·神经心理学研究·

多系统萎缩和帕金森病患者执行功能障碍研究

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【摘要】 **目的** 探讨多系统萎缩和帕金森病患者执行功能障碍特点。**方法** 采用简易智能状态检查量表(MMSE)和蒙特利尔认知评价量表(MoCA),以及Stroop色词测验(SCWT)、数字符号转换测验(DSST)/图形符号转换测验(GSST)、画钟测验(CDT)和连线测验(TMT)评价34例多系统萎缩患者[以小脑共济失调为主要表现型(MSA-C型)21例、以帕金森病综合征为主要表现型(MSA-P型)13例]和18例原发性帕金森病患者的整体认知功能和执行功能。**结果** 各组受试者MoCA评分差异有统计学意义($P=0.019$),其中PD组和MSA-C型组患者评分低于对照组($P=0.015,0.002$)。各组受试者SCWT测验各部分评分($P=0.035,0.013,0.012,0.037$)、DSST评分($P=0.000$)、GSST评分($P=0.000$)、TMT评分($P=0.035$)差异均有统计学意义,其中,MSA-C型组和MSA-P型组患者SCWT-A($P=0.004,0.045$)、SCWT-B($P=0.001,0.036$)和SCWT-D($P=0.023,0.010$)评分均高于对照组,PD组、MSA-C型组和MSA-P型组患者SCWT-C评分($P=0.005,0.014,0.003$)、DSST评分($P=0.003,0.000,0.000$)和GSST评分($P=0.001,0.000,0.000$)均高于对照组,仅MSA-P型组患者TMT评分高于对照组($P=0.006$)。**结论** 多系统萎缩和帕金森病患者均存在不同程度的执行功能障碍,SCWT和DSST/GSST测验有助于评价此类患者的执行功能障碍。

【关键词】 多系统萎缩; 帕金森病; 认知障碍; 神经心理学测验

Analysis on executive dysfunction of patients with multiple system atrophy and Parkinson´s disease

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【**Abstract**】 **Objective** To explore the characteristics of executive dysfunction of patients with multiple system atrophy (MSA) and Parkinson´s disease (PD) by neuropsychological tests. **Methods** Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Stroop Color - Word Test (SCWT), Digital Symbol Substitution Test (DSST)/Graphic Symbol Substitution Test (GSST), Clock Drawing Test (CDT) and Trail Making Test (TMT) were used to assess the overall cognitive and executive function of 34 patients with MSA [21 with cerebellar-predominant (MSA-C) and 13 with parkinsonism-predominant (MSA-P)], 18 patients with primary PD and 14 normal controls. **Results** There was significant difference in MoCA score among different groups ($P=0.019$). PD and MSA-C groups had lower MoCA score than that in normal control group ($P=0.015$, 0.002). There were significant differences in each SCWT score ($P=0.035$, 0.013, 0.012, 0.037), DSST ($P=0.000$), GSST ($P=0.000$) and TMT ($P=0.035$) among different groups. Among them, MSA-C and MSA-P groups had significantly higher SCWT-A ($P=0.004$, 0.045), SCWT-B ($P=0.001$, 0.036) and SCWT-D scores ($P=0.023$, 0.010) than those in normal control group. PD, MSA-C and MSA-P groups had significantly higher SCWT-C ($P=0.005$, 0.014, 0.003), DSST ($P=0.003$, 0.000, 0.000) and GSST scores ($P=0.001$, 0.000, 0.000) than those in normal control group. MSA-P group had significantly higher TMT score than that in normal control group ($P=0.006$). **Conclusions** Patients with MSA and PD may present executive dysfunction to different degrees. SCWT and DSST/GSST tests are useful in assessing executive dysfunction in those patients.

