·临床研究·

情绪对轻中度帕金森病患者认知功能的影响

刘惠苗　李冬　仇福成　董慈　张永志　韩瑞　解冰川　顾平

【摘要】 **目的**　探讨焦虑和抑郁情绪对轻中度帕金森病患者认知功能的影响。**方法**　71例原发性帕金森病患者，采用统一帕金森病评价量表（UPDRS）和Hoehn-Yahr分级评价病情严重程度、汉密尔顿焦虑量表（HAMA，14项）和汉密尔顿抑郁量表（HAMD，24项）评价焦虑和抑郁情绪、简易智能状态检查量表（MMSE）和蒙特利尔认知评价量表（MoCA，北京版）评价认知功能，分析焦虑和抑郁情绪对认知功能的影响。**结果**　71例患者均为轻中度帕金森病患者，出现焦虑61例（85.92%）、抑郁55例（77.46%）、同时出现焦虑和抑郁52例（73.24%）。伴焦虑和抑郁患者UPDRS评分分别高于无焦虑（P = 0.016）和无抑郁（P = 0.000）患者，伴焦虑患者MoCA评分低于无焦虑患者（P = 0.042）。71例患者中49例（69.01%）出现认知功能障碍，其中轻度认知损害28例（39.44%）、痴呆21例（29.58%）。Logistic回归分析显示，仅焦虑是帕金森病患者认知功能障碍的独立危险影响（OR = 10.816，95%CI：1.682～69.560；P = 0.012）。**结论**　伴焦虑或抑郁情绪的帕金森病患者病情更严重，存在焦虑的帕金森病患者认知功能障碍患病率更高、程度更严重。

【关键词】 帕金森病；　焦虑；　抑郁；　认知障碍；　回归分析

Effect of emotion on the cognitive function of patients with mild to moderate Parkinson´s disease

LIU Hui-miao, LI Dong, QIU Fu-cheng, DONG Ci, ZHANG Yong-zhi, HAN Rui, XIE Bing-chuan, GU Ping
Department of Neurology, the First Hospital of Hebei Medical University, Shijiazhuang 050031, Hebei, China
Corresponding author: GU Ping (Email: gpwh2000@126.com)

【**Abstract**】 **Objective**　To explore the effect of anxiety and depression on cognitive function in patients with mild to moderate Parkinson´s disease (PD). **Methods**　A total of 71 patients with primary PD were enrolled in this study. Unified Parkinson´s Disease Rating Scale (UPDRS) and Hoehn-Yahr stage were used to evaluate the severity of the disease. Hamilton Anxiety Rating Scale (14-item version, HAMA-14) and Hamilton Depression Rating Scale (24-item version, HAMD-24) were used to evaluate the anxiety and depression. Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA, Beijing version) were used to evaluate the cognitive function. The impact of anxiety and depression on cognitive function was analyzed. **Results**　All of these patients were diagnosed as mild to moderate PD, including 61 patients (85.92%) with anxiety, 55 patients (77.46%) with depression and 52 patients (73.24%) with concurrent anxiety and depression. The UPDRS score of patients with anxiety and depression were significantly higher than that of patients without anxiety (P = 0.016) or depression (P = 0.000). The MoCA score of PD patients with anxiety were significantly lower than that of patients without anxiety (P = 0.042). Among 71 patients, there were 49 cases (69.01%) with cognitive dysfunction, including 28 patients (39.44%) with mild cognitive impairment (MCI) and 21 cases (29.58%) with dementia. There was no statistical difference of HAMA-14 and HAMD-24 scores among PD patients with different cognitive levels (P > 0.05, for all). Logistic regression analysis showed only anxiety was the independent risk factor for cognitive dysfunction of PD patients (OR = 10.816, 95% CI: 1.682–69.560; P = 0.012). **Conclusions**　The illness of PD patients accompanied by anxiety or depression is more serious. PD patients with anxiety have higher prevalence of cognitive dysfunction.

doi：10.3969/j.issn.1672-6731.2016.02.006
基金项目：2013年度河北省卫生厅医学科学研究课题（项目编号：20130281）
作者单位：050031 石家庄，河北医科大学第一医院神经内科
通讯作者：顾平（Email：gpwh2000@126.com）

【Key words】 Parkinson disease; Anxiety; Depression; Cognition disorders; Regression analysis

This study was supported by Medical Scientific Research Project of Health Department of Hebei, China (No. 20130281).

