipital gray matter, (15) Right pons, (16) Left pons, (17) Right cerebellum, (18) Left cerebellum.

(p-value<0.0001) Figure 3, which show increasing mean ADC values with increasing age. While no significant variation with age for gray matter, cerebellar white matter, basal ganglia, and caudate in between all age groups [Table 3].

Table 1: Distribution of the study group by age and sex.

Age (year)	No.	Male	Female	%
20-29	30	13	17	8.6
30-39	46	20	26	13.1
40-49	65	33	32	18.6
50-59	67	30	37	19.1
60-69	77	33	44	22
70-79	56	25	31	16
≥80	9	6	3	2.6
Total	350	160	190	100.0

Table 2: Mean ADC values ± SD in different ROIs and according to gender.

ROI	Female		Male		p-value
Cerebral Gray matter	888.5447	24.60699	888.0125	24.19411	0.839
Cerebral White matter	750.5697	13.23878	750.7578	13.67047	0.896
Cerebellar white matter	600.5421	10.58217	600.1844	12.28509	0.770
Caudate	777.4053	36.80071	776.3000	37.94158	0.783
Putamen	740.7289	10.32957	739.3750	10.58152	0.228
Thalamus	752.9842	22.99096	755.3375	22.28832	0.334
Pons	631.8421	51.62696	634.1719	53.50968	0.679

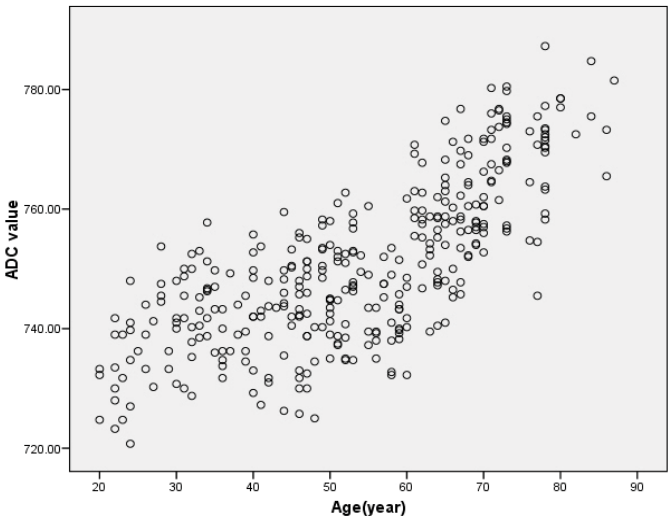

Figure 2: Distribution of white matter ADC values in ($mm^2/sec \times 10^{-6}$) according to age.

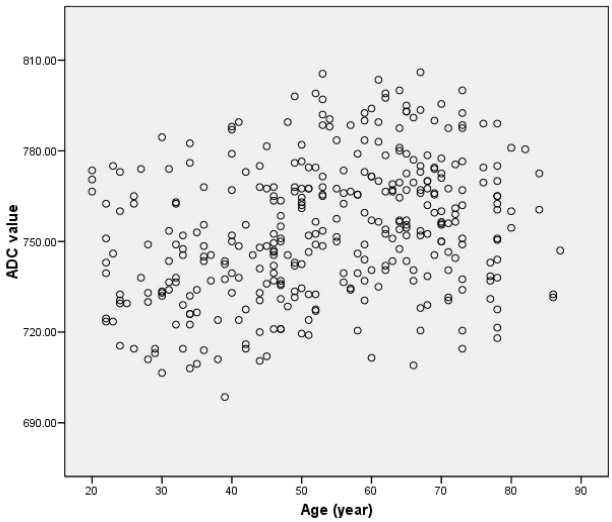

Figure 3: Distribution of thalamic ADC values in ($mm^2/sec \times 10^{-6}$) according to age.

Table 3: Mean ADC values ± SD in different ROIs according to age groups.