【**Key words**】 Multiple system atrophy; Parkinson disease; Cognition disorders; Neuropsychological tests

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随着社会老龄化的逐渐突显，增龄性神经变性病如多系统萎缩（MSA）、帕金森病（PD）等的发病率和明确诊断率逐渐升高。多系统萎缩和帕金森病同为α-突触共核蛋白病，临床症状和影像学表现存在重叠和交叉，故二者鉴别诊断存在一定困难。研究显示，二者在疾病早期即存在认知功能障碍，尤以执行功能障碍显著[1]。目前国内鲜见多系统萎缩和帕金森病患者执行功能障碍特点的文献报道，鉴于此，本研究采用神经心理学测验量表对多系统萎缩和帕金森病患者的认知功能进行评价，以期总结此类疾病患者执行功能障碍特点。

对象与方法

一、研究对象

1. 多系统萎缩组（MSA组） 共计选择2012年12月–2013年11月在解放军总医院神经内科门诊或住院治疗的多系统萎缩患者34例，符合2008年Gilman等[2]提出的很可能（probable）多系统萎缩诊断标准；排除颅脑创伤（TBI）、代谢性疾病、中枢神经系统感染、神经变性病和药物等原因继发的帕金森综合征，药物滥用史、精神疾病病史、影响认知功能的器质性脑病病史、其他中枢神经系统疾病病史、肝肾功能障碍或甲状腺功能障碍、贫血或营养不良、影响神经心理学测验的听觉和视觉障碍。男性24例，女性10例；年龄44～72岁，平均（58.97±7.40）岁；受教育程度为2～17年，平均为（9.53±3.43）年；病程1～5年，中位病程2.25（1.88，4.00）年；其中以小脑共济失调为主要表现的多系统萎缩（MSA-C）型21例、以帕金森综合征为主要表现的多系统萎缩（MSA-P）型13例。

2. 帕金森病组（PD组） 选择同期在我院神经内科门诊或住院治疗的原发性帕金森病患者18例，符合英国帕金森病学会脑库帕金森病临床诊断标准[3]；排除标准同MSA组。男性7例，女性11例；年龄45～69岁，平均（57.94±6.87）岁；受教育程度4～17年，平均病程（8.72±3.38）年；病程1～11年，中位病程3.56（1.00，5.25）年。

3. 正常对照组（对照组） 选择同期在我院进行体格检查的老年健康志愿者共14例，男性7例，女性7例；年龄47～68岁，平均（56.93±7.06）岁；受教育程度3～13年，平均（8.29±2.37）年。

各组受试者性别、受教育程度和病程比较，差异无统计学意义（均$P>0.05$），而MSA-P型组患者年龄高于其他各组（$P=0.012$，0.015，0.001；表1）。

二、研究方法

1. 整体认知功能评价 采用简易智能状态检查量表（MMSE）和蒙特利尔认知评价量表（MoCA）评价受试者整体认知功能。（1）MMSE量表：据不同受教育程度设置分界值，文盲≤17分、小学≤20分、中学≤22分、大学≤23分，即为认知功能障碍[4]。（2）MoCA量表：据不同受教育程度设置分界值，文盲≤17分、小学≤20分、中学及以上≤24分（受教育程度≤12年者评分加1分），为认知功能障碍[4]。

2. 执行功能评价 由同一位受过专业训练的心理测评师在安静独立的房间内对受试者进行测试。采用Stroop色词测验（SCWT）、数字符号转换测验（DSST）/图形符号转换测验（GSST）、画钟测验（CDT）和连线测验（TMT）评价执行功能。（1）SCWT测验：选择4种颜色（黄、红、蓝、绿），每张卡片包含50个字，卡片1由4种颜色的字组成，要求正确读出字义；卡片2由4种颜色的圆点组成，要求正确读出颜色名称；卡片3和卡片4由4种颜色印刷而成，卡片3的要求与卡片1相同，即读出字义，卡片4的要求与卡片2相同，即读出颜色名称，记录受试者完成每张卡片任务的时间。（2）DSST/GSST测验：要求受试者按照答题纸上方给出的数字符号和图形符号对应关系，在数字下的空格内填上对应的符号，在分别进行7和5次练习后记录其在90 s内完成的正确个数。（3）CDT测验：总评分4分，包括轮廓、数字位置、数字数目和指针共4项条目，评分越低、执行功能越差。（4）TMT测验：在一张纸上印25个小圆圈，并标注数字1～25，要求尽快按照数字顺序用直线连接25个小圆圈，记录受试者完成连线的时间。