帕金森病(PD)是一种临床常见的中老年中枢神经系统变性病,以黑质多巴胺能神经元变性缺失和路易小体(LB)形成为病理学特点,临床主要表现为静止性震颤、肌强直、运动迟缓、姿势步态异常等运动症状。近年来,帕金森病非运动症状(NMS)颇受临床关注,包括认知功能障碍和睡眠障碍、焦虑和抑郁症状、易疲乏、冷漠、多汗、尿频等自主神经功能障碍等,其中以认知功能障碍发病率较高。据文献报道,约24%首诊帕金森病患者存在认知功能障碍[1],而30%患者最终进展至帕金森病痴呆(PDD)[2],帕金森病患者发生痴呆的可能性约为正常人的6倍[3],焦虑和抑郁症状可早于运动症状且贯穿疾病全过程,严重影响生活质量。本研究旨在探讨焦虑和抑郁对帕金森病患者认知功能的影响。

对象与方法

一、研究对象

选择2013年5–12月在河北医科大学第一医院神经内科就诊的原发性帕金森病患者71例,均符合英国帕金森病学会脑库帕金森病临床诊断标准[4];同时排除原发性震颤、脑血管病、中枢神经系统感染和中毒、颅脑创伤等疾病导致的帕金森综合征,多系统萎缩(MSA)、进行性核上性麻痹(PSP)、皮质基底节变性(CBD)、路易体痴呆(DLB)等帕金森叠加综合征,严重认知功能障碍并发精神障碍或恶性肿瘤,严重日常生活活动能力下降和文盲,以及曾接受过帕金森病外科手术治疗的患者,男性40例,女性31例;年龄47~84岁,平均(66.50±8.66)岁;病程12~240个月,中位病程60个月;受教育程度6~18年,平均(11.17±3.45)年。

二、研究方法

由经过统一培训的神经内科医师登记患者性别、年龄、病程和受教育程度。入组病例均于疾病“开期”进行统一帕金森病评价量表(UPDRS)评分和Hoehn-Yahr分级,分别采用汉密尔顿焦虑量表(HAMA,14项)、汉密尔顿抑郁量表(HAMD,24项),以及简易智能状态检查量表(MMSE)和蒙特利尔认知评价量表(MoCA,北京版)评价患者焦虑、抑郁和认知功能。

1. 帕金森病严重程度及分期 采用UPDRS量表评价病情严重程度,0~50分为轻度,51~100分为中度,101~199分为重度。Hoehn-Yahr分级共分为5级,1~2级为轻度,单侧或双侧身体受影响,但无平衡障碍;2.5~3级为中度,双侧身体受影响且出现平衡障碍;4~5级为重度,日常生活活动能力严重受影响。

2. 焦虑和抑郁评价 (1)HAMA量表(14项):①躯体性焦虑,包括肌肉系统症状、感觉系统症状、心血管系统症状、呼吸系统症状、胃肠道症状、生殖和泌尿系统症状、自主神经系统症状共7项内容。②精神性焦虑,包括焦虑、紧张、恐惧、失眠、认知功能障碍、抑郁心境和会谈时行为表现共7项内容。评分<7分为无焦虑症状,评分≥7分为有焦虑症状。(2)HAMD量表(24项):①焦虑/躯体化,包括精神性焦虑、躯体性焦虑、胃肠道症状、疑病、自知力共5项内容。②体重减轻。③认知功能障碍,包括负罪感、自杀、激越、人格解体和现实解体、偏执症状、强迫症状共6项内容。④昼夜变化。⑤迟滞症状,包括抑郁、工作和兴趣减少、阻滞、性症状共4项内容。⑥睡眠障碍,包括入睡困难、浅睡眠、早醒共3项内容。⑦绝望感,包括能力减退感、绝望感、自卑感共3项内容。<7分为无抑郁症状,≥7分为有抑郁症状。HAMA和HAMD评分均≥7分者,为同时存在焦虑和抑郁症状。

