Evaluation of attention deficit, hyperactivity, and impulsivity symptoms in patients with type 2 diabetes mellitus

Tip 2 diyabet tanılı hastalarda dikkat eksikliği, hiperaktivite ve dürtüsellik semptomlarının değerlendirilmesi

Ali İnaltekin[1], İbrahim Yağcı[2], Eray Atalay[3]
[1]Assit.Prof., Oltu State Hospital, Department of Psychiatry, Erzurum,Turkey, https://orcid.org/0000-0003-0933-0308
[2]M.D., Kars Harakani State Hospital,Department of Psychiatry, Kars, Turkey, https://orcid.org/0000-0003-0755-2695
[3]Assoc. Prof., Kafkas University,School of Medicine, Department of Internal Medicine, Kars,Turkey, https://orcid.org/0000-0002-9700-7019

SUMMARY

Objective: Type 2 Diabetes Mellitus (DM) is a chronic metabolic disease and a global health problem. Inadequate glycemic control and diabetes self-management can cause many secondary diseases. There are few studies on the association between attention deficit hyperactivity disorder (ADHD) and type 2 DM. Our study compares adult and childhood ADHD symptoms and signs and impulsivity in type 2 DM patients and healthy controls. **Method:** In this case-control study, data were collected voluntarily. The study was carried out with a total of 200 participants, including 100 people in both the Type 2 diabetes group and the healthy control group. The Barratt Impulsivity Scale version 11 (BIS-11), Adult ADHD Self-Report Scale (ASRS), Wender-Utah Rating Scale (WURS) and demographic information form were applied to the participants and compared between the groups. **Results:** The mean ASRS attention score, ASRS hyperactivity score, ASRS total score, WURS total score, BIS total score of the type 2 DM group were significantly higher than the control group. Moreover, the probability of ADHD was evaluated using the cut-off scores in the ASRS and WURS scales, and it was detected in significantly more people in the type 2 DM group. **Discussion:** Our study revealed that attention deficit, hyperactivity, and impulsivity symptoms are more common in type 2 DM patients than controls. Evaluation of these symptoms may be beneficial in the self-management of diabetes and in improving glycemic control.

Key Words: Attention deficit hyperactivity disorder, impulsivity, type 2 diabetes mellitus

ÖZET

Amaç: Kronik, metabolik bir hastalık olan tip 2 Diyabetes Mellitus (DM), küresel bir sağlık sorunudur. Yetersiz diyabet özyönetimi ve glisemik kontrol birçok ikincil hastalığa sebep olabilir. Dikkatsizlik, motor hiperaktivite ve dürtüsellik ile karakterize Dikkat Eksikliği Hiperaktivite Bozukluğu (DEHB) ve tip 2 DM arasındaki ilişki hakkında yeterince çalışma yoktur. Çalışmamızda tip 2 DM hastalarında ve sağlıklı kontrollerde erişkin ve çocukluk çağındaki DEHB belirti ve bulguları ile dürtüselliği karşılaştırmayı amaçladık. **Yöntem:** Araştırmamız bir olgu-kontrol çalışması olup veriler gönüllü katılım esasına göre toplandı. Çalışma Tip 2 diyabet ve sağlıklı kontrol grubunda 100 kişi olmak üzere toplam 200 katılımcı ile gerçekleştirildi. Çalışmaya alınan katılımcılara Erişkin Dikkat Eksikliği Hiperaktivite Bozukluğu Öz Bildirim Ölçeği (EDHÖ), Wender-Utah Derecelendirme Ölçeği (WUDÖ), Barratt Dürtüsellik Ölçeği 11. versiyon (BIS-11), demografik bilgi formu uygulandı ve gruplar arasında karşılaştırıldı. **Bulgular:** Tip 2 DM grubunun ortalama EDHÖ dikkat puanı, EDHÖ hiperaktivite puanı, EDHÖ toplam puanı, WUDÖ toplam puanı, BDÖ toplam puanı, kontrol grubuna göre anlamlı olarak yüksek bulundu. Ayrıca EDHÖ, WUDÖ ölçeklerinde kesme puanlar kullanılarak DEHB olasılığı değerlendirildi ve tip 2 DM grubunda anlamlı olarak daha fazla kişide tespit edildi. **Sonuç:** Çalışmamızda tip 2 DM hastalarında dikkat eksikliği, hiperaktivite ve dürtüsellik semptomları kontrollere göre daha fazla bulundu. Diyabetin öz yönetiminde ve glisemik kontrolün iyileştirilmesinde bu semptomların değerlendirilmesi faydalı olabilir.