3. 统计分析方法 采用SPSS 19.0统计软件进行数据处理与分析。计数资料以率（%）或相对数构成比（%）表示，采用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，采用单因素方差分析，两两比较行LSD-t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，采用Kruskal-Wallis秩和检验（H检验）。以$P\leq0.05$为差异具有统计学意义。

结 果

一、整体认知功能的比较

各组受试者MMSE评分差异无统计学意义（$P=0.264$）；MoCA评分差异有统计学意义（$P=0.019$），

表1 各组受试者临床资料的比较

Table 1. Comparison of clinical data among different groups

Item	Control (N = 14)	PD (N = 18)	MSA-C (N = 21)	MSA-P (N = 13)	Statistic value	*P* value
Sex [case (%)]					5.974	0.113
Male	7 (7/14)	7 (7/18)	16 (76.19)	8 (8/13)		
Female	7 (7/14)	11 (11/18)	5 (23.81)	5 (5/13)		
Age ($\bar{x} \pm s$, year)	56.93 ± 7.06	57.94 ± 6.87	55.86 ± 6.13	64.00 ± 6.53	4.265	0.008
Education ($\bar{x} \pm s$, year)	8.29 ± 2.37	8.72 ± 3.38	8.62 ± 3.34	10.00 ± 3.16	2.151	0.103
Duration [M (P_{25}, P_{75}), year]	—	3.56 (1.00, 5.25)	2.43 (1.25, 3.00)	3.50 (2.00, 5.00)	2.948	0.228

χ^2 test for comparison of sex, Kruskal-Wallis H test for comparison of duration, and one-way ANOVA for comparison of others。—, no data, 此项无数据。PD, Parkinson's disease, 帕金森病; MSA-C, multiple system atrophy with cerebellar-predominant, 以小脑共济失调为主要表现的多系统萎缩; MSA-P, multiple system atrophy with parkinsonism-predominant, 以帕金森综合征为主要表现的多系统萎缩

其中，PD组和MSA-C型组患者MoCA评分低于对照组（P = 0.015，0.002），其余各组差异无统计学意义（均P > 0.05；表2，3）。

二、执行功能的比较

各组受试者SCWT测验各部分评分差异均具有统计学意义（P = 0.035，0.013，0.012，0.037），其中，MSA-C型组和MSA-P型组患者SCWT-A（P = 0.004，0.045）、SCWT-B（P = 0.001，0.036）和SCWT-D（P = 0.023，0.010）评分高于对照组，PD组、MSA-C型组和MSA-P型组患者SCWT-C评分高于对照组（P = 0.005，0.014，0.003），其余各组差异无统计学意义（均P > 0.05；表2，3）。各组受试者DSST和GSST评分差异均有统计学意义（P = 0.000，0.000），其中，PD组、MSA-C型组和MSA-P型组患者DSST（P = 0.003，0.000，0.000）和GSST（P = 0.001，0.000，0.000）评分高于对照组，其余各组差异无统计学意义（均P > 0.05；表2，3）。各组受试者TMT评分差异有统计学意义（P = 0.035），其中，仅MSA-P型组患者评分高于对照组（P = 0.006），其余各组差异无统计学意义（均P > 0.05；表2，3）。而各组受试者CDT评分差异无统计学意义（P = 0.087；表2，3）。