ROI	20-29	30-39	40-49	50-59	60-69	70-79	≥ 80	total	p-value
Cerebral White matter	735.90 8.0	741.98 6.6	743.71 8.9	745.34 7.5	756.64 8.8	767.73 8.4	776.33 5.5	750.65 13.4	0.0001
Cerebral Gray matter	890.46 21.9	888.12 22.7	892.29 28.9	887.57 22.8	884.45 25.3	890.83 21.2	875.72 22.1	888.30 24.3	0.327
Cerebellar white matter	601.63 11.3	602.10 9.3	599.80 11.1	600.02 12.4	599.53 11.1	599.25 11.2	608.33 15.5	600.37 11.3	0.319
Caudate	770.43 37.8	773.70 39.0	780.12 37.9	778.54 37.5	780.50 37.9	772.16 34.1	777.88 36.8	776.90 37.2	0.748
Putamen	739.71 10.7	739.02 10.6	740.73 8.0	740.44 9.6	739.79 11.8	740.41 10.3	740.83 8.5	740.11 10.4	0.986
Thalamus	742.46 21.2	739.15 19.9	748.57 21.0	759.62 21.7	764.57 21.1	757.16 21.0	757.77 18.5	754.06 22.6	0.0001
Pons	630.01 38.8	631.54 55.8	637.77 59.2	627.73 50.9	631.91 53.39	633.50 47.9	657.61 58.0	632.90 52.4	0.765

Discussion

In this study we evaluated ADC values for multiple different regions of human brain in a large adult population including patients of both sexes distributed over a wide age range, which provides the first data in Sulaimaniya city. DWI as one of the promising methods for studying tissue microstructure has become a routine component of brain MRI imaging protocols over the past 2 decades, [13,14] because of its speed, use in diagnosis of many pathological processes, specially its unique ability for early detection of ischemic disorders of CNS. These clinical images provide enormous potential resource for scientific investigation of its quantitative parameters in normal and pathological states of brain. [13]

Diffusion properties of brain have been reported to reflect structural properties and because normal aging is associated with ultra-structural changes which can be easily depicted by DWI and its quantitative parameter, ADC Value. [11] We studied whether ADC values of normal appearing brain would differ across age groups, which besides providing a better understanding of normal aging process it help to better assess disease processes because minor changes may be difficult to detect by visual inspection.

The ADC values of different ROIs we studied are similar to values stated by other studies including Aleksandra Klimas et al. [10] Stefan et al., [11] ADC values of various analyzed brain regions were different, and this is likely due to structural and physiological differences between these regions. [6,15]

the ADC values in the cerebral cortex were significantly higher than those of white matter In all age groups and in both sexes, this finding is in agreement with previous studies by Helenius et al., [16] Gideon et al., [17] Ahlhelm et al. [18] However it is in contrary to RN Sener et al. [19] this consistent difference might be due to the fact that GM has substantially higher blood flow and consists mostly of unmyelinated neurons while WM is made up of mostly myelinated neurons, the mean free water content of GM is higher than that in WM. [20]

In addition the ADC values in the basal ganglia and thalamus were lower than the values in the GM, similar results seen. [16] In thalamus the results vary throughout studies for example, in the study by Fabiano et al. [21] and another by Ni JM et al. [22] they were between 71 and 75 × 10^{-5} mm^2/s, which is near our results, while in the study by Naganawa S et al. [8] they were between 82 and 98 × 10^{-5} mm^2/s. This may be contributed to by different imaging parameters used.

Based on the reports that state differences in ADC values between the two brain hemisphere structures, like Naganawa S, et al. who found statistically significant differences between some right and left white matter regions, and also Kantarci et al. [23] during studying regional diffusivity in mild cognitive impairment showed differences in ADC value of right and left thalamus, and they contributed it to the ultrastructural differences between the two hemispheres, we studied changes in ADC due to laterality, and we found no statistically significant differences for all age groups. This is in agreement with other studies. [24]

No statistically significant difference found between male and female participants in all age groups in our study. This is consistent with Johanna Helenius et al. [16] and Teodora Albu et al. [24] and Watanabe et al. [25] while in Naganawa S, et al. male and female below 60 were different.