3. 认知功能评价 据MMSE和MoCA评分,以及患者及其家属主诉是否有认知功能减退和是否对日常生活有影响分为3组。(1)认知功能正常组:MoCA评分≥26分且无认知功能减退主诉。(2)轻度认知损害组(MCI组):MoCA评分<26分且MMSE评分≥26分,同时有认知功能减退主诉但未影响日常生活。(3)痴呆组:MMSE评分<26分,同时有认知功能减退主诉并影响日常生活[5]。

三、统计分析方法

采用SPSS 13.0统计软件进行数据处理与分

析。计数资料以相对数构成比(%)或率(%)表示,行χ^2检验。呈正态分布的计量资料以均数±标准差($\bar{x}\pm s$)表示,行两独立样本的t检验;不同认知功能组患者情绪的比较采用Kruskal-Wallis秩和检验(H检验)。呈非正态分布的计量资料以中位数和四分位数间距[$M(P_{25}, P_{75})$]表示,行Mann-Whitney U检验。认知功能影响因素的筛查采用单因素和多因素Logistic回归分析。以$P \leqslant 0.05$为差异具有统计学意义。

结　果

一、一般资料

本组71例均为轻至中度帕金森病患者,UPDRS评分为10~78分,中位评分为39分;Hoehn-Yahr分级1~4级,中位分级为2级。其中,焦虑组(HAMA评分≥7分)和抑郁组(HAMD评分≥7分)患者除UPDRS评分分别高于无焦虑组(HAMA评分<7分,$P=0.023$)和无抑郁组(HAMD评分<7分,$P=0.029$)外,其他各项资料(性别、年龄、病程、受教育程度、UPDRS评分和Hoehn-Yahr分级)比较,差异均无统计学意义($P>0.05$;表1,2),具有可比性。

二、认知功能评价

本组患者MMSE评分16~30分,中位评分为27分;MoCA评分10~30分,中位评分23分。虽然,焦虑组和抑郁组患者MMSE评分均略低于无焦虑组和无抑郁组,但差异未达到统计学意义(均$P>0.05$);焦虑组患者MoCA评分低于无焦虑组($P=0.042$),而抑郁组与无抑郁组患者MoCA评分差异无统计学意义($P>0.05$;表1,2)。本组71例患者中22例(30.99%)认知功能正常,49例(69.01%)认知功能障碍,其中轻度认知损害28例(39.44%)、痴呆21例(29.58%)。

三、认知功能与情绪变化的关系

1.认知功能对情绪的影响　认知功能正常组、轻度认知损害组和痴呆组患者HAMA(14项)和HAMD(24项)评分比较,差异无统计学意义(均$P>0.05$,表3)。提示认知功能障碍对帕金森病患者的情绪变化无明显影响。

2.情绪对认知功能的影响　单因素Logistic回归分析显示,焦虑为帕金森病患者认知功能障碍的危险因素($P<0.05$;表4,5)。以焦虑为自变量代入多因素Logistic回归方程,进一步分析显示,焦虑为帕金森病患者认知功能障碍的独立危险因素($OR=10.816$,95%CI:1.682~69.560,$P=0.012$;表6)。

表1　焦虑组与无焦虑组患者一般资料的比较

Table 1.　Comparison of general information between PD patients with or without anxiety

Item	No anxiety (N = 10)	Anxiety (N = 61)	Statistical value	P value
Sex [case (%)]			0.000	1.000
Male	6 (6/10)	34 (55.74)		
Female	4 (4/10)	27 (44.26)		
Age ($\bar{x}\pm s$, year)	65.30 ± 10.93	66.75 ± 8.32	0.489	0.626
Duration [$M(P_{25}, P_{75})$, year]	4.50 (2.75, 7.25)	5.00 (3.00, 9.00)	-0.540	0.589
Education [$M(P_{25}, P_{75})$, year]	12.00 (9.00, 15.25)	12.00 (9.00, 15.00)	-0.870	0.384
UPDRS [$M(P_{25}, P_{75})$, score]	26.50 (36.00, 43.00)	40.00 (31.00, 52.00)	-2.406	0.016
Hoehn-Yahr [$M(P_{25}, P_{75})$, grade]	2.25 (1.00, 2.63)	2.00 (2.00, 3.00)	-0.682	0.496
MMSE [$M(P_{25}, P_{75})$, score]	29.00 (25.00, 30.00)	27.00 (25.00, 29.00)	-1.745	0.081
MoCA [$M(P_{25}, P_{75})$, score]	26.00 (22.25, 28.50)	22.00 (18.50, 25.50)	-2.331	0.020