讨 论

既往研究显示，多系统萎缩早期即可出现认知功能障碍[5]。2013年，Song等[6]研究发现，多系统萎缩患者存在一定程度的认知功能障碍、情感障碍和日常生活活动能力（ADL）障碍，而且，两种亚型（MSA-C型和MSA-P型）患者均存在认知功能障碍，尤其是执行功能障碍。

2008年，Gilman等[2]在1999年多系统萎缩诊断标准基础上提出更新的诊断标准，将痴呆作为排除标准，但大量研究和临床实践均提示多系统萎缩患者的认知功能甚至可达痴呆诊断标准，国内外亦可见以认知功能障碍为首发症状的多系统萎缩个案报道[7-8]。2015年，Cao等[9]研究显示，国内多系统萎缩患者可伴严重认知功能障碍，故痴呆不应成为多系统萎缩的绝对排除标准，甚至有研究显示，11%～15%的多系统萎缩患者存在痴呆[10-11]。本研究有2例多系统萎缩患者MoCA评分 ≤ 17分，病程分别为2和3年，表明多系统萎缩患者病程早期即可能存在较明显的认知功能下降。

多系统萎缩和帕金森病同属α-突触共核蛋白病，二者临床表现（如锥体外系症状、皮质功能障碍等）和影像学特点存在一定重叠[12]，疾病早期较难鉴别。由于α-突触共核蛋白（α-Syn）在不同疾病中具有不同结构特点，故不同疾病患者认知功能障碍特点各异[13]。Krishnan等[14]研究显示，多系统萎缩患者整体认知功能优于帕金森病患者，但额叶皮质功能低于帕金森病患者。本研究结果显示，多系统萎缩患者执行功能障碍较帕金森病患者显著，然而神经心理学测验并不能将二者区别，与Siri等[15]的研究结果相一致，而国内鲜见多系统萎缩与帕金森病患者认知功能障碍比较的研究报道，二者的对比研究多集中于影像学和神经电生理学检测[16]。

本研究结果还显示，除SCWT和TMT测验外，DSST/GSST测验也有助于评价多系统萎缩和帕金森病患者执行功能，且优于SCWT和TMT测验。

多系统萎缩患者执行功能障碍表现为斑片状认知损害，本研究提示我们在临床实践中应对多系统萎缩患者执行功能障碍予以重视和关注。然而

表2　各组受试者神经心理学测验结果的比较($\bar{x} \pm s$,评分)

Table 2.　Comparison of the results of neuropsychological tests among different groups ($\bar{x} \pm s$, score)

Item	Control (N = 14)	PD (N = 18)	MSA-C (N = 21)	MSA-P (N = 13)	*F* value	*P* value
MMSE	28.43 ± 1.16	27.44 ± 1.77	27.43 ± 1.66	27.77 ± 1.59	1.358	0.264
MoCA	26.00 ± 1.47	23.67 ± 2.33	23.14 ± 2.97	24.08 ± 3.28	3.552	0.019
SCWT-A	31.07 ± 5.47	39.61 ± 11.12	42.43 ± 11.32	39.85 ± 14.92	3.047	0.035
SCWT-B	37.07 ± 6.44	45.67 ± 11.42	53.33 ± 17.66	48.62 ± 16.19	3.894	0.013
SCWT-C	37.57 ± 8.80	51.33 ± 14.93	49.29 ± 10.68	53.31 ± 18.23	3.963	0.012
SCWT-D	81.27 ± 11.13	90.61 ± 30.63	101.86 ± 24.72	107.62 ± 33.22	3.012	0.037
DSST	36.00 ± 5.81	27.06 ± 10.97	22.33 ± 6.67	23.15 ± 7.37	9.128	0.000
GSST	39.93 ± 5.44	29.94 ± 9.80	26.71 ± 7.14	26.08 ± 8.96	9.313	0.000
CDT	3.86 ± 0.36	3.50 ± 0.71	3.43 ± 0.75	3.15 ± 0.90	2.287	0.087
TMT	67.00 ± 15.07	73.83 ± 21.90	82.52 ± 35.20	95.62 ± 24.01	3.057	0.035

