

· 临床研究 ·

婴儿期条栅视力与3岁神经发育的前瞻性队列研究

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[摘要] 目的: 探究婴儿期条栅视力与3岁神经发育的关联。方法: 采用前瞻性队列研究设计, 纳入2016年8月—2019年6月在江苏出生队列中招募的1 096个家庭的1 122例儿童。在1岁时, 使用Teller视力卡Ⅱ测量条栅视力。在3岁时, 使用贝利婴幼儿发育量表筛查测试-第3版评估儿童的神经发育情况, 包括认知能力、语言理解、语言表达、精细运动和大运动5个维度。运用泊松回归分析两者的关联。结果: 在1 122例儿童中, 94例(8.4%)出现条栅视力异常。5个维度神经发育欠佳的发生率在3.5%~10.3%。相比条栅视力正常组, 婴儿期条栅视力异常组3岁大运动发育欠佳的风险增加96%(RR=1.96, 95% CI: 1.03~3.70)。排除双胞胎、早产儿、低出生体重儿及辅助生殖受孕出生的儿童后, 该关联仍然显著。结论: 婴儿期条栅视力异常与3岁神经发育的大运动维度发育欠佳风险增加相关。

[关键词] 条栅视力; 神经发育; 认知; 语言理解; 语言表达; 精细运动; 大运动

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Association between infant visual acuity and neurodevelopment at three years of age: a prospective cohort study

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[Abstract] **Objective:** To explore the association between infant visual acuity and neurodevelopment at 3 years of age. **Methods:** We employed a prospective cohort study design. A total of 1 122 children from 1 096 families enrolled in the Jiangsu Birth Cohort between August 2016 and June 2019 were included. At 1 year of age, visual acuity was measured using the Teller Acuity Card II. At 3 years of age, neurodevelopmental status was assessed using the Bayley Scales of Infant and Toddler Development, Version III Screening Test, covering five domains: cognition, receptive communication, expressive communication, fine motor, and gross motor. Poisson regression models were used to examine the associations between infant visual acuity and neurodevelopment at 3 years of age. **Results:** Among the 1 122 children, 94 (8.4%) showed abnormal visual acuity. The prevalence of noncompetent neurodevelopment across five domains ranged from 3.5% to 10.3%. Compared with the group with normal visual acuity in infancy, the group with abnormal visual acuity had a 96% increased risk of being noncompetent development in gross motor domain at age 3 (RR=1.96, 95% CI 1.03–3.70). This association remained stable after excluding twins, preterm infants, low birth weight infants and children conceived via assisted reproductive technology. **Conclusion:** Abnormal visual acuity in infancy was associated with an increased risk of being noncompetent in gross motor development at 3 years of age.

[Key words] visual acuity; neurodevelopment; cognitive; receptive communication; expressive communication; fine motor; gross motor

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神经发育迟缓是目前全球范围内日益严重的儿童健康问题,患病率约为10%且呈持续上升趋势。2023年一项针对我国多地区178 235名儿童的横断面研究发现,1~36个月龄儿童存在神经发育迟缓的患病率为12.5%^[1]。早期神经发育迟缓会对个体的健康状况和功能发展造成长期负面影响,包括注意力不集中、自尊心受损、破坏性行为、体力活动参与不足及久坐行为增加等,这会进一步增加超重和肥胖等不良健康结局的风险^[2-4]。因此,有必要进一步关注神经发育迟缓的影响因素,尤其是生命早期的可识别、可干预因素,为早期预警和精准干预做好准备。既往研究发现多种因素与神经发育迟缓有关,主要集中在出生前因素,例如母亲妊娠疾病、不良环境暴露和不良出生结局等^[5-7]。尽管这些研究为理解神经发育迟缓病因提供了珍贵线索,但关于出生后因素对神经发育的影响研究较少。

