·论著·

# 儿童低水平铅暴露与神经行为关系的研究

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[摘 要] 目的 探讨低水平铅暴露对儿童神经行为的影响。方法 整群随机抽取某市幼儿园 4～6 岁 211 名儿童为研究对象,采指端末梢血 20 μl,原子吸收石墨炉法测定血铅,以血铅水平 100 μg/L 为界,分为高血铅组(≥100 μg/L)和低血铅组(<100 μg/L),采用 Achenbach 儿童行为量表(CBCL)及自拟调查表进行问卷调查,其结果运用 $t$,$\chi^2$ 检验,简相关及多元逐步回归等方法进行统计分析。结果 高血铅组外向行为得分及行为异常率(13.28±6.26,18.26%)显著高于低血铅组(9.98±5.46,7.29%)($t=4.0677$,$\chi^2=5.470$,均 $P<0.05$),血铅值与外向行为中多动、攻击、违纪因子分显著正相关($r=0.3164$,0.2828,0.1886,$P<0.05$),血铅值≥150 μg/L 时,行为异常率显著增加($\chi^2=13.695$,$P<0.05$)。结论 低水平铅暴露对儿童外向行为具有负性影响。

[关 键 词] 低水平铅暴露 神经行为 儿童
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发育的中枢神经系统对铅毒性特别易感和脆弱,其损害是一连续的过程,神经心理、行为的变化早于铅所造成的智力的不可逆损害[1],0～6 岁儿童是铅中毒的高危人群,国内对该群体研究较少,且多局限于铅对学龄儿童智力的损害[2],低水平铅暴露对学龄前儿童行为影响的报道尚不多见。本研究通过探讨铅导致的神经行为变化,以及血铅量和行为效应关系,为预防儿童行为问题及铅对智力损害提供依据。

## 1 对象与方法

### 1.1 对象

随机整群抽取某市居民区幼儿园 4～6 岁 211 名儿童为研究对象,其中男 109 名,女 102 名,以血铅水平 100 μg/L 为界,分为高血铅组(≥100 μg/L)和低血铅组(<100 μg/L)。

### 1.2 方法

1.2.1 血样采集和测定 采指端末梢血 20 μl,血样消化、离心后,用日本岛津 AA-670/GV-5 原子吸收分光光度计(石墨炉法)测定血铅含量。全血铅分析标准物质由中国预防医学科学院提供。每测 15 份血样,测定高、中、低的一份标准物质,测得值均在标准值的允许范围内,同时设 4% 平行样,样本测定差值差异无显著性($P>0.05$)。

1.2.2 儿童行为的测定及影响因素调查 采用 Achenbach 儿童行为量表(CBCL)[3]和自拟调查表,在专业人员指导下,由家长填写,以任一行为因子分大于中国儿童常模或 CBCL 总分超过第 98 百分位即判断为有行为问题,得有效答卷 211 份,表格回收率 100%。

1.2.3 统计分析 用 SPSS 6.0 软件在 AST/586 微机上,采用 $t$,$\chi^2$ 检验,简相关及多元逐步回归分析。

## 2 结果

### 2.1 两组儿童行为比较分析

高血铅组外向行为得分及行为异常率(13.28±6.26,18.26%)显著高于低血铅组(9.98±5.46,7.29%)($t=4.0677$,$\chi^2=5.470$,$P<0.05$),内向得分及 CBCL 总分两组无显著差异($t=1.0815$,1.5623,$P>0.05$)。见表 1。

表 1 两组行为得分及行为异常率比较 ($\bar{x}\pm s$)

| 组别 | 例数 | 内向得分 | 外向得分 | CBCL 总分 | 行为异常率(%) |
|---|---|---|---|---|---|
| 低血铅组 | 96 | 8.08±5.96 | 9.98±5.46 | 21.49±10.45 | 7.29 |
| 高血铅组 | 115 | 7.18±6.09 | 13.28±6.26[a] | 23.81±11.08 | 18.26[a] |

注:a 与低血铅组比较 $P<0.05$

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### 2.2 血铅水平与行为异常率分析

依据血铅水平将研究对象分为Ⅴ组，不同组别行为异常率差异有显著性（$\chi^2 = 13.695$，$P < 0.01$），进一步两两比较，当血铅≥150 μg/L 后 2 组行为异常率显著高于前 3 组（$\chi^2$ 分别为 4.727，6.261，5.168；4.503，5.911，4.928，均 $P < 0.05$），表明血铅≥150 μg/L 时，儿童行为异常率显著增多。见表 2。