PD，Parkinson's disease，帕金森病；MSA-C，multiple system atrophy with cerebellar-predominant，以小脑共济失调为主要表现的多系统萎缩；MSA-P，multiple system atrophy with parkinsonism-predominant，以帕金森综合征为主要表现的多系统萎缩；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；SCWT，Stroop Color-Word Test，Stroop色词测验；DSST，Digital Symbol Substitution Test，数字符号转换测验；GSST，Graphic Symbol Substitution Test，图形符号转换测验；CDT，Clock Drawing Test，画钟测验；TMT，Trail Making Test，连线测验。The same for table below

表3　各组受试者神经心理学测验结果的两两比较*

Table 3.　Paired comparison of the results of neuropsychological tests among different groups*

Paired comparison	MoCA	SCWT-A	SCWT-B	SCWT-C	SCWT-D	DSST	GSST	TMT
Control∶PD	0.015	0.056	0.090	0.005	0.293	0.003	0.001	0.468
Control∶MSA-C	0.002	0.004	0.001	0.014	0.023	0.000	0.000	0.092
Control∶MSA-P	0.061	0.045	0.036	0.003	0.010	0.000	0.000	0.006
PD∶MSA-C	0.536	0.435	0.093	0.635	0.189	0.073	0.215	0.307
PD∶MSA-P	0.668	0.954	0.565	0.686	0.081	0.188	0.191	0.026
MSA-C∶MSA-P	0.316	0.514	0.343	0.397	0.538	0.774	0.823	0.100

*P value

本研究仍存在一定局限性，由于MSA-P型患者发病年龄较晚，导致入组病例年龄分布不均衡；尽管入组患者均未合并严重情绪障碍，但是本研究并未对情绪障碍进行评价，可能对认知功能的评价有所影响；本研究未发现多系统萎缩与帕金森病患者执行功能的差异，尚待大样本多中心临床研究为国人多系统萎缩和帕金森病患者执行功能障碍特点及其差异提供详尽的理论依据。

参　考　文　献

[1] Zweig RM, Disbrow EA, Javalkar V. Cognitive and psychiatric disturbances in Parkinsonian syndromes. Neurol Clin, 2016, 34: 235-246.

[2] Gilman S, Wenning GK, Low PA, Brooks DJ, Mathias CJ, Trojanowski JQ, Wood NW, Colosimo C, Dürr A, Fowler CJ, Kaufmann H, Klockgether T, Lees A, Poewe W, Quinn N, Revesz T, Robertson D, Sandroni P, Seppi K, Vidailhet M. Second consensus statement on the diagnosis of multiple system atrophy. Neurology, 2008, 71:670-676.

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

[4] Jia JP. Guidelines for the diagnosis and treatment of dementia and cognitive impairment in China. Beijing: People's Medical Publishing House, 2010: 120-122.[贾建平. 中国痴呆与认知障碍诊治指南. 北京: 人民卫生出版社, 2010: 120-122.]

[5] Stanzani - Maserati M, Gallassi R, Calandra - Buonaura G, Alessandria M, Oppi F, Poda R, Sambati L, Provini F, Cortelli P. Cognitive and sleep features of multiple system atrophy: review and prospective study. Eur Neurol, 2014, 72(5/6):349 - 359.

[6] Song DD, Yu YX, Dong QW, Zhang HL, Liu JG, Liu Q, Yu J, Qi XK. Assessment of cognitive function, emotions and activities of daily living in patients with multiple system atrophy. Zhonghua Yi Xue Za Zhi, 2013, 93:1948-1951.