视力是视觉功能的重要组成部分,也是获取外部信息的主要途径^[8]。视力异常在我国呈现低龄化趋势,其对随后的身心健康影响需予以更多重视。婴幼儿出生后1年,视力发育逐步稳定,是早期评估视力的关键且稳定的时期。然而,1岁婴幼儿难以配合常规视力检查,可用的定量评估方法有限。条栅视力检查基于优先注视原理,操作简便、结果可量化,在国际上已广泛用于婴儿临床视力评估^[9]。3岁前的大脑具有较强的可塑性,对外界刺激和经验输入较为敏感^[10]。研究发现,视力异常与青春期认知表现欠佳相关,还可能增加抑郁症发病风险^[11-12]。然而,现有研究多聚焦于学龄期至青春期^[13-14]。对于生命早期视力与神经发育之间的关联研究仍然有限。

鉴于此,本课题组开展了一项前瞻性队列研究,旨在探讨婴儿期条栅视力与3岁神经发育的关联,以期改善婴幼儿神经发育情况提供新的思路。

1 对象和方法

1.1 对象

本研究基于江苏出生队列,采用前瞻性队列研究设计,由南京医科大学附属妇产医院于2016年8月—2019年6月招募参与者。研究对象入选标准为:①分娩结局为活产的单双胎妊娠孕妇;②儿童参与1岁时随访;③儿童参与3岁时随访。排除标准为:①1岁随访时间不在(12±1)个月或未能完成右眼条栅视力检查;②3岁随访时间不在(35.0~36.5)个月或未能配合完成贝利婴幼儿发育量表筛查测试-第3版(Bayley scales of infant and toddler devel-

opment, version III screening test, BSID-III)评估。在研究期间,共有1 158个家庭符合纳入标准,其中,因1岁随访时间不在(12±1)个月排除32个家庭,因未完成右眼条栅视力检查排除28个家庭,因3岁随访时间不在35.0~36.5个月排除2个家庭,最终共有1 096个家庭及其1 122例子代纳入分析。所有参与者签署知情同意书,本研究经获得南京医科大学伦理委员会批准[NJMUIRB(2014)248]。

1.2 方法

1.2.1 条栅视力

在儿童1岁时,通过电话方式邀请其至南京医科大学附属妇产医院参加随访。在主要抚养人的陪同下,由经统一培训的专业眼科医生依据使用Teller视力卡(Teller acuity cards II, TAC II)对儿童进行条栅视力检查。TAC II视力检查是目前国际上广泛认可的评估0~36个月龄婴幼儿的首选检测方法^[15]。检查时,受试婴幼儿坐于家长腿上,与检查者相对,检查距离固定为55 cm。测试过程中将TAC II视力卡置于婴幼儿视野内,其中心与双眼高度平行。检查者在吸引婴幼儿注视前方后,持测试卡通过窥孔观察其对条栅刺激的反应,直到测试者判断出受试儿童能够看到的最细的条栅图像,记录相应的最大条栅空间频率作为条栅视力,结果以周/度(cycles per degree, cpd)表示。根据Salomão和Ventura^[9]的方法,计算了婴儿条栅视力的95%置信区间(95% confidence interval, 95% CI)的90%容差限值。低于容差下限的条栅视力测量值被认为是条栅视力异常。此外,所有受试婴幼儿均接受眼部外观检查、红光反射检查以排除可能对视力产生显著影响的其他眼部疾病。

1.2.2 神经发育

当儿童3岁时,通过电话邀请其至南京医科大学附属妇产医院进行现场随访。由经过标准化培训的执业医师,在主要照护者在场的情况下,使用BSID-III评估儿童神经发育情况,该量表具有较好的信度和效度^[16]。实施BSID-III的执业医师均不了解婴儿期视力状况。评估包括5个维度:认知能力、语言理解、语言表达、精细运动和大运动。每个维度均包含若干测试项目。儿童每完成1项任务记1分,最终得到各维度的评分。根据量表评分标准,各能区的结果可分为“存在落后风险”“边缘”和“无明显异常”3个等级。具体而言,认知0~22分、语言理解0~12分、语言表达0~14分、精细运动0~17分、大运动0~18分时,判定为“存在落后风险”;认知23~27分、