表 2 不同血铅水平行为异常率

| 组别 | 血铅(μg/L) | 例数 | 异常人数 | 异常率(%) |
|---|---|---|---|---|
| Ⅰ | <50 | 40 | 3 | 7.50 |
| Ⅱ | 50～ | 56 | 4 | 7.14 |
| Ⅲ | 100～ | 58 | 5 | 8.62 |
| Ⅳ | 150～ | 39 | 10 | 25.64[a] |
| Ⅴ | 250～ | 18 | 6 | 33.33[a] |

注：a 分别与Ⅰ，Ⅱ，Ⅲ组比较 $P < 0.05$

### 2.3 血铅对数值与外向行为各因子分的相关分析

简相关分析显示：血铅对数值与多动、攻击、违纪因子分显著正相关。见表 3。

表 3 血铅对数值与外向行为各因子简相关分析

| 测量指标 | 攻击 | 肥胖 | 违纪 | 分裂 | 多动 | 残忍 | 性问题 |
|---|---|---|---|---|---|---|---|
| 血铅对数值 | 0.2828[a] | 0.1024 | 0.1886[a] | 0.0942 | 0.3164[a] | 0.1183 | 0.0926 |

注：a $P < 0.05$

### 2.4 多元逐步回归分析

用自拟调查表对可能影响儿童外向行为的 18 个高危因子，包括年龄、性别、妊娠及出生情况、哺乳期母亲情绪、婴儿早期喂养、父母职业、文化程度、教养方式、家庭经济状况及气氛、居住环境、饮食习惯和儿童血铅对数值等分别与外向行为各因子进行逐步回归分析，$F$ 界值 $\alpha = 0.1$，结果发现：血铅对数值最终均引入多动、攻击及违纪因子分回归方程，这表明在控制家庭，社会等混杂因素后，铅对儿童外向行为的影响依然存在，并保持统计学意义。

## 3 讨论

探讨铅的损害作用时应注意铅暴露、行为异常及中枢神经改变相关关系的研究[4]，为早期发现铅中毒，预防铅的智力损害具有重要意义。本研究结果表明，内向得分及 CBCL 总分两组间无显著差异，这可能是由于低水平铅暴露对内向得分及 CBCL 总分的影响相对于社会环境而言较小，从而掩盖了它的作用，也可能由于样本的不均衡性或受方法学本身的限制所致。然而高血铅组外向行为得分、行为异常率显著高于低血铅组，血铅值与攻击、多动及违纪因子分显著正相关，这种相关在运用多元逐步回归分析的方法，控制诸多混杂因素后依然存在，并保持原有的统计学意义。当血铅水平大于 150 μg/L 时，行为异常率显著增加，因此可认为血铅值对儿童神经行为的影响存在一定的剂量-效应关系。据本次研究的结果，存在多动、攻击及违纪等行为问题的儿童应列为铅中毒筛查的高危人群，以便早期发现铅中毒病例，及时采取健康教育、环境干预及临床驱铅治疗等妥善措施，阻断铅毒性对智力损害的病理过程。

关于铅影响儿童外向行为的机制，有研究认为：低浓度铅可选择蓄积于海马区及大脑皮层，引起海马功能紊乱的特征形态学改变，而表现为多动、攻击性行为等，在大脑皮层，铅致额前区及枕叶区神经突触形成减少，从而造成或不能控制的不恰当行为与反应[5]。慢性铅暴露能使 5-羟色胺的含量、合成、更新速度以及与其它神经递质的比值发生改变，此外，铅导致 δ-氨基酮戊酸（δ-ALA）增多，使之在中枢神经系统中，起假神经递质作用，阻断突触前抑制过程，使机体呈过度兴奋状态，诸如中枢神经递质的改变，影响脑功能的正常活动，从而产生异常的情绪及行为偏离而发生违纪现象[6]。总之，本研究提示，低水平铅暴露对儿童行为已产生负性影响，唤起全社会对控制铅污染的重视，已成为需要解决的重大公共卫生问题。