χ^2 test for comparison of sex, t test for comparison of age, and Mann-Whitney U test for comparison of others。UPDRS, Unified Parkinson's Disease Rating Scale,统一帕金森病评价量表;MMSE, Mini-Mental State Examination,简易智能状态检查量表;MoCA, Montreal Cognitive Assessment,蒙特利尔认知评价量表。The same for Table 2

表2　抑郁组与无抑郁组患者一般资料的比较

Table 2.　Comparison of general information between PD patients with or without depression

Item	No depression (N = 16)	Depression (N = 55)	Statistical value	P value
Sex [case (%)]			0.000	0.994
Male	9 (9/16)	31 (56.36)		
Female	7 (7/16)	24 (43.64)		
Age ($\bar{x}\pm s$, year)	64.81 ± 10.77	67.05 ± 7.99	0.910	0.366
Duration [$M(P_{25}, P_{75})$, year]	4.50 (2.25, 7.25)	5.00 (3.00, 9.00)	-0.796	0.426
Education [$M(P_{25}, P_{75})$, year]	12.00 (9.00, 15.00)	12.00 (9.00, 15.00)	-0.270	0.787
UPDRS [$M(P_{25}, P_{75})$, score]	39.00 (30.00, 52.00)	39.00 (30.00, 52.00)	-6.057	0.000
Hoehn-Yahr [$M(P_{25}, P_{75})$, grade]	2.00 (2.00, 2.88)	2.00 (2.00, 3.00)	-0.511	0.610
MMSE [$M(P_{25}, P_{75})$, score]	27.50 (25.00, 29.75)	27.00 (25.00, 29.00)	-0.841	0.400
MoCA [$M(P_{25}, P_{75})$, score]	23.50 (18.00, 27.50)	23.00 (19.00, 26.00)	0.891	0.373

讨　论

MMSE量表是由Folstein于1975年编制的,一直用于痴呆的筛查与评价[6],MoCA量表是在MMSE

表3 认知功能正常与异常帕金森病患者焦虑与抑郁程度的比较[$M(P_{25},P_{75})$,评分]

Table 3. Comparison of anxiety and depression in PD patients with or without cognitive dysfunction [M (P_{25}, P_{75}), score]

Group	N	HAMA-14	HAMD-24
Normal cognitive function	22	11.00 (9.00, 14.00)	10.00 (7.00, 13.00)
MCI	28	11.00 (9.00, 14.75)	11.00 (7.00, 14.00)
Dementia	21	11.00 (9.00, 15.00)	11.00 (7.00, 15.00)
H value		3.229	2.174
P value		0.199	0.337

MCI, mild cognitive impairment, 轻度认知损害; HAMA, Hamilton Anxiety Rating Scale, 汉密尔顿焦虑量表; HAMD, Hamilton Depression Rating Scale, 汉密尔顿抑郁量表

量表基础上经过长期的临床摸索和实践改良而成。目前对于认知功能评价,MMSE量表简便,应用最为广泛,但因涵盖认知领域少,敏感性低等原因而受限,MoCA量表在多项研究中均显示对认知功能障碍的筛查优于MMSE量表。

帕金森病患者在病程中出现的认知功能障碍主要与遗传因素、老龄化和环境因素有关,其病理学机制可能与额叶-纹状体环路破坏有关[7]。有研究显示,与震颤型帕金森病相比,姿势步态异常型帕金森病患者病程中认知功能下降程度更明显[8]。据相关文献报道,帕金森病患者认知功能障碍患病率约为55%[9],本组病例患病率为69.01%(49/71),远高于年龄相匹配的社区老年人群[10-11]。有研究显示,帕金森病患者在疾病早中期即可出现轻度认知损害[12]。