语言理解 13~20分、语言表达 15~20分、精细运动 18~22分、大运动 19~23分时,判定为“边缘”;认知 28~33分、语言理解 21~24分、语言表达 21~24分、精细运动 23~27分、大运动 24~28分时,判定为“无明显异常”。根据既往研究,在统计分析时将“存在落后风险”和“边缘”合并定义为“发育欠佳”^[17]。

1.2.3 协变量

研究考虑的协变量包括:分娩年龄(年)、胎龄(周)、视力检查年龄(日)、神经发育检查年龄(连续变量,日)、家庭年收入(<50 000元, 50 000~<100 000元, 100 000~<200 000元, ≥200 000元)、母亲受教育水平(<12年, ≥12年)、母亲孕前体重指数(body mass index, BMI)(<18.5 kg/m², 18.5~23.9 kg/m², 24.0~27.9 kg/m², ≥28.0 kg/m²)、妊娠胎数(单胎, 双胎)、妊娠期高血压疾病(慢性高血压, 妊娠期高血压, 子痫前期)、妊娠合并糖尿病(糖尿病合并妊娠, 妊娠期糖尿病)、母乳喂养时长(<6个月, 6~12个月, ≥12个月)、儿童性别(男, 女)。

1.3 统计学方法

所有统计分析均使用R语言(4.4.2版)完成。描述研究对象基本特征时,采用均数±标准差($\bar{x} \pm s$)描述符合正态分布的连续性资料,采用频数构成比 $[n(\%)]$ 描述定性资料。在组间比较中,对连续性资料采用独立样本 t 检验,对定性资料采用卡方检验。对于存在缺失的数据,采用多重插补法进行处理。考虑到双胎妊娠中同一妊娠单位内个体之间存在非独立性,在分析婴儿期条栅视力与3岁神经发育之间的关联时,采用了基于泊松回归的广义线性混合效应模型,并联合使用稳健方差估计;在排除双胎后的敏感性分析中,采用普通泊松回归模型进行分析,同样使用稳健方差估计。分析结果以相对危险度(relative risk, RR)及其95%CI进行报告。混杂因素定义为同时与暴露和结局相关且不位于潜在因果路径中的协变量。本研究进行了按性别分层分析,开展了敏感性分析以检验结果的稳定性,分别排除了双胎、早产儿、低出生体重儿及辅助生殖受孕出生的儿童。统计检验采用双侧检验, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 研究人群基本特征

本研究共纳入1 096个家庭,包括1 122例儿童。条栅视力95%CI的90%容差限值下限为3.89 cpd,其中94例(8.4%)儿童视力低于此阈值,被判定为条

栅视力异常。表1描述了条栅视力正常和异常人群的基本特征比较。两组间双胞胎率、神经发育检查年龄差异有统计学意义,条栅视力异常组的双胎比例高于正常组($P=0.006$),神经发育检查年龄低于正常组($P=0.028$)。本研究纳入人群与排除人群基本特征比较结果见表2。两组间的家庭年总收入($P=0.011$)、妊娠期高血压疾病患病率($P < 0.001$)、神经发育检查年龄($P=0.035$)的差异有统计学意义。

在1 122例儿童中,认知维度的发育欠佳率为4.6%($n=52$),语言理解维度的发育欠佳率为3.5%($n=39$),语言表达维度的发育欠佳率为4.0%($n=45$),精细运动维度的发育欠佳率为10.3%($n=116$),大运动维度的发育欠佳率为6.9%($n=77$),具体结果见表3。条栅视力异常组的大运动发育欠佳率显著高于条栅视力正常组(12.8% vs. 6.3%, $P=0.013$)。

