

DOI: 10.16781/j.0258-879x.2018.11.1224

· 论 著 ·

老年人抑郁共病糖尿病血糖、血脂水平与认知功能的关系

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[摘要] **目的** 探讨老年人罹患抑郁症及共病 2 型糖尿病后的血糖、血脂水平改变及其与认知功能的关系。

方法 以 2017 年 11 月 1 日至 12 月 30 日接受健康体检的 60~79 岁老年人作为研究对象, 根据入组、排除标准最终纳入抑郁共病糖尿病组(共病组) 59 例、单纯抑郁组 106 例、单纯糖尿病组 84 例、无糖尿病或抑郁症(对照组) 248 例。统计各组老年人下述资料: 基本生理指标(身高、体质量、腰围、臀围与血压)、体质量指数(BMI)及腰臀比(WHR); 血糖、血脂水平; 蒙特利尔认知评估(MoCA)量表评估结果。分析各组间 BMI、WHR、血压、血糖、血脂水平的差异, 以及与 MoCA 量表评估的校正总分、各认知域之间的关系。**结果** (1) 各组老年人在身高、体质量、BMI、WHR 及舒张压方面差异无统计学意义(P 均 >0.05); 收缩压和脉压差异均有统计学意义(P 均 <0.01), 且单纯糖尿病组二者升高最显著。(2) 与对照组相比, 共病组与单纯糖尿病组空腹血糖(FBG)、口服葡萄糖耐量试验(OGTT) 2 h 血糖、糖化血红蛋白(HbA_{1c})均升高(P 均 <0.01), 单纯抑郁组差异无统计学意义($P>0.05$)。共病组的三酰甘油(TG)水平较对照组升高($P<0.05$), 共病组与糖尿病组较对照组的高密度脂蛋白(HDL)均降低($P<0.05$, $P<0.01$)。(3) 各组老年人 MoCA 量表的校正总分差异无统计学意义($P>0.05$); 与对照组相比, 其他 3 组的注意力得分均降低(P 均 <0.01); 共病组的流畅性、定向得分较对照组降低($P<0.05$, $P<0.01$), 同时定向得分较糖尿病组也降低($P<0.05$)。(4) 简单线性回归分析显示, FBG、 HbA_{1c} 对 MoCA 量表的校正总分呈负向影响($b=-0.339$, $P=0.006$; $b=-0.482$, $P=0.023$), FBG、OGTT 2 h 血糖、 HbA_{1c} 对注意力得分呈负向影响($b=-0.119$, $P<0.001$; $b=-0.040$, $P=0.002$; $b=-0.161$, $P=0.006$)。(5) 多元线性回归模型分析显示, FBG 对 MoCA 量表校正总分呈负向影响($B=-0.349$, $P=0.004$)。**结论** 高血糖状态可能是抑郁共病糖尿病老年人认知功能障碍的危险因素。

[关键词] 老年人; 抑郁; 2 型糖尿病; 血糖; 脂类; 认知功能障碍**[中图分类号]** R 749.42; R 587.2 **[文献标志码]** A **[文章编号]** 0258-879X(2018)11-1224-06

Relationship between blood glucose and lipid levels and cognitive function in elderly patients with comorbidity of depression and type 2 diabetes mellitus

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[Abstract] **Objective** To explore the relationship between blood glucose and lipid levels and cognitive function in elderly patients with comorbidity of depression and type 2 diabetes mellitus (T2DM). **Methods** The clinical data from elderly participants (60 to 79 years old) receiving physical examination between Nov. 1 and Dec. 30, 2017 were collected. According to inclusion and exclusion criteria, 59 cases with comorbidity of depression and T2DM were assigned to comorbid group, 106 depression cases were in depression group, 84 T2DM cases were in diabetes group and 248 were in control group (with no diabetes or depression). The general physiological indicators (height, body mass, waist circumference, hip circumference and blood pressure) were collected, the body mass index (BMI) and waist-to-hip ratio (WHR) were calculated, and blood glucose and lipid levels were determined. The Montreal Cognitive Assessment (MoCA) scale was used to assess the cognitive function of the elderly in each group. The differences in BMI, WHR, blood pressure, blood glucose level and blood lipid level among the groups were compared, and the relationships between these indicators and the adjusted total score and scores in each cognitive domain of MoCA scale were analyzed. **Results** (1) There were no significant differences in height,

