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首次发病精神分裂症患者早期认知功能改变研究*

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摘要 目的:探讨首次发病精神分裂症患者早期认知功能损伤情况。**方法:**选取我院 2015 年 1 月~2016 年 1 月收治的 73 例首次发病精神分裂症患者(研究组)和 75 例健康者(对照组)作为研究对象,采用神经心理测验工具评估两组对象认知功能并进行比较。**结果:**BVMT-R 试验中研究组延迟回忆、回忆总数、3 试、2 试和 1 试得分均低于对照组,差异有统计学意义($P<0.05$)。HVLt-R 试验中研究组延迟总数、3 试和 2 试得分均低于对照组,差异有统计学意义($P<0.05$)。研究组沟槽钉板测验中利手与非利手耗时均高于对照组,连线测验中连线测验 A、颜色连线 1 及 2 完成时间均高于对照组,差异均有统计学意义($P<0.05$)。PASAT 测试中研究组尝试数和正确数均低于对照组,差异有统计学意义($P<0.05$)。WAIS-III 测试中研究组符合搜索错误数目高于对照组,而符号搜索正确数目、符号搜索总分及数字符号分数均低于对照组,差异有统计学意义($P<0.05$)。Stroop 色词测验中研究组单词总数、颜色总数和色/词总数均低于对照组,差异有统计学意义($P<0.05$)。WMS-III 测验结果组间比较差异无统计学意义($P>0.05$)。**结论:**首次发病精神分裂症患者早期认知功能广泛损伤。

关键词:精神分裂症;首次发病;认知功能

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The Changes of Neurocognitive Function in Early Stage in Patients with First-Episode Schizophrenia*

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ABSTRACT Objective: To evaluate the changes of neurocognitive function in early stage in patients with first-episode schizophrenia. **Methods:** In this study, 73 cases of patients with first-episode schizophrenia (research group) and 75 cases of health person (control group) were selected from January 2015 to January 2016 in our hospital. The neurocognitive function was evaluated by neuro-psychological testing tool and the data between two group were compared. **Results:** Scores of delayed recall, total recall, 3 trial, 2 trial and 1 trial of research group were lower than those of control group in BVMT-R test, and the difference was statistically significant ($P<0.05$). In HVLt-R test, the scores of total delay, 3 trial and 2 trial of research group were significantly lower than those of control group ($P<0.05$). The consuming time of dominant hands and subdominant hands in pegboard tasks were significantly higher in research group than in control group ($P<0.05$). Completion time of connection test A, color connection 1 and 2 in connection test of research group were significantly higher than those of control group ($P<0.05$). Attempt number and correct number in research group in PASAT test were significantly lower than in control group ($P<0.05$). Number of search errors in research group was higher than in control group, while number of search correct, search total score and digital sign score were significantly lower than in control group ($P<0.05$). Total number of words, color and color / word count in research group were lower than in control group in Stroop color word test, and the difference was statistically significant ($P<0.05$). WMS-III test results between two group had no significant difference ($P>0.05$). **Conclusion:** The neurocognitive function in early stage in patients with first-episode schizophrenia has been extensively damaged.

Key words: Schizophrenia; First-episode; Neurocognitive function

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前言

精神分裂症患者认知功能的早期改变是当前的研究热点,主要涉及执行功能、精细动作、学习和记忆、信息处理速度等内容。有研究指出,精神分裂症患者的执行功能、听觉注意、视觉注意、非语言记忆、语言记忆、智能、运动操作等功能与发病前相比均明显下降^[1]。认知功能受损后患者的生活及工作能力必然会受到严重影响。而对于年龄较低的精神分裂症患者,学业、就业及婚姻等重要事件受到的影响尤为突出^[2]。目前对精神分裂症患者早期认知功能改变的研究多集中在30岁以上人群,对30岁以下发病人群关注较少。在本次研究中选取18~30岁首次发病患者进行研究,采用神经心理测验工具对认知功能进行评估,并与健康人群进行比较。