2.2 婴儿期条栅视力与3岁神经发育的关联

表4展示了婴儿期条栅视力与3岁神经发育的关联。结果发现,与婴儿期条栅视力正常组相比,婴儿期条栅视力异常组3岁时大运动发育欠佳的风险增加,且该关联在所有模型中均具有统计学意义。具体而言,在未校正混杂因素时,与婴儿期条栅视力正常组相比,婴儿期条栅视力异常组3岁时大运动发育欠佳风险增102%(RR=2.02, 95% CI: 1.09~3.74);在调整所有协变量之后,该风险仍增加96%(RR=1.96, 95% CI: 1.03~3.70)。在认知、语言理解、语言表达及精细运动维度,婴儿期条栅视力异常与3岁神经发育欠佳之间均未观察到显著关联。

2.3 婴儿期条栅视力与3岁神经发育关联的性别分层分析

为检验婴儿期条栅视力与3岁神经发育关联是否存在性别差异,本研究进行了子代性别分层分析,结果见表5。在男孩中,与婴儿期条栅视力正常组相比,婴儿期条栅视力异常组3岁时大运动发育欠佳风险增加131%(RR=2.31, 95% CI: 1.03~5.21),在女孩中,二者未见统计学显著关联(RR=1.37, 95% CI: 0.47~4.01),但效应方向一致,且不同性别间效应差异无统计学意义(异质性 $P=0.443$)。在认知、语言理解、语言表达及精细运动维度,婴儿期条栅视力异常与3岁发育欠佳在不同性别亚组中均未见统计学显著关联,且性别分层后的组间效应无显著异质性。

2.4 婴儿期条栅视力与3岁神经发育关联的敏感性分析

为评估婴儿期条栅视力与3岁神经发育关联的稳健性,本研究进一步开展了敏感性分析,结果见

表1 研究人群基本特征
Table 1 Basic characteristics of study population

Characteristics	Control group	Abnormal visual acuity	t/χ^2	<i>P</i>
Parental characteristics	1 008	88		
Maternal age(years, $\bar{x} \pm s$)	30.36 ± 3.79	30.96 ± 3.33	-1.604	0.151
Pre-pregnancy BMI[n(%)]			1.105	0.776
<18.5 kg/m ²	144(14.3)	14(15.9)		
18.5–23.9 kg/m ²	700(69.6)	59(67.0)		
24.0–27.9 kg/m ²	124(12.3)	13(14.8)		
≥28.0 kg/m ²	38(3.8)	2(2.3)		
Household income[n(%)]			3.099	0.377
<50 000 yuan	52(5.3)	8(9.2)		
50 000–<1100 000 yuan	262(26.9)	19(21.8)		
100 000–<1200 000 yuan	455(46.7)	43(49.4)		
≥200 000 yuan	206(21.1)	17(19.5)		
Maternal education[n(%)]			0.007	0.933
<12 years	89(8.8)	7(8.0)		
≥12 years	918(91.2)	81(92.0)		
Mode of conception[n(%)]			0.001	0.999
Spontaneous	868(86.1)	76(86.4)		
ART	140(13.9)	12(13.6)		
Hypertensive disorders of pregnancy[n(%)]			–	0.197
No	976(96.8)	84(95.5)		
Chronic hypertension	7(0.7)	0(0.0)		
Gestational hypertension	10(1.0)	3(3.4)		
Preeclampsia	15(1.5)	1(1.1)		
Diabetes mellitus in pregnancy[n(%)]			–	0.503
No	734(72.8)	59(67.0)		
Diabetes complicating pregnancy	11(1.1)	1(1.1)		
Gestational diabetes mellitus	263(26.1)	28(31.8)		
Infant characteristics	1 028	94		
Sex[n(%)]			1.452	0.228
Boy	532(51.8)	42(44.7)		
Girl	496(48.2)	52(55.3)		
Plurality[n(%)]			7.476	0.006
Singleton	974(94.7)	82(87.2)		
Twins	54(5.3)	12(12.8)		
Gestational age(weeks, $\bar{x} \pm s$)	39.31 ± 1.58	39.29 ± 1.61	0.135	0.891
Preterm birth[n(%)]			0.691	0.406
No	955(92.9)	90(95.7)		
Yes	73(7.1)	4(4.3)		
Low birth weight infant[n(%)]			–	0.359
No	979(95.2)	92(97.9)		
Yes	49(4.8)	2(2.1)		
Breastfeeding duration[n(%)]			2.539	0.281
<6 months	231(22.7)	24(25.8)		
6–12 months	350(34.4)	37(39.8)		
≥12 months	437(42.9)	32(34.4)		
Age at visual acuity assessment($\bar{x} \pm s$)	364.99 ± 8.12	364.06 ± 7.05	1.208	0.283
Age at neurodevelopmental assessment($\bar{x} \pm s$)	1 095.74 ± 7.30	1 094.00 ± 7.72	2.099	0.028

