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Selective Impairment of Attentional Networks of Executive Control in Middle-Aged Subjects with Type 2 Diabetes Mellitus

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Background: The influence of type 2 diabetes mellitus (T2DM) on attention has been elusive. The Attention Network Test (ANT) was developed to evaluate the functioning of 3 individual attentional networks: orienting, alerting, and executive control. The purpose of this study was to use the ANT to assess attentional function and its sub-components in T2DM patients ages 40–60 years.

Material/Methods: Thirty T2DM patients and 30 healthy controls ages 40–60 years were recruited in this investigation. The ANT was used to statistically compare the efficiency among 3 sub-components of the attention networks between middle-aged T2DM patients (n=30) and gender-, age-, and education-matched healthy controls (n=30).

Results: The ANT demonstrated a significant difference in executive control network between the T2DM patients and healthy controls (t=3.242, P=0.002), whereas no significant difference was observed regarding the domains of alerting (t=0.515, P=0.609) and orienting control (t=0.078, P=0.938) between the T2DM patient group and the healthy control group. Moreover, the mean reaction time in the ANT in the T2DM patients was significantly longer compared with that in the healthy controls (t=3.561, P=0.001).

Conclusions: The ANT reveals significant impairment in the executive control of middle-aged patients diagnosed with T2DM, whereas no significant impairment was observed in the domains of alerting and orienting.

MeSH Keywords: Attention • Diabetes Mellitus, Type 2 • Executive Function

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3546 4 — 43

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Background

Type 2 diabetes mellitus (T2DM) is a metabolic disease characterized by hyperglycemia due to insulin resistance and relative insulin deficiency, and involves multiple changes in the structure and function of tissues and organs [1]. Its worldwide prevalence rates are rapidly increasing, and T2DM has become a global health challenge. T2DM can cause dysfunction of the central nervous system, especially cognitive impairment. Individuals with type 2 diabetes are at ~60% greater risk for the development of dementia compared with counterparts without diabetes [2]. Therefore, T2DM is a risk factor for developing cognitive impairment and dementia [3,4]. In type 2 diabetes, cognitive changes mainly affect learning, memory, executive function, and information processing speed [5]. The exact neuroanatomical or neurochemical impacts on cognitive performance with type 2 diabetes are unclear. Previous studies based on functional imaging showed that ischemic changes in the brain, brain atrophy, and cerebral small vessel disease are involved in the cognitive impairments associated with type 2 diabetes [6,7].

Cognitive decline is a state between normal senility and dementia. Given that T2DM is related to a rising risk of dementia, it is important to identify the signs of early cognitive decline in T2DM patients before they develop dementia. Within the impaired cognitive domains of T2DM, attention and executive functions are often involved at the early stage of T2DM patients[8,9]. Attention is defined as a cognitive process selectively focused on one area of the environment but disregarding other areas. Keeping, distribution, and transformation of attention are crucial for the speed and efficiency of the brain from received external stimuli to useful information processing. The investigative tools used by neuropsychologists in these attention studies have been a battery of neuropsychological assessments such as the Trail Making Test Part A and B, the Stroop Color-Word Test (Part III), the Digit-Symbol Modalities Test, the Wisconsin Card Sorting Test (WCST), the Paced Auditory Serial Addition Test (PASAT), the Digit Span Test, and the Brixton Spatial Anticipation Test. A study Using the Color-Word Stroop Test and Digit-Symbol Modalities Test showed that T2DM subjects presented attention dysfunction compared with controls [10]. Similarly, Solanki found that hyperglycemia was significantly and negatively correlated with attention [11]. However, the impact of T2DM on attention function is still controversial. The previous study based on neuropsychological assessment (NPA), after adjustment for differences in IQ between T2DM patients and control subjects, found that attention performance was not significantly reduced [12].

Different neuropsychological scales represent only separate parts of attention which results in less comparability among different paradigms. Human manipulation also leads to poor temporal resolution. Thus, attention can be qualitatively but not accurately or quantitatively detected. These factors cause differences in the experimental results on attentional function in T2DM.