Anahtar Sözcükler: Dikkat eksikliği hiperaktivite bozukluğu, dürtüsellik, tip 2 diyabet

(Turkish J Clinical Psychiatry 2023;26:143-148)
DOI: 10.5505/kpd.2023.85451

The arrival date of article: 10.06.2022 , Acceptance date publication: 12.10.2022

INTRODUCTION

Diabetes mellitus (DM) is an increase in blood glucose due to insufficient secretion of insulin or insufficient use of secreted insulin (1). Type 2 DM, which constitutes 90% of diabetes patients and manifests itself with insufficient insulin function, is a global health problem with increasing prevalence and incidence rates every year (2,3). Mismanagement of diabetes that results in high blood sugar can cause several secondary diseases. The risk of heart attack increases up to 200% in patients with diabetes (4). In severe cases, inadequate glycemic control can result in foot infections and limb amputations (5). In addition, diabetes can cause kidney failure and stroke (6,7). Comorbid somatic diseases and psychological disorders related to diabetes can also be seen (8).

Impulsivity manifests itself in behaviors that lack adequate reflection and foresight. The diagnosis of type 2 diabetes is associated with impulse control disorders, especially eating disorders (9). Moreover, impulsivity has been identified as potential risk factor for developing type 2 DM (9). These findings suggest that impulsivity may impair diabetes self-management through lack of planning and inadequate behavioral regulation.

Attention Deficit Hyperactivity Disorder (ADHD) is a chronic neuropsychiatric disorder that begins in childhood and is characterized by attention deficit, impulsive behavior and hyperactivity (10). ADHD symptoms typically appear in childhood, and approximately 50% of these symptoms are carried over to adulthood (11,12). Studies have reported an increase in the prevalence of ADHD in recent years (13). In parallel, childhood obesity has been increasing over the past years. The comorbidity of ADHD and obesity has been evaluated. Despite the contradictory findings in the studies, meta-analytical evidence indicates a significant relationship between ADHD and obesity, independent of psychiatric comorbidity (14). The relationship between obesity, metabolic syndrome, and ADHD is well known. However, the relationship between ADHD and diabetes, one of the metabolic syndrome components, is not well established.

The present study compares adult and childhood ADHD symptoms and signs and impulsivity in healthy controls and type 2 DM patients.

METHOD

The study was carried out in the internal medicine outpatient clinic of Kafkas University Research Hospital between April 1, 2020, and January 1, 2021. All procedures were performed under the 1964 Declaration of Helsinki and its subsequent amendments, and the Ethics Committee approved the study of Kafkas University Faculty of Medicine at session 04, dated February 2, 2020.

Participants

The patient group (n=99) of this study consists of individuals older than 18 years of age and at least a primary school graduate who applied to the Internal Medicine outpatient clinic of Kafkas University Research and Application Hospital and were diagnosed with type 2 DM for at least one year. A control group was formed with 100 age- and gender-matched healthy individuals. Those with comorbid psychotic, neurocognitive, substance use disorders, or psychotropic drug use were excluded.

Data Collection Tools

Social and Demographic Factors: Initially, the age, gender, education level, and marital status of all participants were assessed using a sociodemographic questionnaire prepared by the researchers.

Adult Attention Deficit Hyperactivity Disorder (ADHD) Self-Report Scale (ASRS): It was developed by the World Health Organization (15). It has two subscales; hyperactivity/impulsivity and attention deficit. It is a five-point Likert-type scale, in which each item is rated between 0 and 4. Those with a total score of 24 or higher on either of the two subscales were considered "highly likely to have ADHD," 17-23 "likely to have ADHD," and 0-16 "unlikely to have ADHD." This scale has a Turkish validity and reliability study (16).