Data were missing for pre-pregnancy BMI(*n*=2), household income(*n*=34), and breastfeeding duration(*n*=11). BMI: body mass index; ART: assisted reproductive technology.

表2 纳入人群与排除人群的一般特征比较

Table 2 Comparison of baseline characteristics between included and excluded participants

Characteristics	Included population	Excluded population	t/χ^2	P
Parental characteristics	1 096	62		
Maternal age (years, $\bar{x} \pm s$)	30.41 \pm 3.76	31.02 \pm 4.05	1.159	0.216
Pre-pregnancy BMI [$n(\%)$]			1.498	0.683
<18.5 kg/m ²	158(14.4)	10(16.4)		
18.5-23.9 kg/m ²	759(69.4)	38(62.3)		
24.0-27.9 kg/m ²	137(12.5)	10(16.4)		
\geq 28.0 kg/m ²	40(3.7)	3(4.9)		
Household income [$n(\%)$]			11.100	0.011
<50 000 yuan	60(5.6)	6(9.8)		
50 000-<100 000 yuan	281(26.5)	14(23.0)		
100 000-<200 000 yuan	498(46.9)	19(31.1)		
\geq 200 000 yuan	223(21.0)	22(36.1)		
Maternal education [$n(\%)$]			0.001	0.999
<12 years	96(8.8)	5(8.2)		
\geq 12 years	999(91.2)	56(91.8)		
Mode of conception [$n(\%)$]			0.001	0.999
Spontaneous	944(86.1)	53(85.5)		
ART	152(13.9)	9(14.5)		
Hypertensive disorders of pregnancy [$n(\%)$]			-	<0.001
No	1 060(96.7)	55(88.7)		
Chronic hypertension	7(0.6)	0(0.0)		
Gestational hypertension	13(1.2)	5(8.1)		
Preeclampsia	16(1.5)	2(3.2)		
Diabetes mellitus in pregnancy [$n(\%)$]			-	0.420
No	793(72.4)	49(79.0)		
Diabetes complicating pregnancy	12(1.1)	0(0.0)		
Gestational diabetes mellitus	291(26.6)	13(21.0)		
Infant characteristics	1 122	66		
Sex [$n(\%)$]			0.787	0.375
Boys	574(51.2)	38(57.6)		
Girls	548(48.8)	28(42.4)		
Plurality [$n(\%)$]			0.634	0.426
Singleton	1 056(94.1)	60(90.9)		
Twins	66(5.9)	6(9.1)		
Gestational age (weeks, $\bar{x} \pm s$)	39.31 \pm 1.58	38.98 \pm 1.63	-1.584	0.104
Preterm birth [$n(\%)$]			0.821	0.365
No	1 032(93.1)	59(89.4)		
Yes	77(6.9)	7(10.6)		
Low birth weight infant [$n(\%)$]			-	0.407
No	1 071(95.5)	61(92.4)		
Yes	51(4.5)	5(7.6)		
Breastfeeding duration [$n(\%)$]			1.921	0.383
<6 months	469(42.2)	23(35.4)		
6-12 months	255(23.0)	14(21.5)		
\geq 12 months	387(34.8)	28(43.1)		
Age at visual acuity assessment ($\bar{x} \pm s$)	364.92 \pm 8.04	365.38 \pm 7.89	0.462	0.649
Age at neurodevelopmental assessment ($\bar{x} \pm s$)	1 095.59 \pm 7.35	1 093.59 \pm 9.33	-1.712	0.035