情绪障碍为帕金森病患者临床较为常见的非运动症状之一[13-14]。目前,对帕金森病患者情绪障碍与认知功能障碍之间的关系尚未完全阐明,一般认为与去甲肾上腺素能和5-羟色胺能神经元损害有关,或由患者对自身认知功能减退而产生的悲观和焦虑情绪所诱发[15-16]。帕金森病伴抑郁的发生率为20%~40%[17-18],发病机制与脑组织5-羟色胺和多巴胺(DA)代谢产物表达下调导致的额叶-皮质下神经网络功能异常有关[19]。临床主要表现为情绪低落(冷漠、悲观、兴趣减少等)、对工作和生活丧失兴趣、注意力不集中、敏感、睡眠障碍、缺乏幽默感、伴自杀倾向等,但较少出现自残和自杀行为[20],其机制为脑组织5-羟色胺和多巴胺代谢产物表达水平下降导致的额叶-皮质下神经网络功能异常[19]。研究显示,HAMD-24评分与MoCA评分呈负相关,抑郁症状可损害帕金森病患者认知功能[21-22]。对本组病例的观察结果显示,伴抑郁的帕金森病患者认知功能障碍患病率呈上升趋势可能与本研究所纳入的轻至中度帕金森病患者抑郁症状和认知功能障碍相对较轻有关。Erro等[23]认为,帕金森病患者出现焦虑症状的主要原因是黑质-纹状体多巴胺能神经元功能异常和右侧尾状核低代谢,临床表现为广泛性焦虑、社交恐惧或惊恐障碍[24-25]。目前认为,焦虑为帕金森病前驱症状[25],对患者感觉、知觉、记忆、思维等认知功能具有不良影响,使其视觉或听觉功能减退,继而导致反应迟钝以及学习、记忆和理解能力下降,影响正常交流[26]。本研究伴焦虑的帕金森病患者的MoCA评分均降低,提示焦虑症状可以诱发或加重认知损害程度;但本研究伴焦虑的帕金森病患者的MMSE评分与无焦虑者之间无明显差异。由于MMSE量表之瞬时记忆和命名测验内容简单,故对轻度认知损害的诊断敏感性较低;而MoCA量表增加了执行能力和注意力测验项目,使轻度认知损害诊断的敏感性有所提高,大量临床研究结果均提示,MoCA量表筛查效果明显优于MMSE量表[27-28],本研究亦获得相同结果。

本研究所纳入的帕金森病患者多伴焦虑与抑郁症状共存,但尚未达到焦虑症和抑郁症的诊断标准。目前关于焦虑与抑郁之间的关系尚无定论,大多数研究认为有以下3种可能:(1)连续谱论,即焦虑症与抑郁症的发病基础相同,是同一种疾病的不同表现形式。(2)二分论,认为焦虑与抑郁是两种不同性质的疾病,共病现象是二者各为一种独立疾病但同时存在于同一患者的临床症状中。(3)共病论,认为焦虑和抑郁共病是一种不同于单纯焦虑障碍和单纯抑郁障碍的独特疾病实体[29]。我们对本组病例的观察未发现帕金森病患者伴焦虑和抑郁共病对其认知功能有显著影响,具体病理生理学机制尚待进一步观察。鉴于情绪障碍和认知功能障碍可严重影响患者生活质量,且前者可能为后者的危险因素,因此,无论是何种机制均应早期诊断并积极治疗其不良情绪,从而提高患者生活质量,预防和延缓病情进展。

本研究为一项非多中心临床试验,由于样本量较小无法进一步分析帕金森病不同临床亚型和发病年龄对认知功能的影响;与此同时,本研究为一

表4 Logistic回归分析变量赋值表

Table 4. Assignment of Logistic regression analysis

Variable	Assignment (score)	
	0	1
Sex	Female	Male
Age (year)	≤60	>60
Duration (year)	≤ 5	> 5
Education (year)	≤12	>12
UPDRS (score)	≤50	>50
Hoehn-Yahr (grade)	≤ 2	> 2
Anxiety	No	Yes
Depression	No	Yes
Anxiety and depression	Anxiety or depression	Coexistence of both

UPDRS, Unified Parkinson's Disease Rating Scale, 统一帕金森病评价量表。The same for Table 5

表5 帕金森病患者认知功能障碍影响因素的单因素Logistic回归分析

Table 5. Univariate Logistic regression analysis of the influencing factors for cognitive dysfunction of PD patients