[收稿日期] 2018-06-26 **[接受日期]** 2018-10-09**[基金项目]** 上海市科委西医引导类项目(16411969900). Supported by Project of Western Medicine Guidance of Science and Technology Commission of Shanghai Municipality (16411969900).**[作者简介]** 杜冰滢, 硕士生, 住院医师. E-mail: 15800614142@163.com

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body mass, BMI, WHR or diastolic blood pressure (DBP) among four groups (all $P>0.05$), while the differences in systolic blood pressure (SBP) and pulse pressure (PP) were significant (both $P<0.01$), with the increase in the diabetes group being most obvious. (2) Compared with the control group, the fasting blood glucose (FBG) level, oral glucose tolerance test (OGTT) 2 h and glycosylated hemoglobin (HbA_{1c}) level were significantly higher in the comorbid group and the diabetes group (all $P<0.01$); while there was no significant difference between the control and the depression groups ($P>0.05$). The triglyceride (TG) level in the comorbid group was significantly higher than that in the control group ($P<0.05$), and the high-density lipoprotein (HDL) levels in the comorbidity and the diabetes groups were lower than that in the control group ($P<0.05$, $P<0.01$). (3) There was no significant difference in the adjusted total score of MoCA scale among the four groups ($P>0.05$). Compared with the control group, the attention scores of the other three groups were significantly lower (all $P<0.01$). The elderly in the comorbid group had significantly lower fluency and orientation scores compared with the elderly in the control group ($P<0.05$, $P<0.01$), and had significantly lower orientation score compared with the elderly in the diabetes group ($P<0.05$). (4) Simple linear regression analysis showed that the adjusted total score of MoCA scale was negatively correlated with FBG and HbA_{1c} levels ($b=-0.339$, $P=0.006$; $b=-0.482$, $P=0.023$), and the attention score was negatively correlated with FBG, OGTT 2h and HbA_{1c} levels ($b=-0.119$, $P<0.001$; $b=-0.040$, $P=0.002$; $b=-0.161$, $P=0.006$). (5) Multiple linear regression analysis revealed that FBG level was negatively correlated with the adjusted total score of MoCA scale ($B=-0.349$, $P=0.004$). **Conclusion** Hyperglycemia may be a risk factor of cognitive dysfunction of elderly patients with comorbid of depression and T2DM.

[Key words] aged; depression; type 2 diabetes mellitus; blood glucose; lipids; cognition disorders

[Acad J Sec Mil Med Univ, 2018, 39(11): 1224-1229]

糖尿病是一种与心理因素密切相关的疾病。糖尿病患者罹患抑郁症等心理障碍的风险明显升高^[1], 同时抑郁症也是 2 型糖尿病的危险因素, 而且抑郁症状会影响糖尿病患者的血糖调节与控制, 从而影响患者的预后^[2]。由于这种双向关系, 共患抑郁症的现象在糖尿病患者中很常见, 发生率为 10.6%~25.3%^[3-4]。

有研究发现, 抑郁症患者往往存在血糖、血脂代谢紊乱^[5-6], 而糖尿病是最容易发生脂质代谢异常的代谢性疾病之一, 其与胰岛素抵抗密切相关^[7-8]。相比于正常老年人, 糖尿病老年人不仅会发生视力丧失、肾脏衰竭、心血管疾病以及糖尿病足等并发症, 而且在众多认知域均存在显著的认知功能障碍^[9-10]。同时, 抑郁症也是与认知功能下降密切相关的一种神经精神疾病^[11]。一项 meta 分析结果表明, 与非抑郁症患者相比, 抑郁症患者在执行功能、记忆、注意力和反应时间等方面均存在较为明显的认知功能障碍^[12]。然而, 抑郁共病糖尿病老年人血脂代谢及认知功能如何改变, 目前国内外尚未见相关报道。本研究旨在探讨抑郁共病糖尿病老年人血糖、血脂代谢的改变和认知功能损害的特点, 分析抑郁共病糖尿病后病情加重的影响因素, 并且结合代谢指标检测, 研究共病老年人认知功能与代谢指标的关系。