表3 不同条栅视力状态儿童神经发育欠佳的频数分布

Table 3 Distribution of the frequency of noncompetent neurodevelopment according to visual acuity status [n(%)]

Noncompetent neurodevelopment	Total(n=1 122)	Control group(n=1 028)	Abnormal visual acuity(n=94)	χ^2	P
Cognition	52(4.6)	47(4.6)	5(5.3)	0.005	0.941
Receptive communication	39(3.5)	35(3.4)	4(4.3)	0.019	0.891
Expressive communication	45(4.0)	41(4.0)	4(4.3)	0.001	0.999
Fine motor	116(10.3)	104(10.1)	12(12.8)	0.398	0.528
Gross motor	77(6.9)	65(6.3)	12(12.8)	4.631	0.031

表4 婴儿期条栅视力与3岁神经发育欠佳的关联

Table 4 Associations between infant visual acuity and noncompetent neurodevelopment at 3 years of age

Outcome	Model 1 ^a		Model 2 ^b	
	RR(95% CI)	P	RR(95% CI)	P
Cognition	1.16(0.46–2.92)	0.748	1.09(0.42–2.84)	0.853
Receptive communication	1.25(0.44–3.52)	0.673	1.25(0.43–3.64)	0.687
Expressive communication	1.07(0.38–3.01)	0.905	1.17(0.40–3.41)	0.746
Fine motor	1.26(0.69–2.29)	0.446	1.16(0.63–2.15)	0.628
Gross motor	2.02(1.09–3.74)	0.025	1.96(1.03–3.70)	0.040

a: Unadjusted for covariates. b: Adjusted for maternal age, household income, maternal education, gestational age, pre-pregnancy BMI, plurality, hypertensive disorders of pregnancy, diabetes mellitus in pregnancy, sex, breastfeeding duration, age at visual acuity assessment, age at neurodevelopmental assessment. RR: risk ratio; CI: confidence interval.

表5 婴儿期条栅视力与3岁神经发育欠佳关联的性别分层分析

Table 5 Associations between infant visual acuity and noncompetent neurodevelopment at 3 years of age stratified by child sex

Variable	Control group[n/N(%)]	Abnormal visual acuity[n/N(%)]	Adjusted RR(95% CI) ^a	P value for heterogeneity
Cognition				0.922
Boy	37/532(7.0)	4/42(9.5)	1.15(0.39–3.39)	
Girl	10/496(2.0)	1/52(1.9)	1.02(0.12–8.51)	
Receptive communication				0.846
Boy	27/532(5.1)	3/42(7.1)	1.30(0.37–4.57)	
Girl	8/496(1.6)	1/52(1.9)	1.68(0.18–15.58)	
Expressive communication				0.796
Boy	33/532(6.2)	3/42(7.1)	1.08(0.31–3.79)	
Girl	8/496(1.6)	1/52(1.9)	1.50(0.17–13.43)	
Fine motor				0.148
Boy	72/532(13.5)	10/42(23.8)	1.56(0.78–3.13)	
Girl	32/496(6.5)	2/52(3.8)	0.48(0.11–2.02)	
Gross motor				0.443
Boy	41/532(7.7)	8/42(19.0)	2.31(1.03–5.21)	
Girl	24/496(4.8)	4/52(7.7)	1.37(0.47–4.01)	

a: Adjusted for maternal age, household income, maternal education, gestational age, pre-pregnancy BMI, plurality, hypertensive disorders of pregnancy, diabetes mellitus in pregnancy, breastfeeding duration, age at visual acuity assessment, age at neurodevelopmental assessment. RR: risk ratio; CI: confidence interval.