Variable	*b*	*SE*	Wald χ^2	*P* value	*OR* value	*OR* 95%CI
Sex	-0.911	0.525	3.011	0.083	0.402	0.144– 1.125
Age	0.380	0.596	0.407	0.523	1.462	0.455– 4.700
Duration	0.519	0.527	0.968	0.325	1.680	0.598– 4.723
Education	0.065	0.574	0.013	0.910	1.067	0.316– 3.284
UPDRS	0.500	0.593	0.711	0.399	1.648	0.516– 5.270
Hoehn-Yahr	0.141	0.515	0.076	0.783	1.152	0.420– 3.160
Anxiety	1.968	0.751	6.859	0.009	7.156	1.641–31.206
Depression	0.730	0.588	1.540	0.215	2.074	0.655– 6.565
Anxiety and depression	0.993	0.560	3.154	0.076	2.700	0.901– 8.093

表6 帕金森病患者认知功能障碍影响因素的多因素Logistic回归分析

Table 6. Multivariate Logistic regression analysis of the influencing factors for cognitive dysfunction of PD patients

Variable	*b*	*SE*	Wald χ^2	*P* value	*OR* value	*OR* 95%CI
Anxiety	2.381	0.950	6.287	0.012	10.816	1.682–69.560
Constant	-4.482	3.010	2.216	0.137		

项横断面研究，仅调查一个时间点的情绪和认知功能，不能显示患者情绪变化的动态结果且缺乏随访；入组病例病情（轻至中度）、认知功能障碍以及抑郁和焦虑程度均较轻，可能存在病例选择偏倚；而且纳入与排除标准中未考虑药物对患者情绪影响等因素。今后将针对上述问题进一步扩大样本量，同时增加重症患者、改善研究方法以获得更加详细、准确的数据。

参 考 文 献

[1] Muslimovic D, Post B, Speelman JD, Schmand B. Cognitive profile of patients with newly diagnosed Parkinson disease. Neurology, 2005, 65:1239-1245.

[2] Hely MA, Reid WG, Adena MA, Halliday GM, Morris JG. The Sydney multicenter study of Parkinson's disease: the inevitability of dementia at 20 years. Mov Disord, 2008, 23:837-844.

[3] Janvin CC, Aarsland D, Larsen JP. Cognitive predictors of dementia in Parkinson's disease: a community - based, 4 - year longitudinal study. J Geriair Psychiatry Neurol, 2005, 18:149-154.

[4] Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. Arch Neurol, 1999, 56:33-39.

[5] Li LF, Xiao JS, Zhang JJ, Zhang H, Liu L, Li F, Zhong ZA. Comparison of screening scales in evaluating cognitive function in mild cognitive impairment patients. Yi Xue Xin Zhi Za Zhi, 2011, 21:420-423.[李兰芳, 肖劲松, 章军建, 张洪, 刘丽, 李飞, 钟子安. 轻度认知功能障碍常用筛查量表的比较分析. 医学新知杂志, 2011, 21:420-423.]

[6] Folstein MF, Robins LN, Helzer JE. The Mini - Mental State Examination. Arch Gen Psychiatry, 1983, 40:812.

[7] Yang RW, Chang LH. Cognitive impariment of Parkinson disease. Yi Xue Zong Shu, 2011, 17:2623-2626.[杨荣文, 常履华. 帕金森患者的认知功能障碍. 医学综述, 2011, 17:2623-2626.]

[8] Yu CY, Liu WG, Chen L, Feng WR. A 2-year follow-up study on cognitive function of patients with Parkinson's disease. Zhonghua Xing Wei Yi Xue Yu Nao Ke Xue Za Zhi, 2014, 23:601-604.[于翠玉, 刘卫国, 陈伶, 冯芜若. 帕金森病患者认知功能两年随访. 中华行为医学与脑科学杂志, 2014, 23:601-604.]

