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间歇性外斜视患儿的注意跟踪能力异常 *

周丽琴[1,2] 左真涛[1] 王 静[3] 傅 涛[3]** 陈 霖[1,2,4]**

([1] 中国科学院生物物理研究所，脑与认知科学国家重点实验室，北京 100101；[2] 中国科学院大学，北京 100049；
[3] 首都医科大学附属北京同仁医院，北京同仁眼科中心，北京市眼科学与视觉科学重点实验室，北京 100730；
[4] 中国科学院脑科学卓越创新中心，上海 200031)

摘要 间歇性外斜视是儿童眼科的常见疾病之一，也是目前眼科学研究的热点领域之一．本研究使用多物体跟踪实验范式，系统考察了间歇性外斜视儿童，相对于弱视儿童以及正常对照儿童，注意的容量是否存在异常．实验结果发现间歇性外斜视儿童和弱视儿童的注意跟踪能力都显著地差于正常对照儿童，而且间歇性外斜视儿童和弱视儿童的跟踪成绩基本没有差别，他们的注意跟踪功能的受损程度相近．本研究首次报道了间歇性外斜视儿童注意能力的行为异常，对进一步研究间歇性外斜视的发病机理和早期临床诊断具有潜在的参考意义．

关键词 间歇性外斜视，弱视，注意跟踪，运动
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斜视是常见的眼科疾病之一，多发于儿童期，病因复杂．全球范围内流行病学的调查研究发现，弱视和斜视在人群中的患病率平均分别为 2.2%和 2.8%[1–5]．中国最新的流行病学调查研究也发现，中国东部地区学龄前儿童以及中国中部地区初中生的弱视患病率分别为 1.2%和 2.5%，令人吃惊的是，斜视患病率分别高达 5.65%和 5.0%[6–7]，远高于国外同类调查研究的结果，但原因目前尚不清楚．其中，最常见的斜视类型是间歇性外斜视(intermittent exotropia，IXT)，分别占 57.81%和 77.8%．间歇性外斜视患者表现出间歇性眼位偏斜、伴有异常视网膜对应，融合功能减弱，并且在显斜期伴有较差的立体视觉[8]．如果不及时治疗和干预，间歇性外斜视可能发展为恒定性外斜视．另外，间歇性外斜视患者会无意识地抑制一只眼睛以保持正常视觉，这种斜视早期的抑制可能会进而发展成弱视[9–13]．不同于其他类型的斜视，间歇性外斜视一般发病较早，患儿早期临床特征不明显，显斜期通常间歇出现，甚至在很长一段时期内仍可维持正常眼位和双眼视功能，临床特征具有随年龄增长逐步发展的特点．这些因素都给间歇性外斜视的早期发现带来困难，容易延误最适宜的治疗和干预时机．除如立体视觉、融合功能等眼科学指标异常之外，Mohney 及其同事发现，外斜视儿童，特别是间歇性外斜视儿童，相对于正常控制组，具有更高的风险在早期成年期发展出多种精神疾病[14–15]．而且他们进一步的研究发现，手术矫正治疗，不管成功与否，并不能降低该风险[16]．这提示间歇性外斜患儿可能还伴有中枢神经系统的异常．因此，间歇性外斜视成为目前眼科学研究的热点领域之一．

但目前关于间歇性外斜视的中枢神经系统功能异常的研究很少，大多数的研究集中在恒定性外斜视或者斜视性弱视的研究上．例如，动物电生理的研究发现斜视引起早期视觉皮层或皮层下结构的功能异常[17–23]．基于体素的形态测量方法(voxel-based morphometry，VBM)和弥散张量成像(diffusion tensor imaging，DTI)等结构脑成像的研究发现，斜

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** 通讯联系人.
傅 涛. E-mail: taofu@ccmu.edu.cn
陈 霖. Tel: 010-64888565, E-mail: linchen@bcslab.ibp.ac.cn
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视患者除枕叶外，大脑的背侧通路(包括后顶叶、前额区等)也存在结构异常[24-25]．斜视性弱视的行为研究也发现，斜视性弱视患者表现出对视觉物体数量的低估[26]，注意瞬脱效应的延长[27]，以及多物体跟踪能力的下降[28]．这些研究表明，除枕叶外，斜视性弱视患者的后顶叶皮层，即负责这些认知功能的关键脑区，也可能存在功能异常[29-31]．功能磁共振成像(functional magnetic imaging，fMRI)的研究结果也验证了这一假设：在完成多物体跟踪任务时，斜视性弱视患者的顶内沟和额眼区的激活明显降低[32]．