表6。当分别排除双胞胎、早产儿、低出生体重儿及辅助生殖受孕出生的儿童后，结果与主分析基本一致。具体而言，与婴儿期条栅视力正常组相比，婴

儿期条栅视力异常组3岁时大运动发育欠佳的风险在排除双胞胎后增加136%(RR=2.36, 95% CI: 1.21~4.58)、在排除早产儿后增加142%(RR=2.42, 95%

CI: 1.25~4.72)、在排除低出生体重儿后增加115% (RR=2.15, 95%CI: 1.13~4.08), 在排除辅助生殖受孕出生的儿童后增加169% (RR=2.69, 95%CI: 1.37~5.28), 而其余神经发育维度未见统计学显著关联。

3 讨论

本研究基于江苏出生队列, 纵向分析了婴儿期条栅视力与3岁神经发育的关联, 发现婴儿期条栅视力异常与3岁大运动发育欠佳风险增加相关, 在排除双胞胎、早产儿、低出生体重儿及辅助生殖受孕出生的儿童后, 该关联仍然显著。这表明婴儿期条栅视力异常可能是影响3岁神经发育的大运动维度的危险因素。

本研究中, 条栅视力异常界值为3.89 cpd, 该数值与既往研究报道的12个月龄婴儿条栅视力参考水平较为接近。已有一项针对中国婴儿条栅视力参考标准的前瞻性研究显示, 12个月龄婴儿的条栅视力均值为3.73 cpd^[18]。此外, 另一项荟萃分析更新了TAC II的年龄特异性参考标准, 指出约12个月龄婴儿单眼条栅视力的正常下限为3.75 cpd^[15]。若采用上述研究中的条栅视力下限作为异常划分依据, 视力异常的分类结果未发生变化。

已有研究探讨了视力异常对认知能力、运动能力的负面影响^[19-22], 本研究与既往发现一致。一项观察性横断面研究对1~42个月龄儿童分析发现, 条栅视力水平与基于BSID-III评估的认知和运动评分

表6 婴儿期条栅视力与3岁神经发育欠佳关联的敏感性分析

Table 6 Sensitivity analysis of associations between infant visual acuity and noncompetent neurodevelopment at 3 years of age

Outcome	Model 1 ^a		Model 2 ^b	
	RR(95% CI)	P	RR(95% CI)	P
Excluding twins				
Cognition	1.38(0.55-3.49)	0.494	1.54(0.59-4.02)	0.376
Receptive communication	1.11(0.34-3.64)	0.859	1.25(0.37-4.25)	0.725
Expressive communication	1.05(0.32-3.41)	0.938	1.35(0.40-4.56)	0.628
Fine motor	1.13(0.57-2.23)	0.735	1.15(0.58-2.31)	0.690
Gross motor	2.21(1.16-4.22)	0.015	2.36(1.21-4.58)	0.012
Excluding preterm births				
Cognition	1.18(0.47-2.97)	0.727	1.17(0.44-3.11)	0.753
Receptive communication	1.03(0.31-3.36)	0.965	1.01(0.29-3.55)	0.985
Expressive communication	0.94(0.29-3.05)	0.913	1.26(0.37-4.36)	0.712
Fine motor	1.24(0.66-2.32)	0.497	1.09(0.56-2.09)	0.807
Gross motor	2.01(1.06-3.83)	0.033	2.42(1.25-4.72)	0.009
Excluding low birth weight infant				
Cognition	1.16(0.46-2.91)	0.757	1.10(0.42-2.88)	0.841
Receptive communication	1.22(0.43-3.42)	0.711	1.04(0.35-3.08)	0.938
Expressive communication	1.12(0.40-3.14)	0.829	1.31(0.44-3.89)	0.622
Fine motor	1.16(0.62-2.16)	0.642	1.02(0.54-1.93)	0.956
Gross motor	2.09(1.13-3.89)	0.019	2.15(1.13-4.08)	0.019
Excluding ART-conceived infants				
Cognition	1.53(0.60-3.89)	0.373	1.73(0.66-4.54)	0.270
Receptive communication	1.26(0.38-4.14)	0.707	1.46(0.42-5.06)	0.551
Expressive communication	1.03(0.31-3.37)	0.962	1.39(0.41-4.71)	0.599
Fine motor	1.32(0.68-2.53)	0.412	1.38(0.70-2.70)	0.351
Gross motor	2.35(1.23-4.49)	0.010	2.69(1.37-5.28)	0.004