1 资料和方法

1.1 研究对象 以 2017 年 11 月 1 日至 12 月 30 日

在上海市杨浦区殷行社区卫生服务中心接受健康体检的 60~79 岁老年人作为研究对象。

抑郁共病糖尿病组 (以下简称共病组) 入组标准: (1) 符合 1999 年世界卫生组织 (World Health Organization, WHO) 2 型糖尿病的诊断分型标准^[13], 即有典型糖尿病症状 (多饮、多食、多尿、体质量下降), 加之符合以下 3 条中任意一条即可诊断: 随机血糖 ≥ 11.1 mmol/L, 或空腹血糖 (fasting blood glucose, FBG) ≥ 7.0 mmol/L, 或葡萄糖负荷后 2 h 血糖 ≥ 11.1 mmol/L; (2) 焦虑自评量表 (self-rating anxiety scale, SAS) 评分 < 50 ^[14]; (3) 简版老年抑郁量表 (geriatric depression scale, GDS) 评分 ≥ 5 ^[15]; (4) 年龄 60~79 岁。单纯抑郁组符合除 (1) 以外的入组标准, 单纯糖尿病组符合除 (3) 以外的入组标准, 对照组只符合 (2) 和 (4) 两条标准。排除标准: (1) 合并严重糖尿病并发症; (2) 既往曾有任何可能影响认知功能的神经系统疾病, 如中枢神经系统感染、脑梗死、颅内出血及颅脑外伤等; (3) 既往有服用抗抑郁药物史; (4) 合并严重临床并发症, 如心、肝、肺、肾衰竭史。根据入组和排除标准, 最终纳入共病组 59 例、单纯抑郁组 106 例、单纯糖尿病组 84 例、对照组 248 例。本研究经长海医院伦理委员会审批; 所有受试者均签署知情同意书且自愿配合。

1.2 一般资料与生物化学指标 入组时对所有老年人分别测量基本生理指标 (身高、体质量、

腰围、臀围、血压),计算体质量指数(body mass index, BMI)及腰臀比(whist-to-hip ratio, WHR)。采集入组老年人的血液及尿液标本,检测血常规、尿常规、FBG、口服葡萄糖耐量试验(oral glucose tolerance test, OGTT) 2 h 血糖、糖化血红蛋白(glycosylated hemoglobin, HbA_{1c})、总胆固醇(total cholesterol, TC)、三酰甘油(triglyceride, TG)、高密度脂蛋白(high-density lipoprotein, HDL)、低密度脂蛋白(low-density lipoprotein, LDL)等。

1.3 评估量表 用评估量表对入组老年人进行评估,评估量表包括:(1)蒙特利尔认知评估(Montreal cognitive assessment, MoCA)量表。由加拿大 Nasreddine 等^[16]根据临床经验并参考简明精神状态量表(mini-mental state examination, MMSE)制定,是对认知功能异常进行快速筛查的评定工具。MoCA 量表北京版由王伟和王鲁宁^[17]翻译修订,常用于轻度认知异常的筛查。评定范围包括视空间结构、命名、注意力、重复句子、流畅性、抽象能力、延迟回忆以及定向力等 8 个认知域,总分 30 分,得分≤24 为轻度认

知异常。(2) SAS 由 Zung 编制,用于评定患者焦虑主观感受。由 20 个项目组成,每个项目按 1~4 级评分,计算原始分数乘以 1.25 最后取整数部分得到标准分^[18],得分≥50 表示焦虑状态^[14]。

(3) GDS。由美国心理学家在含有 30 个项目的标准版基础上设计的简版老年抑郁量表^[19-20],共 15 个项目,用于评估老年人抑郁水平。得分≥5 认为存在抑郁^[15]。

1.4 统计学处理 应用 SPSS 21.0 软件进行统计学分析。计量资料以 $\bar{x} \pm s$ 表示,各组间比较采用单因素方差分析,两两比较采用 LSD-*t* 检验。计数资料以频数表示,组间比较采用 χ^2 检验。采用多元线性回归模型分析方法评价各指标对认知功能的影响。检验水准(α)为 0.05。

2 结果

2.1 各组老年人一般资料比较 根据入组、排除标准,最终纳入共病组 59 例、单纯抑郁组 106 例、单纯糖尿病组 84 例、对照组 248 例。各组老年人在年龄、性别以及文化程度上的差异均无统计学意义(P 均>0.05,表 1)。