Wender-Utah Rating Scale (WURS): It was designed

to evaluate the childhood signs and symptoms of ADHD in adults. The self-report scale is in five-point Likert-type, consisting of 25 items, in which each item is rated between 0 and 4. The cut-off score for the diagnosis of ADHD is accepted as 36 and above. The Turkish validity and reliability of the scale were established, and the cut-off point was determined as 36 (17).

Barratt Impulsivity Scale version 11 (BIS-11): It was developed to measure impulsivity. BIS-11 is a 4-point Likert-type scale in which each item is rated between 1 and 4. This scale has a Turkish validity and reliability study (18).

Data Evaluation

The data were evaluated using the SPSS (24.0) software package. The data were presented in tables as the number of individuals, percentage, arithmetic mean, and standard deviation. Statistical significance level was determined as 0.05.Kolmogorov Smirnov test, kurtosis, and skewness values were used to assess the conformity of the data to normal distribution. The independent sample t-test was used to determine the difference between the means of the two groups, and the Chi-square test was used for categorical variables.

RESULTS

The study consisted of 54 women and 45 men (n = 99) in the type 2 DM group and 56 women and 44 men (n = 100) in the control group. The mean age of participants was 56.30±9.63 years in the type 2 DM group and 57.42±6.19 years in the control group. The mean education period was 7.36±2.91 years in the type 2 DM group and 6.70±2.09 years in the control group. There were five alcohol users, 18 smokers in the type 2 DM group, six alcohol users, 20 smokers in the control group. There was no statistically significant difference between the groups in terms of age, education, gender, alcohol, and cigarette use (p=0.332, p=0.660, p=0837, p=0.769, p=0.744, respectively) (Table 1). The mean Body mass index (BMI) was 30.98±4.81 in the type 2 DM group and 26.39±3.70 in the control group. In the type 2 DM group, 76 were married, 23 were unmarried; in the control group, 92 were married, and eight were unmarried. A significant difference was detected between the groups in terms of BMI and marital status (p<0.001 and p=0.03, respectively) (Table 1).

Table 1. Demographic Characteristics of Type 2 DM and Control Groups

		Type 2 DM Group n=99	Control Group n=100	p
Age (Mean–Sd)		56.30–9.63	57.42–6.19	0.332
Education (Year) (Mean–Sd)		7.36–2.91	6.70–2.09	0.660
BMI (Mean–Sd)		30,98–4,81	26.39–3.70	<0.001
		n (%)	n (%)	
Gender	Female	54 (54.5)	56 (56)	
	Male	45 (45.5)	44 (44)	0.837
Smoking		18 (18.2)	20 (20)	0.744
Uses alcohol		5 (5.1)	6 (6)	0.769
Marital Status	Married	76 (76.8)	92 (92)	
	Single	23 (23.2)	8 (8)	0.03

Sd : Standart Deviation, BM : Body Mass Index, p<0.05

The mean ASRS attention score of the type 2 DM group was 13.19±6.14, ASRS hyperactivity score was 14.71±5.70, ASRS total score was 28.24±11.07, WURS total score was 37.24±17.87, BIS total score was 61.55±10.78; the mean ASRS attention score of the control group was 7.04±3.97, ASRS hyperactivity score was 4.82±4.38, ASRS total score was 12.86±9.74, WURS total score was 15.02±9.53, BIS total score was 51.46±8.76, and there was a statistically significant difference between the groups (all p<0.001) (Table 2).

Those who scored 24 points or more from any of the two subscales of ASRS (ASRS (24)) were 13 in the type 2 DM group, 4 in the control group; those who scored 17 or higher (ASRS (17)) were 42 in the type 2 DM group, 9 in the control group; those who scored 36 or more in the total WURS score

Table 2. Comparison of Type 2 DM andControl Groups According to ASRS, WURS, BIS Scores

	Type 2 DM Group n=99	Control Group n=100	P
	Mean–Sd	Mean–Sd	
ASRS attention	13,.19–6.14	7.04–3.97	<0.001
ASRS hyperactivity	14.71–5.70	4.82–4.38	<0.001
ASRS Total	28.24–11.07	12.86–9.74	<0.001
WURS Total	37.24–17.87	15.02–9.53	<0.001
BIS-11 Total	61.55–10.78	51.46–8.76	<0.001