1 资料与方法

1.1 一般资料

选取我院2015年1月~2016年1月收治的73例首次发病精神分裂症患者(研究组)和75例健康者(对照组)作为研究对象。研究组入组标准^[3]:^①按《美国精神障碍诊断与统计手册(第4版)》中的《DSM-IV-TR轴I障碍用临床定式检查》确诊为精神分裂症;^②年龄18~30岁;^③首次发作期,病程≤3年,不足量间断治疗时间<3个月,足量连续治疗时间<1个月;排除标准:^④合并头部外伤、脑器质性疾病等有临床意义的疾病;^⑤智力低下无法执行测试者;^⑥近3个月内合并酒精或药物滥用者。对照组患者为健康志愿者,通过网络及海报招募。对照组入组标准:^①年龄18~30岁;^②按《美国精神障碍诊断与统计手册(第4版)》中的《DSM-IV-TR轴I障碍用临床定式检查》排除精神分裂症,近亲无精神及神经疾病;排除标准:^④合并头部外伤、脑器质性疾病等有临床意义的疾病;^⑤智力低下无法执行测试者;^⑥近3个月内合并酒精或药物滥用者。研究组男性43例,女性30例,年龄18~29岁,平均年龄(24.05±3.51)岁,平均受教育年限(14.52±3.16)年。对照组75例,男性40例,女性35例,年龄18~30岁,平均年龄(24.12±3.48)岁,平均受教育年限(14.38±3.09)年。两组研究对象均无色弱及色盲、无口吃,视力≥4.6,利手均为右利手。两组研究对象一般资料比较差异无统计学意义(P>0.05)。研究经我院医学伦理委员会批准,研究对象入组前均签署知情同意书。

1.2 评估方法

评估工具为中文版成套神经心理测验工具^[4]:^①词汇学习与记忆:学习能力、即刻回忆词汇能力和保持能力测试工具为

霍普金斯词汇学习测验-修订版(The Hopki verbal learning test-revision, HVLTR),将12个汉语和单词呈现给被试者,即刻隐蔽词汇让被试者回忆,回忆不要求顺序,将此结果作为即刻回忆数。重复呈现3次,统计总和作为回忆总数。在呈现30min后让被试者再次回忆,作为延迟回忆数;^②视觉学习与记忆:视觉学习速率和回忆测试工具为视觉空间记忆测验(Brief Visuospatial Memory Test-revised, BVMT-R),将1张画有6幅图的卡片给患者记忆,记忆时间10s,即刻要求被试者通过记忆画图,根据相符程度评分,作为即刻回忆。重复3次上述步骤,统计总分作为回忆总数。在记忆25min后再次回忆画图,作为延迟回忆分数。保持百分比=(延迟回忆分数/2试与3试中分数高者)×100.00%;^③精细动作:测试工具为沟槽钉板测验,让被试者将金属钉置入“3×3”金属板孔中,记录利手和非利手耗时;^④信息处理和执行功能:工具为连线测验。心理能力和认知能力采用连线测验A测试,让被试者将纸上的1~25的数字尽可能快的按照升序连接,记录耗时。颜色连线1让被试者按顺序连接不同颜色的数字圆圈,记录耗时。颜色连线2同样让被试者连接圆圈,过程中连续变换数字颜色,记录耗时。知觉转换能力和习惯性反应抑制能力采用Stroop色词测验测试,通过3部分不同颜色单词刺激,最后让被试者以最快速度读出单词的颜色。心理运动、书写运动和注意力集中能力采用《韦克斯勒成人智力量表(第三版)》(Wechsler Adult Intelligence Scale (Third Edition), WAIS-III)数字符号测试,让被试者参照视觉匹配数字和符号,120s内画正确数为分数。WAIS-III符号搜索让被试者匹配目标符号和靶符号,限时120s。符号搜索总分=正确数-错误数;^⑤工作记忆和信息处理:工具为《韦克斯勒记忆量表(第三版)》(Wechsler Memory Scale (Third Edition), WMS-III),让被试者顺序和反序操作两个相同长度的数字序列,分别作为顺行空间和逆行空间广度评分及总分;^⑥听觉:工具为定步调听觉连续加法测验(Paced Auditory Serial Addition Test, PASAT),通过录音带呈现随机数字,并要求被试者运算加法,记录尝试数和正确数。

1.3 统计学方法

计量资料采用均数±标准差($\bar{x} \pm s$)表示,并采用独立样本t检验,P<0.05时差异有统计学意义。

2 结果

2.1 两组患者BVMT-R结果对比

研究组延迟回忆、回忆总数、3试、2试和1试得分均低于对照组,差异有统计学意义(P<0.05)(表1)。

表1 两组患者BVMT-R结果对比(分, $\bar{x} \pm s$)

Table 1 Comparison of BVMT-R between two group (score, $\bar{x} \pm s$)