Posner et al. [13] developed a brief computerized battery called the Attention Network Test (ANT), based on attentional network theory. Alerting, orienting, and executive control, which are 3 functionally and anatomically specified brain networks, make up ANT [13,14]. ANT has been used to examine attention network functions in patients with neurological disorders, including Parkinson's disease, essential tremor, Alzheimer's disease, Wilson's disease, and multiple sclerosis [15–21]. Fuentes et al. [15] found a significant difference in alerting efficiency between AD patients and the control group. Zhou et al. [21] discovered that PD patients showed a selective dysfunction in the orienting network but there were no significant differences in Mini-Mental State Examination (MMSE), Verbal Fluency Test (VFT), or Digit Span Test (DS) between PD patients and control groups. Moreover, Lv et al. proved that testing the attentional function of individuals with ANT can identify MCI objectively and efficiently [22]. This suggests that the ANT is more sensitive than the neuropsychological scale and shows that the attention function lesion is anterior to the neuropsychological scale. To the best of our knowledge, there is no research about T2DM patients identifying the early stages of MCI through testing the attention networks with ANT.

Considering the many contradictory research results across attention domains of T2DM, it is unclear whether there is a comprehensive attentional deficit or a deficit in a specific attention network in people with T2DM. The present study used the ANT to investigate the attentional function and its sub-components in middle-aged T2DM patients (40–60 years). From earlier studies based on neuropsychological assessment [23], we assumed that T2DM patients would be more impaired than the healthy controls in attention tasks and that the efficiency of the executive control network is lower in people with T2DM.

Material and Methods

Study subjects

This study was approved by the Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong University and we obtained informed consent from all subjects. Thirty T2DM (HbA1c >6.5%) patients aged 40–60 years admitted to the Shandong Provincial Hospital affiliated to Shandong University from July to December 2016, and 30 age-, sex-, and education level-matched healthy volunteers were recruited in this study. Demographic features of the participants are summarized in Table 1. The enrolled T2DM patients met the 1999

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Table 1. Comparison of demographic characteristics between the T2DM and control groups (x±s).

	T2DM (n=30)	Controls (n=30)	*t* Value (chi-square)	*p* Value
Age (years)	48.56±6.31	47.52±6.72	0.56	0.58
Education Level (years)	9.68±2.25	10.44±2.58	–1.11	0.27
BMI (kg/m^2)	26.55±4.35	25.84±3.12	0.66	0.51
MMSE Score	28.40±1.94	28.88±1.50	–0.98	0.33
Gender, male	15 (30)	14 (30)	0.067*	0.50
HbA1c (%) [normal range: <6%]	9.30±2.19	**5.40**±0.30	8.77	**0.00**
Duration of T2DM (years)	5.76±4.99	–	–	–

Values are mean ± standard deviation or n (%). BMI – body mass index; HbA1c – glycated hemoglobin A1c; MMSE – Mini-Mental State Examination.

World Health Organization (WHO) diabetes diagnostic criteria [24] for at least 1 year. Participants were examined by Mini-Mental State Examination (MMSE) before the experiment to evaluate general mental status. All participants with anxiety or depression as assessed with the Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMD), respectively, were excluded from the study.

Exclusion criteria

We excluded subjects who had: 1) History of neurologic disorder (e.g., transient ischemic attack or stroke, Parkinson's disease, and epilepsy); 2) History of major neuropsychiatric disorder (bipolar disorder, psychotic depression, schizophrenia, dementia) or alcohol or drug abuse based on DSM-IV criteria; (3) Thyroid disease; (4) Use of medications known to affect cognition (such as benzodiazepines, prednisone); (5) Liver and kidney function insufficiency; (6) Visual impairment; or (7) A MMSE score ≤23.

Baseline data

The 30 T2DM patients were ages 40–60 years with a mean age of 48.56 years, and had an education level of 7–15 years with a mean of 9.68 years. In the T2DM group, the mean HbA1c level was 9.30% (range: 6.4–13.3%). The mean BMI (body mass index) was 26.55 kg/m^2 (range: 17.3–38.06 kg/m^2), the mean MMSE score was 28.40 (range: 24–30), and the mean duration of T2DM was 6 years (range: 1–15 years). In the control group, the participants were ages 40–60 years, with a mean age of 47.52 years and an education level of 8–15 years with a mean of 10.44. The mean HbA1c level was 5.40% (range: 5.0–5.8%). The mean MMSE score was 28.88 (range: 26–30). The mean BMI was 25.84 kg/m^2 (range: 20.81–31.86 kg/m^2). No significant difference was noted in age, body mass index, MMSE score, education level, or sex between the 2 groups (all P>0.05).