The mean ADC values of all studied white matter regions show statistically significant change with age, we found gradually increased ADC values with increasing age, but mainly in patients over 60 years old, other studies like Johanna et al. [16] found a trend to higher ADC values with age, so that in patients under 60 years old all white matter regions showed lower ADC values than in the subject groups over 60 years old, this result is also in agreement with Naganawa et al. [8]

Higher ADC values with increasing age in the thalamus was found, in other studies like Stefan T et al. [11] and Ni et al., [22] differences found in thalamus but it was not statistically significant. these differences are explained by changes that occur during aging like enlargement of extracellular space by the decrease of neurons and myelinated fibers, change of capillary walls, and loss of pericytes, [26,27] and also by studying autopsy data which indicate that myelin contents are stable to age 50, and thereafter a 10-15% loss of myelinated fibers occurs until the 8th decade. This change in ADC values which occur with ageing is small in comparison to the change that occur during acute stroke or other disease states, for example a 40-50% reduction in ADC values needed to diagnose acute stroke, [11] while in our studied age groups only 4.2% difference was found between white matters of first and last group, but despite this patients age may need to be considered in measuring ADC values for proper interpretation of the findings.

ADC values in cortical gray matter regions show no change with age. And to the best of our knowledge no reports of age related regional diffusion changes in the cortical gray matter have been reported. Ni et al. [22] found that concentration of NAA in cortex was relatively stable after correction was made for the effect of atrophy.

We note some limitation of this study, related to the manual selection of ROIs, because it is difficult to select an identical site in a structure because of the variability of the brain size. Regarding The size of the ROIs, we tried to draw identical sizes as much as possible, because small ROIs could provide partial information on the analyzed structure and larger ROIs can encompass information from different cerebral structures. Histogram analysis is a promising method; however there is lack of spatial information and whole brain analysis may not demonstrate subtle abnormal regional changes at the early stage of disease.

Conclusion

This study has shown that the ADC values change with cerebral structures and in some structures it change with aging, reflecting different diffusion states in brain due to microstructural changes, this emphasizes the role of measuring ADC values in proper interpretation of DWI in clinical practice.

Competing Interests

The authors declare that they have no competing interests.