表 1 各组老年人一般资料比较

Tab 1 Comparison of general characteristics of the elderly among the four groups

Characteristic	Control $N=248$	Comorbid $N=59$	Depression $N=106$	Diabetes $N=84$	P value
Age (year), $\bar{x} \pm s$	65.75 ± 5.87	65.31 ± 6.79	65.88 ± 5.42	67.10 ± 6.51	0.260
Gender ^a n/n	123/125	33/26	51/55	44/40	0.345
Education ^b n/n	176/64 ^c	45/13 ^d	80/26	62/22	0.233

^a: Male/female; ^b: <12 years/≥12 years; ^{c, d}: There were missing eight and one data, respectively

2.2 各组老年人基本生理指标比较 各组老年人的身高、体质量、BMI、WHR、舒张压差异无统计学意义(P 均>0.05),收缩压和脉压差异有统计学意义(P 均<0.01)。与对照组相比,其他 3 组老年人的收缩压均升高,以单纯糖尿病组升高最显著,差异有统计学意义($P < 0.05$, $P < 0.01$)。与对照组相比,其他 3 组老年人的脉压均升高,以单纯糖尿病组升高最显著,单纯糖尿病组和单纯抑郁组与对照组比较差异均有统计学意义($P < 0.01$, $P < 0.05$),共病组与对照组比较差异无统计学意义($P > 0.05$)。见表 2。

2.3 各组老年人血糖、血脂水平比较 各组老年人的 FBG、OGTT 2 h 血糖、HbA_{1c} 水平差异有统计学意义($P < 0.01$)。与对照组相比,共病组与单纯糖尿病组的 FBG、OGTT 2 h 血糖、HbA_{1c} 水平均升高,差异均有统计学意义

(P 均<0.01),而单纯抑郁组与对照组比较差异无统计学意义($P > 0.05$)。共病组的 TG 水平较对照组升高,差异有统计学意义($P < 0.05$),共病组与糖尿病组的 HDL 较对照组均降低,差异有统计学意义($P < 0.05$, $P < 0.01$)。各组间的 TC、LDL 水平差异均无统计学意义(P 均>0.05)。见表 3。

2.4 各组老年人 MoCA 量表评分比较 各组老年人 MoCA 量表评估的校正总分差异无统计学意义($P > 0.05$)。进一步比较不同认知域时发现,与对照组相比,其他 3 组的注意力得分均降低,差异有统计学意义(P 均<0.01);共病组的流畅性、定向得分低于对照组($P < 0.05$, $P < 0.01$),定向得分低于单纯糖尿病组($P < 0.05$)。各组老年人的视空间结构、命名、重复句子、抽象能力、延迟回忆得分差异均无统计学意义(P 均>0.05)。见表 4。

表 2 各组老年人基本生理指标比较

Tab 2 Comparison of general physiological indicators of the elderly among the four groups

Indicator	Control <i>n</i> =248	Comorbid <i>n</i> =59	Depression <i>n</i> =106	Diabetes <i>n</i> =84	$\bar{x} \pm s$ <i>P</i> value
Height /cm	164.59±8.40	164.89±9.54	166.73±7.03	161.44±8.78	0.283
Body mass <i>m</i> /kg	65.22±9.26	65.62±10.80	64.92±9.46	61.89±8.82	0.588
BMI	24.04±2.14	24.29±4.63	23.13±1.91	23.91±2.59	0.652
Waistline /cm	84.26±7.26	88.22±11.31	83.72±10.03	82.47±8.72	0.472
Hipline /cm	95.95±6.02	96.79±6.58	95.62±7.56	92.78±6.09	0.396
WHR	0.87±0.48	0.89±0.54	0.88±0.75	0.89±0.60	0.825
SBP <i>p</i> /mmHg	141.96±19.03	158.63±16.36*	151.06±21.41*	159.25±20.20**	<0.001
DBP <i>p</i> /mmHg	90.07±16.62	93.88±7.90	89.23±13.21	90.65±15.78	0.891
PP <i>p</i> /mmHg	53.96±15.55	64.75±14.67	61.84±18.92*	68.60±19.21**	0.001