Attentional networks test (ANT)

Apparatus

The ANT was run via E-Prime 2.0 on an IBM-compatible notebook computer running Windows XP. A refresh rate of 85 Hz and a resolution of 1024×768 pixels were used to display the stimuli. The participants sat in a pleasant environment where they could view the stimuli presented on the computer screen, and responses were recorded automatically by clicking a mouse button. The completion time was approximately 25 min.

Stimuli

There was a cross ("+") in the center of the screen, and the target appeared either above or below the cross. The target was an arrow on a gray screen, pointing either to the left or the right. There were 2 arrows on both sides in the identical direction (Congruent condition), or in the opposite direction (incongruent condition), or lines without arrowheads (neutral condition). The job for participants was to respond to the direction of the central arrow and press the mouse button as fast and correctly as possible according to the orientation of the central arrow. For example, if the central arrow indicates the left, then one should press the left button, and vice versa. The target stimulus remained on the screen until the participant responded, but the response time could not be over 2700 ms. Cues were composed of a 100-ms asterisk shown about 400 ms before the target. Center cue, double cue, spatial cue, and no cue were the 4 kinds of cue conditions: (1) no cue, only a fixation was shown; (2) center cue, which was at the central fixation point; (3) double cue, there were 2 asterisks appearing above and below the fixation cross; (4) spatial cue, a single asterisk presented at the target location (either above or below the central fixation point). The reaction time (RT) and accuracy (ACC) were recorded.

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Experimental procedures

The entire experiment contained 3 blocks. The first block was a 12-trial practice of about 1 min, after which feedback about the speed and accuracy was provided. In the other 2 experiments, blocks with 96 trials per block did not show feedback, and each took roughly 10 min. Between 2 blocks, participants were allowed to take a break. Each trial stood for one of 48 conditions in equivalent proportions: 4 cue types × 2 target locations ×2 target directions ×3 congruencies, with 2 repetitions. A random order was utilized to organize the presentation of the trials. The whole experiment required approximately 20 min.

ANT records

The RT and ACC in 12 conditions (3 target types×4 cues) were recorded. The median value was assessed. To avoid the influence of extreme values, standard deviations (SD) were calculated for each condition and RTs outside mean ±2SD of each condition were not included.

Three RTs were calculated according to the following formulas:
RT A=RT no cue-RT double cue
RT O=RT center cue-RT spatial cue
RT E=RT incongruent-RT Congruent

Statistical analysis

Statistical analysis was performed with SPSS 20.0 (Statistical Program for Social Sciences, SPSS Inc, Chicago, IL, USA). The independent-samples *t* test was used to assess the significance of differences between the T2DM and control groups. The main effect and interaction of cue condition and Flanker type for RT data and accuracy between 2 groups were statistically evaluated using analysis of variance (ANOVA). A *P* value of less than 0.05 was considered statistically significant.

RT: Full-factor model F_{group}=144.39, P=0.00, df=1, $F_{Flanker\ type}$=140.90, P=0.00, df=2, $F_{cue\ condition}$=14.87, P=0.00, df=3, $F_{group * FlankerType}$=2.31, P=0.10, df=2, $F_{group * cue\ condition}$=0.36, P=0.78, df=3, $F_{Flanker\ type * cue\ condition}$=0.64, P=0.70, df=6, $F_{group * FlankerType * cue\ condition}$=0.22, P=0.97, df=6. Full-factor model showed that there was no significant difference between the two-level interaction effect and the first-order interaction effect. In order to make the model more accurate in fitting the data, firstly, the two-level interaction effect group * FlankerType * cue condition was removed from the model. The results showed that there was no significance for the 3 primary interactions. $F_{group * FlankerType}$=2.33, P=0.098, df=2, $F_{group * cue\ condition}$=0.37, P=0.78, df=3, $F_{Flanker\ type * cue\ condition}$=0.64, P=0.70, df=6. Then, we removed 3 first-order interaction effects and obtained a three-factor analysis model with no interaction: F_{group}=145.89, P=0.00, df=1, $F_{Flanker\ type}$=141.15, P=0.00, df=2, $F_{cue\ condition}$=15.11, P=0.00, df=3.