如上所述，这些研究主要集中在斜视性弱视患者，或是恒定性外斜视患者中，尚缺乏对在病程上处于更早期阶段的间歇性外斜视患者的直接研究．因此，本研究拟利用多物体跟踪实验范式，初步探讨间歇性外斜视患儿(尚未发展为恒定性外斜视或弱视)是否已经存在注意等认知功能的异常．

1 材料与方法

1.1 受试

所有受试均来自北京同仁医院眼科门诊，由作者傅涛诊断．

本实验收集间歇性外斜视患者27例(15男12女)，年龄7.5～13.0岁，平均(9.5±1.57)岁，外斜度数(13.4±3.45) Δ(三棱镜6 m)，最佳矫正远视力(best-corrected distant visual acuity，BCDVA)为(1.01±0.08) lg*MAR*，屈光度为(−2.13±1.98) *D*．所有间歇性外斜视患者都不伴随弱视症状，并且都在眼正位时进行实验．

收集年龄匹配的弱视患者28例(20男8女)，年龄7.0～13.0岁，平均(9.4±1.95)岁，BCDVA为(0.74±0.37) lg*MAR*，屈光度为(0.78±4.22) *D*．所有弱视患者均无动眼神经功能障碍，眼位正常无偏斜．

随机收集眼位及矫正视力正常的年龄匹配[7.0～11.5岁，平均(9.5±1.56)岁]一般近视儿童23例(11男12女)作为正常对照组，BCDVA为(1.00±0.06) lg*MAR*，屈光度为(−2.15±1.46) *D*．

本研究严格按照首都医科大学附属北京同仁医院伦理委员会的要求进行．所有受试的法定监护人均在实验前签署了知情同意书．

Table 1 Clinical diagnostic data of three group

Patient		IXT	Amblyopia	Control
Sex		15 males, 12 females	20 males, 8 females	11 males, 12 females
Age (years)		9.54±1.57	9.41±1.95	9.52±1.56
Diopter (*D*)		−2.13±1.98	0.78±4.22	−2.15±1.46
BCDVA (lg*MAR*)		1.01±0.08	0.74±0.37	1.00±0.06
BCNVA (lg*MAR*)		1.11±0.15	0.76±0.34	1.08±0.16
Ocular position (Δ) (33 cm)		X(T) −9.81±7.41 Δ	0 abnormal	0 abnormal
Ocular position (Δ) (6 m)		X(T) −13.40±3.45 Δ	0 abnormal	0 abnormal
Worth four-dot test	Near (33 cm)	12 fusion, 4 suppression, 10 diplopia	15 fusion, 7 suppression, 5 diplopia	22 fusion, 0 suppression, 1 diplopia
	Distance (6 m)	7 fusion, 14 suppression, 4 diplopia	7 fusion, 18 suppression, 2 diplopia	14 fusion, 7 suppression, 2 diplopia
Stereoacuity		12 normal, 14 abnormal	4 normal, 23 abnormal	21 normal, 2 abnormal

BCDVA: Best-corrected distant visual acuity. Tested by the standard logarithmic vision chart. BCNVA: Best-corrected near visual acuity. Tested by the Regan 96% contrast letter chart. Stereoacuity: >60 s of arc by TNO stereotest means abnormal near stereopsis.

1.2 设备与刺激

所有刺激图形呈现在显示屏(MacBook Pro)上，屏幕大小29.16°×21.87°，刷新频率为60 Hz．屏幕背景为黑色(0.11 cd/m^2)．注视点是绿色圆点(CIE chromaticity coordinates and luminance value: x = 0.31，y = 0.63；45.67 cd/m^2)，大小为0.06°．刺激图形是灰色圆盘(18.74 cd/m^2)，大小为1.71°．实验过程中，受试双眼到屏幕的距离约为60 cm．

1.3 实验流程

实验使用经典的多物体跟踪范式[33]．如图1所

示，在每个试次的最开始，屏幕上先呈现 8 个灰色圆盘，位置随机，并且任意 2 个圆盘中心之间的距离均大于 2.28°．受试需要盯住呈现在屏幕中央的注视点，然后示意主试启动正式测试．在提示阶段，其中的 1～4 个圆盘闪烁 2.4 s，以提示它们是受试需要跟踪的目标．提示完成后，所有的圆盘以 1.83°/s～2.74°/s 的速度在屏幕上以任意轨迹随机运动．圆盘的随机运动满足如下限制条件：a．圆盘在运动过程中永远不会重叠，最小距离为 2.28°；b．物体运动边界距屏幕边缘 1.42°，当圆盘运动到运动边界时，会以随机角度弹回．整个运动过程持续 8 s，运动结束后所有的圆盘都停下并一直呈现在屏幕上．受试被要求在整个测试过程中把目光盯在注视点上，跟踪指定的目标图形，并在圆盘停下后指出哪些圆盘是最开始提示的圆盘，由主试点击鼠标进行记录．受试被告知本试次正确的目标总个数，并被鼓励尽可能选出所有目标．