a: Unadjusted for covariates. b: Adjusted for maternal age, household income, maternal education, gestational age, pre-pregnancy BMI, plurality, hypertensive disorders of pregnancy, diabetes mellitus in pregnancy, sex, breastfeeding duration, age at visual acuity assessment, age at neurodevelopmental assessment. For variables excluded in the various sensitivity analyses, the corresponding variables are no longer included in the model for adjustment. RR: risk ratio; CI: confidence interval; ART: assisted reproductive technology.

呈正相关^[20]；一项多国家前瞻性研究发现在早产儿中，2、4、6个月时条栅视力较好的婴儿，在12个月时运动发展指数较高^[21]；另有一项系统综述表明，在脑性瘫痪患儿中，视力与12个月龄及以上时的认知能力呈正相关^[22]。随着生活方式的改变和便携式电子设备的广泛使用，儿童视力异常的发生呈现低龄化趋势，加强早期视力筛查和发育监测，有助于及早识别神经发育风险、把握干预窗口期。

性别分层分析提示，婴儿期条栅视力异常与3岁大运动发育欠佳之间的关联在男孩中具有统计学意义，而在女孩中未达到统计学显著水平。然而，性别分层分析的异质性检验未达到统计学显著性，提示尚无充分证据支持不同性别间存在效应差异。既往关于生命早期性别的神经发育差异的研究结论尚不一致。Monir等^[23]发现女孩的BSID-III量表维度得分往往高于男孩，而Kaplan等^[24]研究未发现性别差异，可能是由于不同研究的神经发育评估年龄及方法存在差异。

视力异常对儿童神经发育欠佳影响的可能机制：视力可能通过影响生命早期视觉输入而参与神经可塑性的调节。在关键发育时期，即使是轻微的视力受限或视觉输入减少，也可能对大脑物理结构的发育产生深远影响^[25]。此外对于大运动发育，良好的视力有助于个体获取环境信息和运动轨迹反馈，从而调整行走策略并更好地适应周围环境^[26-27]。

本研究存在局限性。第一，本研究使用的BSID-III，其临床应用已得到验证，有良好的信度和效度^[16]，但并非是诊断量表。第二，本研究的样本量较小，视力异常和神经发育欠佳的例数较少。随着队列研究参与者的持续招募，将会更有效地探索两者之间的关联。第三，本研究同时分析了多个神经发育维度，未进行多重检验校正，可能增加第I类错误的风险。第四，尽管已考虑了诸多人口统计学和临床特征，但仍可能存在残余混杂。例如，出生后儿童行为及父母的视力状况，如高度近视、斜视、弱视及相关遗传性眼病等未被纳入模型进行调整^[28]，可能导致风险效应被高估或低估。

综上所述，本研究表明婴儿期条栅视力异常可能是3岁大运动发育欠佳的潜在风险因素。未来应重点关注婴儿期条栅视力异常儿童的后续发育状况，加强随访监测，并结合长期随访和机制研究进一步阐明二者之间的关联，为生命早期视觉异常筛查及神经发育风险干预提供科学依据。

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The authors declare that there is no conflict of interests.

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QU Yue was responsible for data analysis, manuscript writing, and revision; JIANG Mengting was responsible for data analysis and methodology design; LÜ Hong, JIANG Yangqian, and JIANG Tao were responsible for guiding the design of the paper framework and data collection; LIN Yuan was responsible for project coordination; DU Jiangbo and LI Jiong were responsible for research supervision and guidance.

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