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·论著(译文)·

# Relationship Between Low-Level Lead Exposure and Neurobehaviors of Preschool Children

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**Abstract: Objective** To study the effects of exposure to low-level lead on neurobehaviors of preschool children. **Methods** Blood lead levels were measured in 211 preschool children aged 4 - 6 years in a kindergarten without known exposure to lead sources; the 211 children were assigned into two groups: low blood lead level group (LL group, $<100$ μg/L) and high blood lead level group (HL group, $\geqslant 100$ μg/L). Their neurobehaviors were assessed with Achenbach child behavior checklist (CBCL) to study the relationship between blood lead and CBCL total behavior scores (TBPs), internalizing and externalizing scores (Ints and Exts). **Results** The Exts and incidence of abnormal behavior problems in the HL group ($13.28 \pm 6.26$ and 18.26%, respectively) were much higher than those in the LL group ($9.98 \pm 5.46$ and 7.29%, respectively) ($t = 4.0677$, $\chi^2 = 5.470$, $P < 0.05$). The blood lead level was positively correlated significantly with the scores for hyperactivity, attack and disobedience ($r = 0.3164$, 0.2828, 0.1886, $P < 0.05$). When the blood lead levels of children reached or exceeded 150 μg/L, the incidence of abnormal behavior problems increased significantly. **Conclusions** Low-level lead exposure can have adverse effects on neurobehaviors of preschool children.

**Key words:** Low-level lead exposure; Neurobehavior; Child

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The developing central nervous system is most sensitive to lead toxicity; lead toxicity is a continuous process that causes adverse effects on the development of neropsychology, neurobehavior and intelligence of preschool children. The harmful effects on intelligence persists into adulthood and appears to be irreversible[1]. Children aged 0 - 6 years are considered susceptible and are a high-risk population for adverse effects of lead poisoning. Over the past several years, there has been growing attention that lead toxicity has harmful effects on the child's intelligence. However, reports on the effects of exposure to low-level lead on neurobehaviors of preschool children are rare[2]. The aim of this study was to investigate the effects of exposure to low-level lead on neurobehaviors of preschool children and the relationship between the dose-effect of blood lead and behavioral scores in order to formulate effective prophylaxis regiments for childhood lead poisoning.

## Methods

### Subjects

With cluster random sampling, 211 urban preschool children aged 4 - 6 years (109 boys and 102 girls) from one kindergarten without known lead sources in a city residential district were enrolled in this study. They were assigned into two groups: low blood lead level group (LL group, $<100$ μg/L) and high blood lead level group (HL, $\geqslant 100$ μg/L) according to their blood lead levels.

### Methods

Digital blood samples were collected and blood lead levels were measured with automatic absorption spectrometry in 211 children. Meanwhile, their neurobehaviors and individual conditions were assessed with Achenbach child behavior check list (CBCL)[3] and a self-designed questionnaire, which involves

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some factors affecting neurobehaviors, such as age, sex, and cultural and family background. The child with neurobehavior scores exceeding the norm for Chinese children or with CBCL total behavior scores (TBPs) beyond the ninety-eighth percentile is thought to have abnormal behavioral problems.

**Statistical analysis**

All statistical analyses were performed with the Statistical Package for Social Science, all values were presented as mean ± standard deviation ($\bar{x} \pm s$), differences between the two groups were analyzed using student's T test, and the effects of different lead exposure levels on neurobehaviors were analyzed using $\chi^2$ test. The simple correlated analysis was done to analyze correlations between the lead exposure level and the scores of externalizing factors; confounding factors were controlled with stepwise regression analysis to study the influences of lead exposure on neurobehaviors.

## Results

Differences of behavior scores and the rate of behavior problems between the LL and HL groups were given in Table 1. The externalizing scores (Exts) and incidence of abnormal behavior problems in the HL group (13.28 ± 6.26 and 18.26%, respectively) were significantly higher than those in the LL group (9.98 ± 5.46 and 7.29%, respectively) ($t = 4.0677$, $\chi^2 = 5.470$, $P < 0.05$). However, there was no difference in the TBPs and internalizing scores (Ints) between the LL group and HL group (see Table 1).

Differences of the incidence of abnormal behavior problems among various blood lead levels were given in Table 2. Based on the blood lead levels (<50 μg/L, 50 μg/L~, 100 μg/L~, 150 μg/L~, 250 μg/L~), the subjects were assigned into five group: Group Ⅰ, Group Ⅱ, Group Ⅲ, Group Ⅳ and Group Ⅴ. There were significant differences in the incidence of abnormal behavior problems among the 5 groups ($\chi^2 = 13.695$, $P < 0.01$); the incidence of abnormal behavior problems in Group Ⅳ and Ⅴ (blood lead level ≥150 μg/L) were higher than that of Group Ⅰ, Ⅱ and Ⅲ ($\chi^2 = 4.727, 6.261, 5.168$; $4.503, 5.911, 4.928$; $P < 0.05$) (see Table 2).