References

1. Le Bihan E, Breton D, Lallemand P, Grenier E, Cabanis M, Laval J. MR imaging of intravoxel in coherent motions: Application to diffusion and perfusion in neurologic disorders. Radiology. 1986;161:401-407.
2. Taylor DG, Bushell MC. The spatial mapping of translational diffusion coefficients by the NMR imaging technique. Phys Med Biol. 1985;30:345-349.
3. Xing D, Papadakis NG, Huang CL, Lee VM, Carpenter TA, Hall LD. Optimized diffusion-weighting for measurements of apparent diffusion coefficient (ADC) in human brain. Magn Reson Imaging. 1997;15:771-784.
4. Stejskal E, Tanner J. Spin diffusion measurements: Spin-echos in the presence of a time-dependent field gradient. J Chem Phys. 1965;42:288-292.
5. Azim C. Effect of imaging parameters on the accuracy of apparent diffusion coefficient and optimization strategies. Diagn Interv Radiol. 2016;22:101-107.
6. Luminita M, Lucian D. Apparent diffusion coefficient of the normal human brain for various experimental conditions. AIP Conference Proceedings. 2017;1796:040005.
7. Zhong J. Basics of diffusion measurements by MRI. In: T. Moritani, (editors). Diffusion-weighted MR imaging of the brain. (2nd edition). London: Springer Dordrecht Heidelberg. 2009. p. 3.
8. Naganawa S, Sato K, Katagiri T, Mimura T, Ishigaki T. Regional ADC values of the normal brain: differences due to age, gender, and laterality. Eur Radiol. 2003;13:6-11.
9. Mascalchi M, Filippi M, Floris R, Fonda C, Gasparotti R, Villari N. Diffusion weighted MR of the brain: methodology and clinical application. Radiol Med 2005;109:155-197.
10. Klimas A, Drzazga Z, Kluczewska E, Hartel M. Regional ADC measurements during normal brain aging in the clinical range of b values: A DWI study. Clinical Imaging. 2013;37:637-644.
11. Engelter ST, Provenzale JM, Petrella JR, De-Long DM, MacFall JR. The effect of aging on the apparent diffusion coefficient of normal-appearing white matter. American Journal of Roentgenology. 2000;175:425-430.
12. Maas LC, Mukherjee P. Diffusion MRI: Overview and clinical applications in neuroradiology. Applied Radiology. 2005;34:44-60.
13. Chun T, Filippi CG, Zimmerman RD, Ulug AM. Diffusion changes in the aging human brain. AJNR Am J Neuroradiol. 2000; 21:1078-1083.
14. Tournier JD. Diffusion MRI in the brain – Theory and concepts. Progress in Nuclear Magnetic Resonance Spectroscopy. 2019;113:1-16.
15. Le Bihan D, Turner R, Douek P, Patronas N. Diffusion MR imaging: Clinical applications. AJR Am J Roentgenol. 1992;159:591-599
16. Helenius J, Soinne L, Perkio J, Salonen O, Kangasmaki A, Kaste M, et al. Diffusion-weighted MR imaging in normal human brains in various age groups. AJNR Am J Neuroradiol. 2002;23:194-199.
17. Gideon P, Thomsen C, Henriksen O. Increased self-diffusion of brain water in normal aging. J Magn Reson Imaging. 1994;4:185-188
18. Ahlhelm F, Hagen T, Schneider G, Dorenbeck U, Nabhan A, Reith W. ADC mapping of normal human brain. Med Sci Monit. 2004;10: MT121-125.
19. Sener RN. Diffusion MRI: Apparent Diffusion Coefficient (ADC) values in the normal brain and a classification of brain disorders based on ADC values. Computerized Medical Imaging and Graphics. 2001;25:299-326.
20. De Groot J, Chusid JG. Correlative neuroanatomy. Stamford, Conn: Appleton & Lange; 1991;319.
21. Fabiano AJ, Horsfield MA, Bakshi R. Interhemispheric asymmetry of brain diffusivity in normal individuals: A diffusion-weighted MR imaging study. AJNR Am J Neuroradiol. 2005;26:1089-1094.
22. Ni JM, Chen S, Liu JJ, Huang G, Shen TZ, Chen XR. Regional diffusion changes of cerebral grey matter during normal aging—A fluid-inversion prepared diffusion imaging study. European Journal of Radiology. 2010;75:134-138.
23. Kantarci K, Jack CR Jr, Xu YC, Campeau NG, O'Brien PC, Smith GE, et al. Mild cognitive impairment and Alzheimer disease: Regional diffusivity of water. Radiology. 2001;219:101107
24. Albu TA, Malaescu I. Alterations of contralateral white matter in glioma and meningioma patients: A numerical diffusion-weighted imaging approach. Int J Clin Exp Med. 2019;12:2575-2582
25. Memi Watanabe M, Sakai O, Ozonoff A, Kussman S, Jara H. Age-related apparent diffusion coefficient changes in the normal brain. Radiology. 2013;266:575-582.
26. Chun T, Filippi CG, Zimmerman RD, Ulug AM. Diffusion changes in the aging human brain. Am J Neuroradiol. 2000;21:1078-1083.
27. Meier-Ruge W, Ulrich J, Bruhlmann M, Meier E. Age-related white matter atrophy in the human brain. Ann NY Acad Sci. 1992;673:260-269.