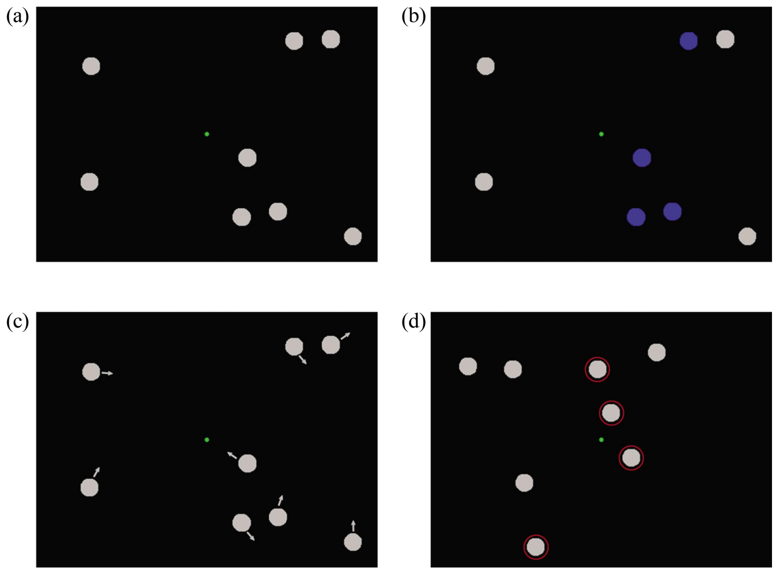

Fig. 1 Illustration of the procedure of the experiment

(a) Initial phase. 8 disks were presented on the screen. (b) Cuing phase. One to four randomly selected disks blinked for 2.4 s to indicate their status as targets. The blue color indicates that an item blinked, designating a target, at the beginning of each trial. (c) Motion phase. All eight disks moved linearly in an independent and random manner with the restriction that no overlap or occlusion was allowed for the items during their motion. The velocities of the moving items was 1.83°/s～2.74°/s. (d) Target selection. Subjects were instructed to track the four targets attentively, and pointed out these targets at the end of each trial.

本研究中，需要跟踪的目标个数分为 1、2、3 或 4 等 4 种条件．正式实验之前有 4 个练习试次，每个条件各练习 1 次．正式实验包含 40 个试次，每个条件 10 个试次，所有条件随机打乱．整个实验过程持续 13～18 min．

1.4 结果计算

同以往的研究类似[28]，每个条件下校正猜测率后的跟踪正确率按如下公式计算：

$$跟踪正确率 = 100*(c-n/t)/(1-n/t)$$

其中，未经校正的原始的正确跟踪比例(c)，n 是需要跟踪的目标个数(1，2，3 或 4)，t 是圆盘总数(本研究中是 8 个)．

2 实验结果

统计分析使用的是 SPSS 22(SPSS Inc., Chicago, IL，USA)，首先对 3 组受试的年龄和性别分别进行单因素方差分析(analysis of variance，ANOVA)．结果表明，3 组受试在年龄 ($F(2, 75) = 0.04$，$P > 0.95$)和性别($F(2, 75) = 1.56$，$P > 0.22$)两个因素上都没有显著性差别．

然后，对跟踪正确率进行 3×4 的混合 ANOVA 分析，受试类型是组间因素(三水平：间歇性外斜视组，弱视组，正常对照组)，跟踪目标个数为组内因素(四水平：1，2，3，4)．分析结果发现，跟

踪目标个数($F(3，225) = 49.26$，$P < 0.001$，$\eta^2 = 0.40$)和受试类型($F(2，75) = 3.47$，$P = 0.036$，$\eta^2 = 0.09$)的主效应都显著，但两者之间的交互作用不显著($F(6，225) = 1.857$，$P = 0.111$，$\eta^2 = 0.05$)．对跟踪个数进行进一步的配对 t 检验发现，与以往研究类似[28, 34-35]，跟踪个数 1 和 2 时，跟踪成绩没有显著差异($t(77) = 1.23$，$P = 0.224$)．但是当跟踪个数为 3 或 4 时，则相对跟踪 1 个目标时的成绩有显著下降(1 vs.3: $t(77)=4.52$，$P = 0.000$；1 vs.4: $t(77)= 8.85$，$P = 0.000$)，并且相对于目标个数为 2 时的跟踪成绩也显著性更差(2 vs.3: $t(77) = 5.08$，$P = 0.000$；2 vs.4: $t(77) = 10.62$，$P = 0.0000$)．跟踪个数为 4 时的成绩，也显著低于跟踪 3 个目标时的成绩 ($t(77) = 6.63$，$P = 0.000$)．对受试类型进行独立 t 检验发现，间歇性外斜视组($t(38) =-2.92$，$P = 0.006$)和弱视组($t(49) =-2.18$，$P = 0.034$)的跟踪成绩都显著低于正常对照组，但间歇性外斜视组和弱视组之间没有差别($t(53) =-0.49$，$P = 0.624$)．