[7] Li LP, Qi XK, Liu JG, Duan F, Zhao M. Multiple system atrophy with cognitive dysfunction as the initial symptom: a case report. Zhonghua Nei Ke Za Zhi, 2008, 47:83.[李丽萍, 戚晓昆, 刘建国, 段枫, 赵敏. 以认知功能障碍为首发症状的多系统萎缩一例. 中华内科杂志, 2008, 47:83.]

[8] Spaccavento S, Del Prete M, Loverre A, Craca A, Nardulli R. Multiple system atrophy with early cognitive deficits: a case

report. Neurocase, 2013, 19:613-622.
[9] Cao B, Zhao B, Wei QQ, Chen K, Yang J, Ou R, Wu Y, Shang HF. The global cognition, frontal lobe dysfunction and behavior changes in Chinese patients with multiple system atrophy. PLoS One, 2015, 10:E0139773.
[10] Kim HJ, Jeon BS, Kim YE, Kim JY, Kim YK, Sohn CH, Yun JY, Jeon S, Lee JM, Lee JY. Clinical and imaging characteristics of dementia in multiple system atrophy. Parkinsonism Relat Disord, 2013, 19:617-621.
[11] Auzou N, Dujardin K, Biundo R, Foubert-Samier A, Barth C, Duval F, Tison F, Defebvre L, Antonini A, Meissner WG. Diagnosing dementia in multiple system atrophy by applying Movement Disorder Society diagnostic criteria for Parkinson's disease dementia. Parkinsonism Relat Disord, 2015, 21:1273-1277.
[12] McCann H, Stevens CH, Cartwright H, Halliday GM. α-Synucleinopathy phenotypes. Parkinsonism Relat Disord, 2014, 20 Suppl 1:62-67.
[13] Spillantini MG, Crowther RA, Jakes R, Cairns NJ, Lantos PL, Goedert M. Filamentous alpha-synuclein inclusions link multiple system atrophy with Parkinson's disease and dementia with Lewy bodies. Neurosci Lett, 1998, 251:205-208.
[14] Krishnan S, Mathuranath PS, Sarma S, Kishore A. Neuropsychological functions in progressive supranuclear palsy, multiple system atrophy and Parkinson's disease. Neurol India, 2006, 54:268-272.
[15] Siri C, Duerr S, Canesi M, Delazer M, Esselink R, Bloem BR, Gurevich T, Balas M, Giladi N, Santacruz P, Marti F, Tolosa E, Rubino A, Meco G, Poewe W, Pezzoli G, Wenning G, Antonini A. A cross-sectional multicenter study of cognitive and behavioural features in multiple system atrophy patients of the parkinsonian and cerebellar type. J Neural Transm (Vienna), 2013, 120:613-618.
[16] Li B, Jiang D, Wang X, Yang RM. Comparison study on sympathetic skin responses in Parkinson's disease and multiple system atrophy patients. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2012, 12:603-607.[李彬, 姜丹, 王训, 杨任民. 帕金森病与多系统萎缩患者交感神经皮肤反应电位的比较研究. 中国现代神经疾病杂志, 2012, 12:603-607.]

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Neuropsychological Formulation: A Clinical Casebook published

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This forward-looking book defines and illustrates the process and themes of formulation in neuropsychology and places it in the vanguard of current practice. The book explains the types of information that go into formulations, how they are gathered, and how they are synthesized into a clinically useful presentation describing psychological conditions resulting from neurological illness or injury. Cases highlight the relevance and flexibility of narrative- and diagram-based formulation methods in approaching a diverse range of issues and conditions, from decisional capacity to cultural considerations, Huntington's disease to deep dyslexia. Throughout this volume, formulation is shown as integral to treatment and rehabilitation planning alongside clinical assessment, cognitive testing, and diagnosis. Neuropsychologists, clinical psychologists and rehabilitation specialists will find Neuropsychological Formulation of critical importance not only to the literature of the field, but also to the developing role of clinical neuropsychology within healthcare systems.

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Animal Models of Neurodevelopmental Disorders published

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