ACC: Full-Factor Model: F_{group}=2.19, P=0.14, df=1, $F_{Flanker\ type}$=14.71, P=0.000, df=2, $F_{cue\ condition}$=0.61, P=0.61, df=3, $F_{group * FlankerType}$=3.27, P=0.039, df=2, $F_{group * cue\ condition}$=0.50, P=0.68, df=3, $F_{Flanker\ type * cue\ condition}$=0.85, P=0.53, df=6, $F_{group * FlankerType * cue\ condition}$=0.33, P=0.92, df=6. The full-factor model showed that there was no significance between two-level interaction effect and the first-order interaction effect. In order to make the model more accurate in fitting the data, firstly the two-level interaction effect group * FlankerType * cue condition was removed from the model. The results showed that only one-level interaction had significance. $F_{group * FlankerType}$=3.92, P=0.038, df=2, $F_{group * cue\ condition}$=0.51, P=0.68, df=3, $F_{Flanker\ type * cue\ condition}$=0.90, P=0.50, df=6. Then, we removed the statistically significant interaction effect, and obtained an interactive three-factor analysis of variance model containing only group * FlankerType. F_{group}=2.21, P=0.14, df=1, $F_{Flanker\ type}$=14.86, P=0.000, df=2, $F_{cue\ condition}$=0.62, P=0.60, df=3, $F_{group * FlankerType}$=3.30, P=0.04, df=2.

Results

Comparison of 3-network efficiency

A 3-factorial design of variance was used to assess the RT: 2 (group: T2DM and control groups) × 4 (cue condition: no cue, center cue, double cue, spatial cue) × 3 (Flanker type: neutral, Congruent, incongruent) (Table 2) and ACC data (Table 3). For RT analysis, the main effect of the group was significant (F_{group}=145.89, *P*=0.00), and the main effect of the Flanker type was significant ($F_{Flanker\ type}$=141.15, *P*=0.00), and the main effect of the cue condition was significant ($F_{cue\ condition}$=15.11, *P*=0.00). There was no significant interaction between the group and Flanker type ($F_{group * Flanker\ type}$=2.33, *P*=0.10). The RT of the diabetes mellitus group (711.45±92.39) was higher than that of the control group (641.16±4.78), and that of target type incongruent (743.73±90.94) was higher than that of Congruent (645.61±78.59) and Neutral (635.36±7.44), with statistical significance. There was no significant difference between Congruent and Neutral. The difference between type center (686.75±97.79) and no (700.36±87.96) was not significant, which was longer than double (661.14±92.10) and spatial (651.34±94.76). But, there was no significant difference between double and spatial. There was a no significant interaction between the group and cue condition ($F_{group * cue\ condition}$=0.37, *P*=0.78) or between the Flanker type and cue condition ($F_{Flanker\ type * cue\ condition}$=0.64 P=0.70).

For the mean accuracy, the significant main effect of Flanker type was observed ($F_{Flanker\ type}$=14.86, *P*=0.000). There were no significant main effects of group [F_{group}=2.21, *P*=0.14] and cue condition ($F_{cue\ condition}$=0.62, *P*=0.60). Incongruent (0.9809±0.05941) was lower than that of Congruent (0.9985±0.01143) and Neutral (0.9967±0.01614), but there was no statistical significance

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Table 2. Mean reaction times (ms) under each cue condition between the T2DM and control groups (x±s).

Flanker type	Cue condition			
	Center	Double	No	Spatial
T2DM group				
Congruent	689.45±68.38	659.01±69.05	704.00±72.85	657.24±88.19
Incongruent	808.54±67.25	781.72±75.92	796.42±73.54	771.45±80.76
Neutral	680.83±66.09	642.77±64.51	700.83±68.71	645.16±71.65
Control group				
Congruent	619.10±76.77	608.38±65.23	643.78±63.11	593.70±62.48
Incongruent	723.60±85.40	692.63±75.78	724.20±85.78	665.37±79.14
Neutral	608.12±66.68	590.03±59.73	640.62±63.76	584.35±56.81

Data are represented as mean ±SD.

Table 3. Mean accuracy (%) under each cue condition between the T2DM and control groups (x±s).