接下来分别对各跟踪个数下的受试类型作组间单因素 ANOVA，发现当跟踪目标个数为 1 或 2 时，受试类型的主效应不显著(跟踪个数为 1 时，$F(2，75) = 2.14$，$P = 0.124$，$\eta^2 = 0.05$；跟踪个数为 2 时，$F(2，75) = 0.61$，$P = 0.545$，$\eta^2 = 0.02$)．当跟踪目标个数为 3 时，受试类型的主效应边缘显著($F(2，75) = 2.50$，$P = 0.089$，$\eta^2 = 0.063$)．对此条件进行进一步的独立 t 检验发现，间歇性外斜视组和弱视组的成绩均显著差于正常对照组($t(48) = -2.32$，$P = 0.025$；$t(49) = -2.01$，$P = 0.05$)，而间歇性外斜视组和弱视组之间没有差异($t(53) = 0.10$，$P = 0.921$)．当跟踪目标个数为 4 时，受试类型的主效应显著($F(2，75) = 3.97$，$P = 0.023$，$\eta^2 = 0.096$)，表现为间歇性外斜视组和弱视组的成绩都显著差于正常对照组($t(48) = -2.94$，$P = 0.005$；$t(49) = -2.33$，$P = 0.024$)，间歇性外斜视组和弱视组之间没有差异($t(53) = -0.54$，$P = 0.593$)．

以跟踪正确率为因变量，跟踪目标个数为自变量作逻辑曲线拟合．间歇性外斜视组、弱视组和正常对照组的拟合结果如图 3．图中的水平虚线为 75%成绩水平．间歇性外斜视组、弱视组和正常对照组在 75%正确率水平的平均跟踪个数分别是 4.18、4.34、5.35．拟合结果再一次表明间歇性外斜视患儿和弱视患儿的注意跟踪能力受损，他们在 75%正确率水平的跟踪容量小于正常儿童．相对于正常儿童，他们在目标个数超过 2 时有明显的跟踪障碍，并且差距随目标个数增加明显增大．但是间歇性外斜视组和弱视组的跟踪成绩基本没有差别，他们的注意跟踪功能的受损程度不相上下．

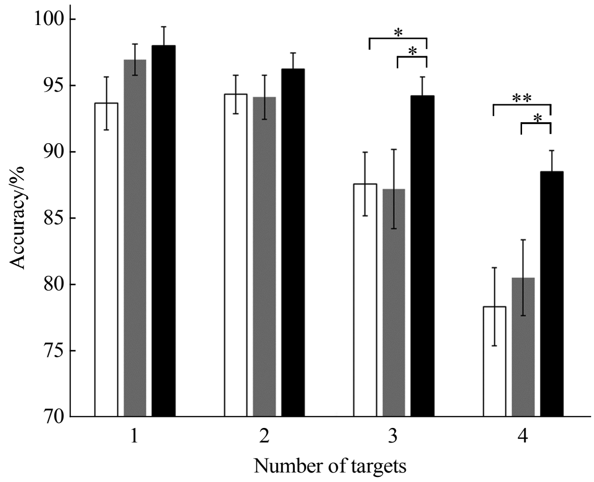

Fig. 2　Group corrected accuracy means on the multiple-object tracking task

The corrected-for-guessing accuracy means for IXT, amblyopia and control group. Main effects of group and target number are significant. *$P < 0.05$; **$P < 0.01$. □: IXT; ▩: Amblyopia; ■: Control.