BIS-11: Barratt Impulsivity Scale version 11, ASRS: attention deficit hyperactivity disorder Self-Report Scale, Sd:Standart Deviation, WURS: Wender-Utah rating scale

Table 3. Comparison of Type 2 DM and Control Groups According to ASRS and WURS Cut-off Scores

	Type 2 DM Group n=99	Control Group n=100	p
Scales (cutscore)	n (%)	n (%)	
ASRS (24)	13 (13.1)	4 (4)	0.02
ASRS (17)	42 (42.4)	9 (9)	<0.001
WURS (36)	41 (41.4)	6 (6)	<0.001

ASRS: attention deficit hyperactivity disorder Self -Report Scale , WURS: Wender -Utah rating scale

(WURS (36)) were 41 in the type 2 DM group, 6 in the control group. Comparison using these cut-off scores revealed a statistically significant difference between the groups (p =0.02, p<0.001 and p0.001, respectively) (Table 3).

DISCUSSION

This case-control study compared the type 2 DM and control groups regarding attention deficit, hyperactivity, and impulsivity symptom scores using the ASRS, WURS, and BIS scales and revealed significantly higher in the type 2 DM group. In addition, evaluating the ASRS and WURS scales according to the cut-off scores determined for the diagnosis of ADHD revealed that the number of people diagnosed with ADHD was significantly higher in the type 2 DM group than in the control group.

The diagnosis of type 2 diabetes has been associated with impulse control disorders (9). Impulsivity has been evaluated as a risk factor for the development of type 2 DM(19-21). Besides, Eckstrand et al. linked food stimuli-related impulsivity to high insulin resistance (22). Our study also determined a significantly higher impulsivity score in type 2 DM patients than in the control group. As impulsivity may impair diabetes self-management, its assessment is crucial in patients with type 2 DM.

There are only a limited number of studies evaluating the relationship between ADHD and type 2 DM. A study examining the Swedish national health registry to investigate the relationship between adult ADHD and metabolic disease reported a higher prevalence of type 2 DM in adults with ADHD than those without ADHD (23). A study conducted in Taiwan in which adolescents and young adults with ADHD were followed up to 9 years found that those diagnosed with ADHD had a higher risk of developing type 2 DM than controls (24). Considering these studies, the results of our study are consistent with the literature.

In adults with type 2 DM, decreased white matter volume and cortical/subcortical atrophy were detected, especially in the frontal region (25,26). The deterioration in cognitive functions in patients with type 2 DM was also associated with the decreased blood circulation of the frontal and parietal lobes (27). Damage to these regions can cause attention deficit, disorders in emotion regulation, and behavioral deterioration.

In ADHD, attention deficit, hyperactivity and disturbance in emotion regulation are seen. According to various neuroimaging studies, the lateral and medial prefrontal cortices, the lateral-inferior parietal and parietal-temporal-occipital cortices on the surface of the right hemisphere, and the cortico-striatal and cortico-cerebellar networks form the center of attention in the brain (28,29). These areas play a role in the formation of cognitive, emotional, and behavioral functions (30). Type 2 DM most commonly affects the frontal and hippocampus areas, explaining the risk of later developing ADHD symptoms.

Our study has limitations. The small number of cases in the patient and control groups can be considered a relative limitation. However, a preliminary power analysis was performed using G*Power3.1 to test the difference between the mean of two independent groups using the medium effect size (d= 0.50) and alpha=0.05. Accordingly, a total of 128 participants was required, with two equally sized groups of n=64 to achieve a power of 0.80. According to this a priori power analysis, our sample size can be considered sufficient. Another limitation of our study is the use of self-evaluation questionnaires without a diagnosis by a psychiatrist. Future studies to be conducted with larger sample groups using psychiatric interviews can provide more precise results.

CONCLUSION

Our study shows that attention deficit, hyperactivity, and impulsivity symptoms are more frequent in type 2 DM patients than controls. These symptoms may be risk factors for type 2 DM patients or adversely affect treatment compliance. Easy-to-use questionnaire-based patient screening can be made to support diabetes management by developing interventions tailored to these symptoms. This, in turn, can enable diabetes self-management and blood sugar control.

Conflicts of interest: The authors declare that they have no conflict of interest.