Flanker type	Cue condition			
	Center	Double	No	Spatial
T2DM group				
Congruent	1.00±0.00	1.00±0.00	1.00±0.00	1.00±0.01
Incongruent	0.98±0.05	0.97±0.08	0.98±0.09	0.97±0.09
Neutral	1.00±0.00	1.00±0.02	1.00±0.01	1.00±0.02
Control group				
Congruent	1.00±0.02	1.00±0.00	1.00±0.02	1.00±0.00
Incongruent	0.99±0.02	0.97±0.05	1.00±0.01	0.99±0.02
Neutral	1.00±0.02	1.00±0.01	1.00±0.02	1.00±0.01

Data are represented as mean ±SD.

between Congruent and Neutral. There was significant interaction between group and Flanker type ($F_{\text{group * Flanker type}}$=3.30, P=0.04). No significant interaction was noted between Flanker type and cue condition ($F_{\text{Flanker type* cue condition}}$=0.90, P=0.50). No significant interaction existed between group and cue condition ($F_{\text{group * cue condition}}$=0.51, P=0.68)

Alerting effect

The alerting effect was statistically compared between 2 groups, as illustrated in Table 4. The comparison results demonstrated no significant difference regarding the domain of alerting effect between the T2DM patients and healthy controls (t=0.515, P=0.609).

Orienting effect

The orienting effect was statistically compared between 2 groups, as illustrated in Table 4. The comparison results demonstrated no significant difference regarding the domain of orienting effect between the T2DM patients and healthy controls (t= 0.078, P=0.938).

Executive control effect

The effect of executive control was statistically compared between 2 groups, as illustrated in Table 4. There was a significant main effect on the executive effect between 2 groups (t=3.242, P=0.002). The findings indicated that executive control network efficiency of T2DM patients was significantly lower than that of their healthy counterparts. Patients with T2DM had higher costs associated with the interference of irrelevant Flanker information.

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Table 4. Comparison of ANT results between the T2DM and control groups (x±s).

Parameter	T2DM (n=30)	Controls (n=30)	*t* Value	*p* Value
Alerting RT (ms)	41.96±29.21	38.00±24.90	0.515	0.609
Orienting RT (ms)	35.81±27.91	35.24±23.04	0.078	0.938
Executive control RT (ms)*	117.91±37.80	83.51±37.25	3.242	0.002
Overall mean RT (ms)*	713.60±73.13	640.71±71.63	3.561	0.001
Accuracy (%)	98.38±2.83	99.08±1.01	–1.180	0.244

Values are expressed as mean ±SD. RT – reaction time. * P<0.01.

Overall mean RT

The overall mean RT was statistically compared between 2 groups, as illustrated in Table 4. A significant difference was noted regarding the overall mean RT between the 2 groups (t=3.561, P=0.001). In the T2DM group, patients had a longer overall mean RT compared with that of their healthy counterparts in the control group, whereas no significant difference was observed in the accuracy between the 2 groups (t=–1.180, P=0.244).

Discussion

We firstly investigated the attentional networks based on the ANT in T2DM patients in this research. We found there was a significant difference in the executive control network but there was no significant difference in MMSE scores between the T2DM patients and healthy controls, which verified that the ANT is more sensitive than the neuropsychological scale and is superior to the neuropsychological scale on the attention function impairment. No significant differences were noted in alerting and orienting network. The RT of the executive control network was significantly longer in T2DM patients (117.91 ms) than in healthy controls (83.51 ms), indicating that the executive control network efficiency of patients with T2DM was lower. The deficits of the executive control network indicate that patients with diabetes had higher costs associated with the interference of irrelevant Flanker information.

A global delay in RTs emerged in T2DM patients compared with the normal group. This is in keeping with the results of a previous study reporting that attention was impaired in T2DM. Resting-state functional magnetic resonance imaging showed that T2DM patients exhibited disruption of functional integration within attention-related brain networks, including the dorsal attention network and ventral attention [25]. Studies performed by neuropsychological assessments also showed that T2DM or hyperglycemia was significantly and negatively correlated with attention [10,11].