Groups	Cases (n)	Delayed recall	Total recalls	3 trial	2 trial	1 trial	Holding percentage (%)
Research group	73	8.09±3.38	20.12±7.83	8.80±3.17	7.05±3.08	4.33±2.42	92.12±27.04
Control group	75	10.93±1.27	27.41±4.89	10.98±1.39	9.75±2.04	6.52±2.47	99.06±19.67
T		6.731	6.772	5.393	6.270	5.447	1.782
P		<0.05	<0.05	<0.05	<0.05	<0.05	>0.05

2.2 两组患者 HVLT-R 结果对比

统计学意义($P<0.05$)(表 2)。

研究组延迟总数、3 试和 2 试得分均低于对照组, 差异有

表 2 两组患者 HVLT-R 结果对比(分, $\bar{x}\pm s$)Table 2 Comparison of HVLT-R between two group(scores, $\bar{x}\pm s$)

Groups	Cases (n)	Total delays	3 trial	2 trial	1 trial
Research group	73	7.69 $\pm$ 2.15	8.82 $\pm$ 1.89	8.07 $\pm$ 1.77	5.98 $\pm$ 2.83
Control group	75	9.15 $\pm$ 1.73	10.53 $\pm$ 1.14	9.52 $\pm$ 1.61	7.17 $\pm$ 1.76
T		4.557	6.643	5.216	1.776
P		<0.05	<0.05	<0.05	>0.05

2.3 两组患者沟槽钉板测验与连线测验结果对比

连线测验中连线测验 A、颜色连线 1 及 2 完成时间均高于对照

研究组沟槽钉板测验中利手与非利手耗时均高于对照组, 组, 差异均有统计学意义($P<0.05$)(表 3)。表 3 两组患者沟槽钉板测验与连线测验结果对比($s, \bar{x}\pm s$)Table 3 Comparison of pegboard tasks and connection test between two groups($s, \bar{x}\pm s$)

Groups	Cases(n)	Dominant hands	Subdominant hands	Completion time for connection test a	Time for color connection 1	Time for color connection 2
Research group	73	85.03 $\pm$ 30.82	96.86 $\pm$ 41.25	51.18 $\pm$ 27.42	53.26 $\pm$ 25.95	116.83 $\pm$ 51.37
Control group	75	59.16 $\pm$ 7.38	67.09 $\pm$ 10.82	27.34 $\pm$ 8.43	29.93 $\pm$ 9.46	66.09 $\pm$ 15.52
T		6.980	5.970	7.109	7.228	8.088
P		<0.05	<0.05	<0.05	<0.05	<0.05

2.4 两组患者 PASAT 结果对比

异有统计学意义($P<0.05$)(表 4)。

PASAT 测试中研究组尝试数和正确数均低于对照组, 差

表 4 两组患者 PASAT 结果对比(个, $\bar{x}\pm s$)Table 4 Comparison of PASAT between two groups(times, $\bar{x}\pm s$)

Groups	Cases(n)	Trials	Corrections
Research group	73	35.87 $\pm$ 9.34	31.53 $\pm$ 11.21
Control group	75	46.27 $\pm$ 3.58	44.80 $\pm$ 5.14
T		8.899	9.215
P		<0.05	<0.05

2.5 两组患者 WAIS-III 结果对比

目、符号搜索总分及数字符号分数均低于对照组, 差异有统计

研究组符合搜索错误数目高于对照组, 而符号搜索正确数 学意义($P<0.05$)。见表 5。表 5 两组患者 WAIS-III 结果对比(个, $\bar{x}\pm s$)Table 5 Comparison of WAIS-III between two groups(times, $\bar{x}\pm s$)

Groups	Cases(n)	Search errors	Search corrections	Search total score (scores)	Digital sign score (scores)
Research groups	73	2.18 $\pm$ 1.72	29.52 $\pm$ 8.57	27.14 $\pm$ 10.12	60.83 $\pm$ 14.96
Control groups	75	0.93 $\pm$ 1.62	45.78 $\pm$ 7.85	45.89 $\pm$ 8.09	90.34 $\pm$ 10.91
T		4.552	12.042	12.467	13.681
P		<0.05	<0.05	<0.05	<0.05

2.6 两组患者 Stroop 色词测验结果对比

研究组单词总数、颜色总数和色 / 词总数均低于对照组, 差异有统计学意义($P<0.05$)(表 6)。

2.7 两组患者 WMS-III 测验结果对比

逆行、顺行及总分组间比较差异无统计学意义($P>0.05$)(表 7)。

表 6 两组患者 Stroop 色词测验结果对比($\bar{x} \pm s$)
Table 6 Comparison of Stroop color word test between two groups($\bar{x} \pm s$)