1 mmHg=0.133 kPa. BMI: Body mass index; WHR: Waist-to-hip ratio; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PP: Pulse pressure. **P*<0.05, ***P*<0.01 vs control group

表 3 各组老年人血糖、血脂水平比较

Tab 3 Comparison of blood glucose and lipid levels of the elderly among the four groups

Indicator	Control <i>n</i> =248	Comorbid <i>n</i> =59	Depression <i>n</i> =106	Diabetes <i>n</i> =84	$\bar{x} \pm s$ <i>P</i> value
FBG <i>c_B</i> /(mmol • L ⁻¹)	5.50±0.57	7.78±2.07**	5.49±0.54 ^{△△}	7.44±1.86**	<0.001
OGTT (2 h) <i>c_B</i> /(mmol • L ⁻¹)	7.40±1.72	14.40±3.96**	7.14±1.65 ^{△△}	14.24±3.19**	<0.001
HbA _{1c} (%)	5.77±0.39	6.98±1.40**	5.72±0.30 ^{△△}	6.79±0.99**	<0.001
TC <i>c_B</i> /(mmol • L ⁻¹)	5.36±1.03	5.22±1.25	5.23±0.91	5.14±1.00	0.322
TG <i>c_B</i> /(mmol • L ⁻¹)	1.48±0.92	1.79±1.44*	1.48±0.89	1.62±0.84	0.123
LDL <i>c_B</i> /(mmol • L ⁻¹)	3.45±0.90	3.33±1.02	3.34±0.88	3.39±1.11	0.709
HDL <i>c_B</i> /(mmol • L ⁻¹)	1.59±0.59	1.40±0.42*	1.54±0.42	1.41±0.43**	0.012

FBG: Fasting blood glucose; OGTT: Oral glucose tolerance test; HbA_{1c}: Glycosylated hemoglobin; TC: Total cholesterol; TG: Triglyceride; LDL: Low-density lipoprotein; HDL: High-density lipoprotein. **P*<0.05, ***P*<0.01 vs control group; ^{△△}*P*<0.01 vs comorbid group

表 4 各组老年人 MoCA 量表认知域得分比较

Tab 4 Comparison of cognitive domain scores of MoCA scale in the elderly among the four groups

Item	Control <i>n</i> =248	Comorbid <i>n</i> =59	Depression <i>n</i> =106	Diabetes <i>n</i> =84	$\bar{x} \pm s$ <i>P</i> value
Visuospatial	3.88±1.20	3.74±1.26	3.83±1.14	3.70±1.24	0.653
Naming	2.46±0.77	2.40±0.82	2.46±0.75	2.31±0.78	0.452
Attention	5.24±0.93	4.72±1.30**	4.90±1.16**	4.86±1.29**	0.001
Language	0.77±0.80	0.74±0.84	0.68±0.74	0.73±0.75	0.594
Fluency	0.95±0.21	0.88±0.33*	0.92±0.27	0.93±0.26	0.206
Abstraction	0.99±0.86	1.09±0.80	0.97±0.83	0.99±0.83	0.856
Delayed recall	2.89±1.60	2.78±1.66	2.71±1.59	2.85±1.61	0.713
Orientation	5.84±0.46	5.62±0.72**	5.76±0.58	5.83±0.46 [△]	0.029
Total score	23.76±3.83	22.83±4.75	23.09±3.91	23.06±4.28	0.234

MoCA: Montreal cognitive assessment. **P*<0.05, ***P*<0.01 vs control group; [△]*P*<0.05 vs comorbid group

2.5 BMI、WHR、血压、血糖、血脂水平对认知功能的影响 分别以 MoCA 量表评估的校正总分、注意力、流畅性、定向得分作为因变量，以 BMI、WHR、血压、血糖、血脂水平作为自变量进行简单线性回归分析。结果显示，BMI、WHR、血压、

血脂水平对认知功能无影响，血糖水平对认知功能有一定影响。其中 FBG、HbA_{1c} 对校正总分呈负向影响 (*b* = -0.339, *P* = 0.006; *b* = -0.482, *P* = 0.023)，FBG、OGTT 2 h 血糖、HbA_{1c} 对注意力得分均呈负向影响 (*b* = -0.119, *P* < 0.001;