The main finding of our study is that the executive network is influenced by T2DM. Executive control response time is a high-level cognitive processing process including judgments, selection, and conversion of attention. We found that this index in T2DM was significantly increased compared to the control group. The findings are similar to earlier studies that indicated attention and executive functions are more vulnerable to damage in subjects with T2DM [26]. Executive control is described as resolving the conflict among thoughts, feelings, and responses. One study performed the assessments of medical and psychological field and a sequence of computerized tasks, which includes processing speed tasks, verbal and visuospatial working memory (WM) updating (n-back) tasks, and the Wisconsin Card Sorting Test (WCST), and results showed that the T2DM group differed from healthy older controls in the percentage of perseverations and the percentage of perseverative errors (WCST) [27]. Another study based on WCST and PASAT found significant differences in executive function and information processing between T2DM and normal individuals [28]. Similarly, Umegaki H also reported that cognition and executive dysfunction in the participants with DM decreased, which could be partly explained by hyperglycemia [29]. All the above studies are consistent with our findings.

Neuroimaging studies show that the executive control network involves frontal areas, including the anterior cingulate cortex, lateral prefrontal cortex, and basal ganglia [30-32]. Performing the WCST activates a complex network of brain regions, mainly including the bilateral prefrontal cortex, especially the dorsolateral part [33]. Poorer performance in the WCST of DM in previous research may indicate the inactivation of the prefrontal cortex, which may be one reason for the reduction of executive control network efficiency. A study showed that T2DM was associated with specific anatomical abnormalities of smaller gray matter volumes in the anterior cingulate, which may also contribute to the deficits in executive control network [34]. Particular correlations were found between cortical thickness and executive control network in relative regions by functional neuroimaging and lesion studies, which includes the anterior cingulate, lateral prefrontal, and right inferior frontal gyri [35]. T2DM-related gray matter loss was distributed mainly among

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anterior cingulated and frontal lobes; white matter loss was distributed in frontal and temporal regions [36]. These regions (anterior cingulated and frontal lobes) include many dopamine-rich areas of the brain. The executive network is modulated by dopamine [13,31]. Cortical atrophy of these regions influences the imbalances of dopamine, which plays a pivotal role in the impairment of the executive control network in T2DM patients. Insulin administration into the central nervous system (CNS) of rats has been demonstrated to improve the expression of dopamine transporter protein in the ventral tegmental area (VTA)/substantia nigra [37]. Increases in dopamine transporter protein result in a depressed synaptic concentration of dopamine. Decreased dopamine in the VTA may decrease levels of dopamine in the frontal cortex through the VTA-frontal lobe dopaminergic pathways and affect the executive control network of T2DM patients.

The alerting network is associated with attaining and keeping a high sensitivity of incoming stimuli and is associated with the thalamic, frontal, and temporoparietal junction [31]. It is related to the cortical projection of the norepinephrine system [38,39]. In this study, no significant difference was found in alerting network between T2DM patients and control groups, which indicated that alerting function was not involved in early stages of T2DM. It is possible that later diabetes mellitus will impair alertness, but this needs further verification.

The orienting network is involved in the selection of information from sensory input; the temporal, parietal junction, superior parietal lobe, and frontal eye fields are involved [40]. Blocking cholinergic input to the superior parietal lobe affects the ability to change attention to cues [41]. The main function of cholinesterase (CHE) is to rapidly hydrolyze neurotransmitter acetylcholine (ACh) in cholinergic synapses and terminate cholinergic nerve signal transmission. Studies have shown that the activity of CHE in serums and tissues of T2DM patients increases [42,43], which decreases the serum concentration of acetylcholine and may affect orienting network efficiency. However, we did not find an abnormal orienting network in T2DM patients compared with the control group. Consistent with our study, in a study based on Montreal Cognitive Assessment (MoCA), none of 30 community-dwelling adults with T2DM aged 50 years and above showed impairment in orientation [34]. However, it is possible that later diabetes mellitus impairs orientation, but this needs further verification.

Some limitations in our study should be acknowledged. First, the sample size for each group was relatively small because of difficulty in recruiting subjects with poor control of T2DM. Second, smokers were included in both groups. Third, all participants were right-handed and left-handed subjects were not investigated.

Conclusions

In summary, in our study, T2DM patients demonstrated selective impairment of executive control, whereas the orienting and alerting domains were not affected. The experimental results suggested that ANT can assist in recognizing early-stage MCI objectively and efficiently. Further studies are required with improved experimental design and method, enlarged sample size, and combined with methods such as functional magnetic resonance to clarify the damage mechanism by which T2DM can affect attention function.

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