Groups	Cases(n)	Total words	Total colors	Total colors and words
Research groups	73	83.21± 16.47	56.25± 14.08	33.06± 10.42
Control groups	75	102.65± 15.46	75.59± 14.06	43.89± 9.76
T		7.406	8.360	6.528
P		<0.05	<0.05	<0.05

表 7 两组患者 WMS-III 测验结果对比($\bar{x} \pm s$)
Table 7 Comparison of WMS-III between two group($\bar{x} \pm s$)

Groups	Cases(n)	Retrograde motion	Total points	Direct motion
Research groups	73	7.65± 2.13	16.03± 3.48	8.49± 1.98
Control groups	75	8.04± 1.98	17.01± 3.15	8.74± 1.82
T		1.262	1.797	0.800
P		>0.05	>0.05	>0.05

3 讨论

有研究指出,认知功能受损后生活及社会功能均有不同程度下降,对患者的负面影响极大^[5]。Graham^[6]等的研究指出,精神分裂症患者多伴有不同程度的认知功能下降。目前关于精神分裂症患者认知功能损伤的研究较多,但多集中在 30 岁以上人群,对 30 岁以下人群的关注较少。而 30 岁之前是人生各方面发展成熟的关键时期,学业、事业、婚姻及后代等重大事件多发生在该时期。因此,了解该时期精神分裂症患者认知功能改变情况有着重要意义。本次研究选取 18~30 岁首次发病精神分裂症患者作为研究对象。

词汇、视觉的学习与记忆功能是认知功能的重要内容。本次研究中,BVMT-R 试验研究组延迟回忆、回忆总数、3 试、2 试和 1 试得分均低于对照组,差异有统计学意义($P<0.05$)。同时,HVLT-R 试验中研究组延迟总数、3 试和 2 试得分也均低于对照组,差异有统计学意义($P<0.05$)。这表明 18~30 岁首次发病精神分裂症患者的词汇、视觉的学习与记忆功能均明显受损,该结论与国外文献报道结论一致^[7]。陈大春^[8]等的研究指出,首次发病精神分裂症患者的学习记忆功能与信息检索和编码能力紧密相关,信息检索和编码能力下降后学习记忆功能也随之下降。还有研究认为,学习记忆功能的下降和患者颞叶结构的改变有一定关系^[9]。

执行功能是认知功能的另一要素,是个体完成任务时认知神经功能协调与否的具体体现。del^[10]等的研究认为,良好的执行功能要求个体以优化、灵活和协同的加工过程完成特定任务。本次研究中,研究组在连线测验中连线测验 A、颜色连线 1 及 2 完成时间均高于对照组,差异均有统计学意义($P<0.05$)。而 Stroop 色词测验中研究组单词总数、颜色总数和色/词总数均低于对照组,差异有统计学意义($P<0.05$)。该结果表明首次发病精神分裂症患者的执行功能下降显著,与国内外文献报道结论相符^[11]。但目前对执行功能障碍隶属范围的划分仍有争议。有研究认为执行功能障碍是一般神经心理功能受损的范畴^[12]。也有研究认为是认知障碍中独立的损伤维度^[13]。

有研究认为,精神分裂症患者精细动作受损,本次研究结果也证实了该结论^[14]。研究结果显示研究组沟槽钉板测验中利手与非利手耗时均高于对照组,差异均有统计学意义($P<0.05$)。精细动作主要考察眼手协调速度和能力,精细动作受损表明患者动作完成存在障碍。精神分裂症患者抗干扰能力、注意力集中能力下降已是共识。有研究指出,认知形成、抗干扰、注意力集中等能力的下降对患者信息处理能力有极大影响^[15-17]。进一步的研究发现,精神分裂症患者的病前智能状况和发病后信息处理速度的下降相关^[18,19]。本次研究中研究组连线测试、PASAT 测试、WAIS-III 测试和 Stroop 色词测验结果均较对照组差,表明首次发病精神分裂症患者信息处理能力明显下降,这与 Wu^[20]等的研究结论一致。

研究已证实,信息处理能力和精细动作属皮质下神经认知功能,而执行功能、视觉和言语记忆能力属大脑皮质认知功能。因此,结合本次研究结果可认为 18~30 岁首次发病精神分裂症患者皮质和皮质下神经认知功能均受到损害。综上所述,18~30 岁首次发病精神分裂症患者早期认知功能广泛损伤。本次研究作为横断面研究存在一定局限,如对认知功能受损的规律、特异性指标等尚未涉及,有待进一步研究。

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