Longitudinal cognitive dysfunction in patients with obstructive sleep apnea syndrome after transient ischemic attack

Yuan-Yuan Meng[1], Yong-Chao Yu[2], Ben Nie[3], Li-Juan Xu[3], Mei Lu[4], Kun Yu[5]

[1]Department of Neurology, Shengli Oilfield Central Hospital, Dongying, Shandong 257034, China;
[2]Department of Intervention, Qingdao Hiser Hospital, Qingdao, Shandong 266034, China;
[3]Department of Oncology, Qingdao Hiser Hospital, Qingdao, Shandong 266034, China;
[4]Department of Geriatrics, Qilu Hospital of Shandong University, Jinan, Shandong 250012, China;
[5]Department of Otorhinolaryngology, Shengli Oilfield Central Hospital, Dongying, Shandong 257034, China.

To the Editor: Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive episodes of upper airway obstruction (partial or complete) during sleep, which leads to recurrent arterial hypoxemia and sleep fragmentation. Untreated OSAS in middle-aged patients cause impairments in attention, vigilance, some aspects of memory, and executive function.[1] Transient ischemic attack (TIA) is characterized by a transient episode of neurological dysfunction caused by focal brain ischemia. By definition, TIA should not bring persistent deficits but it does increase the risk of long-term cognitive impairment.[2] OSAS is an independent risk factor for TIA. However, transient or persistent cognitive impairment after TIA in OSAS patients remains unclear. Therefore, we conducted a prospective cohort study on cognitive function after TIA to provide insight into the characteristics and influence factors of cognitive function in OSAS patients within 2 years.

Totally, 163 moderate and severe OSAS patients who were admitted to the Stroke Unit of Shengli Oilfield Central Hospital between 2012 and 2017 were consecutively enrolled. Inclusion criteria: (i) patients aged ≥45 years with predominant OSAS exhibiting at least apnea-hypopnea index (AHI) ≥20/h; (ii) an event of neurological symptoms within 7 days. Exclusion criteria: (i) patients with some other sleep disorders, such as rapid eye movement sleep behavior disorder; (ii) mini-mental state examination score less than 24; (iii) patients had intracerebral space-occupying lesion or other neurological diseases that could impact their cognitive function or respiratory function; (iv) patients with major depression; (v) the presence of acute or chronic cardiopulmonary diseases that affected pulmonary function; and (vi) patients with magnetic resonance imaging (MRI) contraindication or developed incident stroke during follow-up. Besides, 134 patients with moderate and severe OSAS but without TIA were recruited as control group.

Baseline neuropsychological assessment, basic clinical features, vascular risk factors, hospital anxiety and depression scale (HADS), and MRI were evaluated within 7 days after admission, at 6-month, and 2-year follow-up. All patients were scored according to the ABCD2 scoring method.

No significant difference was found between OSAS patients with and without TIA in age, sex, education level, sleep parameters, mean score of the HADS-D, and presence of vascular risk factors ($P > 0.05$). For OSAS patients with TIA, the function of cognitive domain including executive function ($P < 0.001$), attention ($P < 0.001$), and information processing speed ($P < 0.001$) decreased continuously at baseline, 6-month and 2-year follow-up, whereas the other cognitive function remained stable [Table 1]. There was a significant association of TIA event with decline in executive function (odds ratio [OR] = 0.046, 95% confidence interval [CI]: 0.025–0.084, $P < 0.001$), attention (OR = 4.112, 95% CI: 2.971–5.692, $P < 0.001$), and information processing speed (OR = 7.258, 95% CI: 4.768–11.048, $P < 0.001$) in OSAS patients. The multiple linear regression analysis revealed that age and ABCD2 scores were the adverse risk factors for executive dysfunction. Age, hypertension, Fazekas score, and ABCD2 scores were the adverse risk factors for attention dysfunction and reduced information processing speed.

In this study, moderate and severe OSAS patients showed functional impairment in multiple cognitive domains in the first 2 years after TIA. Among them, the working memory remained relatively intact. However, the cognitive domains

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Correspondence to: Kun Yu, Department of Otorhinolaryngology, Shengli Oilfield Central Hospital, No. 31 Jinan Road, Dongying, Shandong 257034, China
E-Mail: fishstudy@163.com

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Table 1: Cognitive domain compound *z* scores within 2 years after TIA.

Items	Cognitive domain compound Z scores									
	Within 7 days after admission			At 6 months after TIA			At 2 years after TIA			
	TIA Group (*N* = 163)	Control Group (*N* = 134)	*P*	TIA Group (*N* = 163)	Control Group (*N* = 134)	*P*	TIA Group (*N* = 163)	Control Group (*N* = 134)	*P*
Information processing speed	−0.178 (−0.325 to −0.030)	0.317 (0.203–0.431)	0.000	−0.160 (−0.299 to −0.022)	0.291 (0.167–0.416)	0.000	−0.220 (−0.370 to −0.070)	0.291 (0.180–0.401)	0.000
Executive function	0.224 (0.067–0.381)	−0.210 (−0.322 to −0.097)	0.001	0.316 (0.161–0.471)	−0.322 (−0.429 to −0.215)	0.000	0.433 (0.294–0.572)	−0.424 (−0.529 to −0.319)	0.001
Attention	−0.179 (0.334–0.240)	0.320 (0.214–0.426)	0.000	−0.182 (−0.316 to −0.047)	0.301 (0.172–0.429)	0.000	−0.254 (−0.406 to −0.102)	0.384 (0.285–0.483)	0.000
Working memory	0.050 (−0.110 to 0.211)	0.027 (−0.084 to 0.140)	0.671	0.588 (−0.086 to 0.204)	0.009 (−0.118 to 0.136)	0.593	0.169 (−0.128 to 0.162)	0.021 (−0.099 to 0.143)	0.358

Data were shown as mean (95% confidence interval). Cognitive domain compound scores represent the mean of individual test z scores within a cognitive domain. TIA: Transient ischemic attack.

included attention, executive function, and information processing speed were severely impaired. This mild neurological event has only transient effects on cognitive function.[3] However, the persistent cognitive complaints reported following such transient events may arise in moderate and severe OSAS patients. We suppose that long-term hypoxemia and sleeping fragmentation can lead to widespread microstructural brain tissue damage and permanent neuronal damage, which are the pathological basis of cognitive dysfunction. Possibly, the acute ischemic lesion leads to disruption of networks involved in cognitive processing and further accelerates the cognitive decline.[4]

Vascular risk factors are associated with reduced performance on both the cognitive screening task.[5] Our results suggest that the presence of vascular risk factors (hypertension and low-density lipoprotein cholesterol) and age were associated with reduced performance of the executive function measures, attention, and information processing speed. Moreover, the ABCD2, which also loads heavily on vascular risk factors, was associated with cognitive decline.

In summary, the decline of cognitive function, including attention, executive function, and information processing speed, showed in OSAS patients was a dynamic process, especially in the first 2 years after TIA. Early onset and persisting cognitive impairment was more likely to occur in moderate and severe OSAS patients with TIA. Furthermore, long-term management of vascular risk factors may reduce the risk of cognitive impairment.

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Conflicts of interest

None.

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