$b = -0.040, P = 0.002; b = -0.161, P = 0.006$)。

将单因素分析具有统计学意义的因素 FBG、OGTT 2 h 血糖、HbA_{1c} 纳入多元线性回归方程作为自变量,以校正总分为因变量,得出在校正了可能影响认知功能的相关因素后,FBG 仍对认知功能评分有独立的负向影响 ($B = -0.349, P = 0.004$; 表 5)。模型经检验 $F = 8.162, P = 0.004, R^2 = 0.150$ 。

表 5 多元线性回归模型分析 MoCA 量表校正总分的影响因素

Tab 5 Multiple linear regression analysis of influencing factors of adjusted total score of MoCA scale

Variable	β	SE	B	t value	P value
FBG	-0.136	0.122	-0.349	-2.857	0.004
OGTT (2 h)	0.017	0.075	0.018	0.238	0.081
HbA _{1c}	-0.007	0.391	-0.034	-0.088	0.093

MoCA: Montreal cognitive assessment; FBG: Fasting blood glucose; OGTT: Oral glucose tolerance test; HbA_{1c}: Glycosylated hemoglobin; β : Standard coefficient; SE: Standard error; B: Unstandardized coefficient

3 讨论

本研究显示,当老年人罹患抑郁症以及共病糖尿病时,收缩压较对照老年人升高 ($P < 0.01$),糖尿病、抑郁老年人较对照老年人脉压升高 ($P < 0.01, P < 0.05$)。糖尿病老年人以及抑郁症共病糖尿病的老年人发生脂质代谢异常,尤其表现为 HDL 水平降低 ($P < 0.01, P < 0.05$)。糖尿病、抑郁以及共病老年人较对照老年人均会出现不同程度、不同认知域的认知功能损害,其中在注意力方面表现最为突出 (P 均 < 0.01),共病组降低差异最为显著。多元线性回归模型分析发现,FBG 水平升高是认知功能下降的独立影响因素 ($B = -0.349, P = 0.004$)。

随着年龄的增长,老年人动脉硬化情况加重,血管壁弹性明显降低,因此老年人血压具有收缩压升高、脉压增大等特点。同时,老年人易合并其他代谢疾病以及靶器官损伤。血糖升高、HDL 降低、TG 升高等会促进动脉硬化的程度^[21],而糖尿病患者常合并有上述代谢功能紊乱,因此共病老年人收缩压与脉压较单纯抑郁症老年人往往升高。此外,抑郁症状会影响血压调节以及脂质代谢的神经内分泌系统,抑郁患者往往存

在与高血压、脂质代谢紊乱相关的病理生理基础^[22]。本研究也发现抑郁症老年人脉压升高的情况,提示这些老年人存在血压调节功能异常。

任会鹏等^[23]发现,抑郁症患者会出现认知功能损害,尤其在共病糖尿病后认知功能受损更为严重。本研究结果发现抑郁症老年人存在某些认知域功能障碍以及在共病糖尿病后认知功能得分降低更为明显,与既往研究结果^[23]一致。糖尿病除了可以并发多器官慢性损害外,还可以加速认知功能障碍的发展,增加痴呆的患病风险^[24]。研究显示,糖尿病患者工作记忆、注意力、执行功能、信息处理速度等方面均出现不同程度的下降^[25]。本研究也发现糖尿病以及共病老年人在注意力等多个认知域存在障碍。多元线性回归模型分析结果显示,认知功能评分主要受 FBG、OGTT 2 h 血糖、HbA_{1c} 水平的负向影响,提示高血糖以及血糖调节功能紊乱会影响老年人认知功能。本课题组在前期研究中发现,血糖调节异常的老年人外周血中细胞因子、炎症因子、核转录因子及其基因产物等含量增加,而这些因子可以透过血脑屏障到达中枢神经系统,并最终导致脱髓鞘病变及脑白质损伤,出现认知功能障碍(资料未发表)。上述结果在本课题组的动物实验^[26]中也得到验证。这与糖尿病并发认知功能障碍的炎症机制^[27]相吻合。

综上,本研究通过对影响抑郁共病糖尿病老年人认知功能相关因素的分析,提示应尽早发现老年人的抑郁症状与血糖受损情况,并及时进行合理治疗与干预,将认知功能损害降到最低,这为临床诊断和预防此类疾病提供了重要的参考依据。

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