Correspondence address: M.D. İbrahim Yağcı, Kars Harakani Devlet Hastanesi Psikiyatri Kliniği Merkez/kars 36000 Kars - Türkiye, ibrahimyagci53@hotmail.com

REFERENCES

1. Alberti KGMM, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO Consultation. Diabet Med 1998;15(7):539-53.

2.Bruno G, Runzo C, Cavallo-Perin P, Merletti F, Rivetti M, Pinach S, Novelli G, Trovati M, Cerutti F, Pagano G. Incidence of Type 1 and Type 2 Diabetes in Adults Aged 30-49 Years. The population-based registry in the province of Turin, Italy. Diabetes Care 2005;28(11):2613-9.

3.Holman N, Young B, Gadsby R. What is the current prevalence of diagnosed and yet to be diagnosed diabetes in the UK. Diabet Med 2014;31(5):510-1.

4.Emerging Risk Factors Collaboration; Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, Ingelsson E, Lawlor DA, Selvin E, Stampfer M, Stehouwer CD, Lewington S, Pennells L, Thompson A, Sattar N, White IR, Ray KK, Danesh J. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010 Jun 26;375(9733):2215-22. doi: 10.1016/S0140-6736(10)60484-9.

5.Van Damme H, Limet R. Amputation in diabetic patients. Clin Pediatr Med Surg 2007;24(3):569-582.

6.Saran R, Li Y, Robinson B, Ayanian J, Balkrishnan R, Bragg-Gresham J, Chen JTL, Cope E, Gipson D, He K, Herman W, Heung M,Hirth RA, Jacobsen SS,Kalantar-Zadeh K, Kovesdy CP, Leichtman AB, Lu Y, Molnar MZ, Morgenstern H, Nallamothu B, O'Hare AM, Pisoni R, Plattner B, Port FK, Rao P, Rhee CM, Schaubel DE, Selewski DT, Shahinian V, Sim JJ, Song P,Streja E, Tamura MK, Tentori F, Eggers PW, Agodoa LYC, Abbottet KC. US Renal Data System 2014 Annual Data Report: Epidemiology of Kidney Disease in the United States. Am J Kidney Dis 2015;66(1):1-305.

7.Tuomilehto J, Rastenyte D, Jousilahti P, Sarti C, Vartiainen E. Diabetesmellitus as a risk factor for death from stroke: prospective study of the middle-aged Finnish population. Stroke 1996;27(2):210-5.

8.Çelik S, Kayar Y, Önem Akçakaya R, Uyar ET, Kalkan K, Yazısız V, Aydın Ç, Yücel B. Correlation of bingeeating disorder with level of depression and glycemic control in type 2 diabetes mellitus patients. Gen Hosp Psychiatry 2015;37(2):116-9.

9.de Jonge P, Alonso J, Stein DJ, Kiejna A, Aguilar-Gaxiola S, Viana MC, Liu Z, O'Neill S, Bruffaerts R, Caldas-de-Almeida JM, Lepine JP, Matschinger H, Levinson D, de Girolamo G, Fukao A, Bunting B, Haro JM, Posada-Villa JA, Al-HamzawiAO, Medina-Mora ME, Piazza M, Hu C, Sasu C, Lim CCW, Kessler RC, Kate M. Associations between DSM-IV mental disorders and diabetes mellitus: a role for impulse control disorders and depression. Diabetologia. 2014;57(4):699–709.

10.Thapar A, Cooper M. Attention deficit hyperactivity disorder. Lancet 2016;387:1240–50.

11.Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA.Theworldwideprevalence of ADHD: a systematic review and metaregression analysis. Am J Psychiatry 2007;164:942-8.

12.Moreno-Alcázar A, Ramos-Quiroga JA, Radua J, Salavert J, Palomar G, Bosch R, Salvador R, Blanch J, Casas M, Mckenna PJ, Pomarol-Clotet E. Brain abnormalities in adults with attention deficit hyperactivity disorder revealed by voxel-based morphometry. Psychiatry Res Neuroimaging 2016;254:41–7.

13.Feldman HM, Reiff MI. Attention deficit–hyperactivity disorder in children and adolescents. N Engl J Med 2014;370:838-46.

14.Cortese S, Tessari L. Attention-deficit/hyperactivity disorder (ADHD) and obesity: update 2016. Curr Psychiatry Rep 2017;19:4.