[9] Li D, Wang XJ, Luo WF, Zhu TG, Hu WD, Mao CJ, Liu CF. The impact of uric acid on different cognitive domains of patients with Parkinson's disease. Zhonghua Shen Jing Ke Za Zhi, 2010, 43:400-402.[李丹, 王晓君, 罗蔚峰, 朱婷鸽, 胡伟东, 毛成洁, 刘春风. 尿酸对帕金森病患者不同认知功能域影响分析. 中华神经科杂志, 2010, 43:400-402.]

[10] Chen DH, Qu ZW, Jiang Q, Zhang M, Pei Y, Zhu LN, Sun XR, Fu WZ, Yang ZD, Qin HY, Fu HM, Zhang J, Yuan J, Lu Y, Tang Q, Sun YY. Investigation and analysis of the risk factors for the community elderly with mild cognitive impairment. Zhonghua Xing Wei Yi Xue Yu Nao Ke Xue Za Zhi, 2013, 22:413-416.[陈定华, 瞿正万, 江琦, 张明, 裴瑜, 朱莉娜, 孙喜蓉, 傅伟忠, 杨振东, 秦虹云, 傅红梅, 张洁, 袁杰, 卢瑛, 唐强, 孙一颖. 社区老年人轻度认知功能损害危险因素调查. 中华行为医学与脑科学杂志, 2013, 22:413-416.]

[11] Luck T, Riedel-Heller SG, Kaduszkiewicz H, Bickel H, Jessen F, Pentzek M, Wiese B, Koelsch H, van den Bussche H, Abholz HH, Moesch E, Gorfer S, Angermeyer MC, Maier W, Weyerer S; AgeCoDe Group. Mild cognitive impairment in general practice: age - specific prevalence and correlate results from the German study on aging, cognition and dementia in primary care patients (AgeCoDe). Dement Geriatr Cogn Disord, 2007, 24:307-316.

[12] Gu JP, Liu ZG, Gan J, Zhou MZ, Lu LX, Wu JY. Analysis of cognition disorder and its correlative factors in Parkinson disease. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2009, 9:252-256.[顾剑萍, 刘振国, 干静, 周明珠, 陆丽霞, 吴佳英. 帕金森病认知障碍及相关因素分析. 中国现代神经疾病杂志, 2009, 9:252-256.]

[13] Jia SH, Chen HB, Zhang WW. Characteristics and influencing factors of non - motor symptoms in Parkinson's disease. Zhonghua Yi Xue Za Zhi, 2010, 90:1886-1889.[贾树红, 陈海波, 张玮玮. 帕金森病患者非运动症状特点及其影响因素. 中