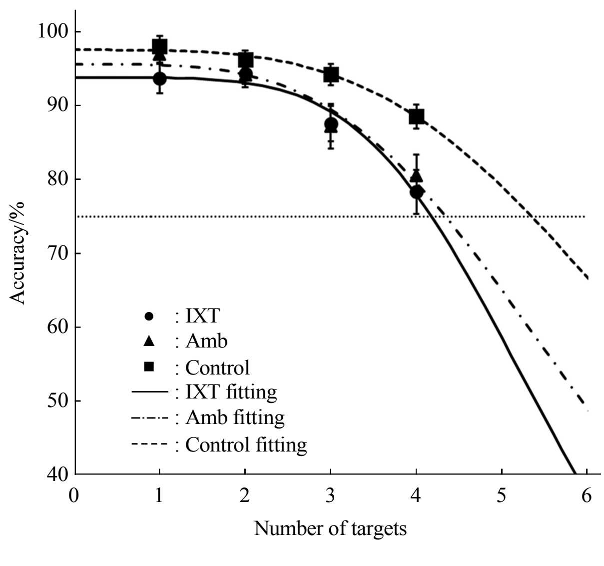

Fig. 3　Logistic curve fitting to the corrected-for-guessing accuracy means obtained from the experiment

Logistic curves were fitting to the data for IXT, amblyopia,and control group. The graph depicts corrected-for guessing accuracy means plotted against number of targets tracked. The horizontal dotted line represents performance at a 75% accuracy level. The number of targets tracked at this level is 4.18, 4.34, 5.35 for, respectively, IXT, amblyopia and control group. Accuracy for all subjects declines as the number of targets increases, when the number of targets is larger than 2. The IXT patients and amblyopic patients perform worse than control subjects once the number of targets surpasses 2. And the departure from control performance, increases as the number of balls tracked increases.

3 讨 论

本研究系统地考察了间歇性外斜视儿童，相对于弱视儿童以及正常健康对照儿童，在多物体跟踪能力上的差别．结果发现，3 组儿童的跟踪成绩都随着跟踪目标个数的增加而逐渐降低，但间歇性外斜视组和弱视组的跟踪成绩在跟踪目标个数为 3 和 4 时都表现出更显著的降低．当跟踪目标个数为 1 或 2 时，尽管间歇性外斜视组的跟踪成绩也表现出下降趋势，但没有达到统计上的显著性，一个可能的原因是因为天花板效应的存在．这一发现表明，间歇性外斜视患儿，虽然没有发展为弱视或恒定性外斜视，已经出现多物体注意跟踪能力的下降，即使是在他们的眼位处于正常状态时也如此．

该结果表明，间歇性外斜视患儿已经具有注意方面的认知功能异常或障碍．以往关于斜视的脑成像研究发现，斜视病例存在后顶叶、前额区等注意相关脑区的结构异常[24-25]．因此，进一步的研究可以考察间歇性外斜视患儿是否也同样具有注意相关的脑区异常．因为注意是人脑重要的基础认知功能之一，同时也是实现大脑其他重要认知功能的基础，所以这方面的研究将为临床间歇性外斜视注意功能的康复提供重要参考．

本研究首次报道了尚未发展为恒定性外斜视或弱视的间歇性外斜视患儿已经存在注意认知功能的异常，对间歇性外斜视的早期临床诊断具有潜在的参考意义．

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Abnormal Attentive Tracking in Children With Intermittent Exotropia*

ZHOU Li-Qin[1,2], ZUO Zhen-Tao[1], WANG Jing[3], FU Tao[3]**, CHEN Lin[1,2,4]**

([1] *Key Laboratory of Brain and Cognitive Science, Institute of Biophysics, Chinese Academy of Sciences, Beijing* 100101, China;
[2] *University of Chinese Academy of Sciences, Beijing* 100049, China;
[3] *Beijing Tongren Eye Centre, Beijing Tongren Hospital, Capital Medical University, Beijing Ophthalmology and Visual Science Key Laboratory, Beijing* 100730, China;
[4] *The Innovation Center of Excellence on Brain Science, Chinese Academy of Sciences, Shanghai* 200031, China)

Abstract Intermittent exotropia is a common pediatric ocular disease, which is also a hot research area in ophthalmology. In this study, we tested the tracking ability of children with intermittent exotropia using multiple object tracking (MOT) paradigm, and compared with amblyopic children and normal children. The experimental results showed that the tracking capacity of children whether with intermittent exotropia or amblyopia was significantly decreased as compared with normal children, and children with intermittent exotropia suffers the same degree of damage with children with amblyopia. It is the first report of the abnormal attentive ability of children with intermittent exotropia, which may be beneficial to future research of pathogenesis and early diagnosis of the disease.

Key words intermittent exotropia, amblyopia, attentive tracking, motion
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**Corresponding author.
FU Tao. E-mail: taofu@ccmu.edu.cn
CHEN Lin. Tel: 86-10-64888565, E-mail: linchen@bcslab.ibp.ac.cn

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