15.Kessler RC, Adler L, Ames M, Demler O, Faraone S, Hırıpı E, Howes MJ, Jın R, Secnık K, Spencer T, Ustun TB, Walters EE. The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. Psychol Med 2005; 35:245-56.

16.Dogan S, Oncu B, Varol-Saracoglu G, Kucukgoncu S. Validity and reliability of the Turkish version of the Adult ADHD Self-Report Scale (ASRS-v1.1). Anadolu Psikiyatri Derg 2009;10:77-87.

17.Güleç H, Tamam L, Yazıcı Güleç M, Turhan M, Karakuş G, Stanford MS. Psychometric properties of the Turkish version of the barratt impulsiveness scale 11. Klinik Psikofarmakol Bulteni 2008; 18: 251-8

18.Oncu B, Olmez S, Senturk V. Validity and reliability of the Turkish version of the Wender Utah Rating Scale for attention-deficit/hyperactivity disorder in adults. Turk Psikiyatri Derg 2005;16(4): 252-9.

19.Čukić I, Mõttus R, Realo A, Allik J. Eluci dating the links between personality traits and diabetes mellitus: Examiningt he role of facets, assessment methods, and selected mediators. Pers Individ Dif 2016; 94:377-82.

20.Terracciano A, Sutin AR, McCrae RR, Deiana B, Ferrucci L, Schlessinger D, Uda M, Costa PT. Facets of personality linked to under weight and over weight. Psychosom Med 2009; 71(6):682-9.

21.Jacobs E, Hoyer A, Brinks R, Icks A, Kuß O, Rathmann W. Healthcare costs of Type 2 diabetes in Germany. Diabet Med 2017; 34(6):855–61.

22.Eckstrand KL, Mummareddy N, Kang H, Cowan R, Zhou M, Zald D, Silver HJ, Niswender KD, Avison MJ. An insulin resistance associated neural correlate of impulsivity in type 2 diabetes mellitus. PLoS One 2017; 12(12):e0189113.

23.Chen Q, Hartman CA, Haavik J, Harro J, Klungsøyr K, Hegvik TA, Wanders R, Ottosen C, Dalsgaard S, Stephen V. Faraone SV, HenrikLarsson H. Common psychiatric and metabolic comorbidity of adult attention-deficit/hyperactivity disorder: a population-based cross-sectional study. PLoS One 2018;13:e0204516.

24.Chen M-H, Pan T-L, Hsu J-W, Huang K-L, MD; Su T-P, Li C-T, Lin W-C, Tsai S-J, Chang W-H, Chen T-J, Bai Y-M. Risk of type 2 diabetes in adolescents and young adults with attention deficit/hyperactivity disorder. J Clin Psychiatry 2018;79(3):429.

25.Hsu JL, Chen YL, Leu JG, Lee CH, Tsai YF, Hsu CY, Bai CH, Leemans A. Microstructural white matter abnormalities in type 2 diabetes mellitus: a diffusion tensör imaging study. Neuroimage 2012;59:1098-105.

26.Novak V, Last D, Alsop DC, Abduljalil AM, Hu K, Lepicoysky L, Cavallerano J, Lipsitz LA. Cerebral blood flow velocity and periventricular white matter hyperintensities in type 2 diabetes. Diabetes Care 2006;29:1529–34.

27.Niwa H, Koumoto C, Shiga T, Takeuchi J, Mishima S, Segawa T, Atsumi T, Shimizu C, Koike T, Yoshioka N. Clinical analysis of cognitive function in diabetic patients by MMSE and SPECT. Diabetes Res Clin Pract 2006;72:142-7.

28.Duncan J, Owen AM. Common regions of the human frontal lobe recruited by diverse cognitive demands. Trends Neurosci 2000;23:475-83.

29.Goldman-Rakic PS. Topography of cognition: parallel distributed networks in primate association cortex. Annu Rev Neurosci 1988;11:137-56.

30.Makris N, Meyer JW, Bates JF, Yeterian EH, Kennedy DN, Caviness VS. MRI-Based topographic parcellation of human cerebral white matter and nuclei II. Rationale and applications with systematics of cerebral connectivity. Neuroimage 1999;9:18-45.