华医学杂志, 2010, 90:1886-1889.]
[14] Politis M, Wu K, Molloy S, G Bain P, Chaudhuri KR, Piccini P. Parkinson's disease symptoms: the patient's perspective. Mov Disord, 2010, 25:1646-1651.
[15] Feng LJ, Zhang N, Cheng Y, Du HJ. Cognitive functions and behavioral and psychological symptoms in patients with Alzheimer's disease and patients with vascular dementia. Zhongguo Xin Li Wei Sheng Za Zhi, 2011, 25:334-338.[冯丽君, 张楠, 程焱, 杜红坚. 阿尔茨海默病和血管性痴呆患者的认知功能和精神行为症状. 中国心理卫生杂志, 2011, 25:334-338.]
[16] Perri R, Fadda L, Caltagirone C, Carlesimo GA. Word list and story recall elicit different patterns of memory deficit in patients with Alzheimer's disease, frontotemporal dementia, subcortical ischemic vascular disease, and Lewy body dementia. J Alzheimers Dis, 2013, 37:99-107.
[17] Aarsland D, Marsh L, Schrag A. Neuropsychiatric symptoms in Parkinson's disease. Mov Disord, 2009, 24:2175-2186.
[18] Starkstein SE, Merello M, Jorge R, Brockman S, Bruce D, Petracca G, Robinson RG. A validation study of depressive syndromes in Parkinson's disease. Mov Disord, 2008, 23:538-546.
[19] Chen HB. Anxiety and depression of Parkinson's disease. Zhonghua Nei Ke Za Zhi, 2008, 47:168-169.[陈海波. 帕金森病的焦虑抑郁. 中华内科杂志, 2008, 47:168-169.]
[20] Ravina B, Camicioli R, Como PG, Marsh L, Jankovic J, Weintraub D, Elm J. The impact of depressive symptoms in early Parkinson disease. Neurology, 2007, 69:342-347.
[21] Chen JP, Yao JX, Wu Y, Chen Y, Mao CJ, Liu CF. Cognitive dysfunctions associated with essential tremor and Parkinson's disease. Zhonghua Yi Xue Za Zhi, 2014, 94:2412-2416.[陈菊萍, 姚建新, 武燕, 陈赟, 毛成洁, 刘春风. 特发性震颤与帕金森病的认知障碍. 中华医学杂志, 2014, 94:2412-2416.]
[22] Korczyn AD, Gurevich T. Parkinson's disease: before the motor symptoms and beyond. J Neurol Sci, 2010, 289:2-6.
[23] Erro R, Pappatù S, Amboni M, Vicidomini C, Longo K, Santangelo G, Picillo M, Vitale C. Anxiety is associated with striatal dopamine transporter availability in newly diagnosed untreated Parkinson's disease patients. Parkinsonism Relat Disord, 2012, 18:1034-1038.
[24] Dissanayaka NN, Sellbach A, Matheson S, O'Sullivan JD, Silburn PA, Byrne GJ, Marsh R, Mellick GD. Anxiety disorders in Parkinson's disease: prevalence and risk factors. Mov Disord, 2010, 25:838-845.
[25] Prediger RD, Matheus FC, Schwarzbold ML, Lima MM, Vital MA. Anxiety in Parkinson's disease: a critical review of experimental and clinical studies. Neuropharmacology, 2012, 62:115-124.
[26] Jacob EL, Gatto NM, Thompson A, Bordelon Y, Ritz B. Occurrence of depression and anxiety prior to Parkinson's disease. Parkinsonism Relat Disord, 2010, 16:576-581.
[27] Chen L, Liu WG, Zhao YY, Hua P, Wang Y, Zhang N. Evaluation of using Montreal Cognitive Assessment in patients with Parkinson's disease with cognitive impairment. Zhonghua Shen Jing Ke Za Zhi, 2011, 44:200-201.[陈伶, 刘卫国, 赵燕燕, 华平, 王阳, 张宁. 蒙特利尔认知评估量表在帕金森病认知障碍患者中的应用价值. 中华神经科杂志, 2011, 44:200-201.]
[28] Nasreddine ZS, Phinips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, Cummings JL, Chertkow H. The Montreal Cognitive Assessment (MoCA): a brief screening tool for mild cognitive impairment. J Am Geriatr Soc, 2005, 53:695-699.
[29] Asnis GM, Praag HM. Panic disorder: clinical, biological, and treatment aspects. New York: John Wiley&Sons, 1995: 80-98.

（收稿日期:2015-11-11）

Systems Biology of Alzheimer's Disease published

Systems Biology of Alzheimer's Disease (ISBN: 978-1-4939-2626-8, eBook ISBN: 978-1-4939-2627-5) will be published by Humana Press in 2016. The editors of this book are Juan I. Castrillo and Stephen G. Oliver, Department of Biochemistry and Cambridge Systems Biology Centre, University of Cambridge.

Alzheimer's disease (AD) and many other neurodegenerative disorders are multifactorial in nature, involving a combination of genomic, epigenomic, network dynamic and environmental factors. A proper investigation requires new integrative Systems Biology approaches, at both the experimental and computational level. The interplay of disease mechanisms and homeostatic networks will underlie the time of onset and rate of progression of the disease.

This book addresses such an integrated approach to AD. It aims to present Systems Biology, including both experimental and computational approaches, as a new strategy for the study of AD and other multifactorial diseases, with the hope that the results will translate into more effective diagnosis and treatment, as well as improved public health policies.

Written for the highly successful Methods in Molecular Biology series, practical and cutting-edge *Systems Biology of Alzheimer's Disease* is intended for post-graduate students, post-doctoral researchers and experts in different fields with an interest in comprehensive Systems Biology strategies applicable to AD and other complex multifactorial diseases (including other neurodegenerative diseases and cancers). This book aims to complement other excellent volumes and monographs on AD that cover fundamental, physiological or medical aspects of the disease.

The price of eBook is 103.52€, and hardcover is 124.99€. Visit link.springer.com for more information.