Simple correlated analysis between blood lead logarithm and the scores of externalizing factors was performed. The results showed that the blood lead level was positively correlated significantly with the scores for hyperactivity, attack and disobedience ($r = 0.3164, 0.2828, 0.1886$, $P < 0.05$) (see Table 3).

**Table 1** Comparisons of behavior scores and the incidence of abnormal behavior problems between the LL group and HL group ($\bar{x} \pm s$)

| Group | n | Ints | Exts | TBPs | behavior problems(%) |
|---|---|---|---|---|---|
| LL | 96 | 8.08±5.96 | 9.98±5.46 | 21.49±10.45 | 7.29 |
| HL | 115 | 7.18±6.09 | 13.28±6.26[a] | 23.81±11.08 | 18.26[a] |

Note: a vs LL group $P < 0.05$

**Table 2** Differences of the incidence of abnormal behavior problems among various blood lead level groups

| Group | Blood lead (μg/L) | n | Number of cases with behavior problems | Incidence of behavior problems (%) |
|---|---|---|---|---|
| Ⅰ | <50 | 40 | 3 | 7.50 |
| Ⅱ | 50~ | 56 | 4 | 7.14 |
| Ⅲ | 100~ | 58 | 5 | 8.62 |
| Ⅳ | 150~ | 39 | 10 | 25.64[a] |
| Ⅴ | 250~ | 18 | 6 | 33.33[a] |

Note: a vs Group Ⅰ, Ⅱ 0r Ⅲ $P < 0.05$

**Table 3** Simple correlated analysis between blood lead logarithm and the scores of externalizing factors

| Index | Attack | Obesity | Disobedience | Abruption | Hyperactivity | Brutality | Sexual problem |
|---|---|---|---|---|---|---|---|
| Blood lead logarithm | 0.2828[a] | 0.1024 | 0.1886[a] | 0.0942 | 0.3164[a] | 0.1183 | 0.0926 |

Note: a $P < 0.05$

Regression analysis was used among the scores of externalizing factors, blood lead logarithm and poten-

tial confounding factors, such as age, sex, and cultural and family background. The results showed that the blood lead level had significantly positive correlation with the scores for hyperactivity, attack and disobedience. Moreover, it remained after confounding factors were controlled by stepwise regression analyses.

## Discussion

There is a critical need for the study to obtain more precise information on the correlation among lead, neurobehaviors and subtle central nervous system dysfunction[4], to discover children with lead poisoning earlier and to prevent harmful effects on their intelligence. Based on this study, there were no significant differences in TBPs and Ints between the LL group and HL group. This may result from less harmful effect of exposure to low-level lead compared to the social environment. Or this may be due to the inhomogeneous samples or restriction by methodology itself. However, the results showed that the Exts of the HL group were higher than those of the LL group. The blood lead level was positively correlated significantly with the scores for hyperactivity, attack and disobedience, and it remained when adjusted for potential confounding factors by stepwise regression analyses. When the blood lead levels of the children exceeded 150 μg/L, the incidence of abnormal behavioral problems increased significantly, showing a dose-effect between the blood lead level and abnormal behavioral problems. Based on the above findings, it is suggested that children with hyperactivity, attack and disobediences should be screened for lead poison ing to enable preventive strategies , such as health edu -cation, environmental intervention, and clinical treatment.

As for the mechanism of lead influencing externalizing neurobehaviors, it has been reported that low-level lead exposure can cause a selective accumulation of lead in the hippocampus and cerebral cortex, resulting in characteristic morphologic changes, such as a significant increase in size and numerical density of mossy fibers, the granule cell layer and the commissural－associational area of the dentate molecular layer, causing functional disturbance of the hippocampus, which induces hyperactivity and attack. Meanwhile, lead exposure decreases the numerical density of nerve synapses in the prefrontal cortex, resulting in inability to inhibit appropriate behavioral responses clinically[5]. Long-term lead exposure affects the content, synthesis, rebirth of 5-HT and the ratio to other neurotransmitters. Moreover, lead can increase the content of δ－ALA that acts as a false neurotransmitter in the central nervous system. This interdicts the process of presynaptic inhibition, causing excessive excitement. In other words, lead may cause variable changes in several neurotransmitter systems, which has a harmful impact on the well－balanced function of the brain to conduce abnormal emotion and behavior, such as disobediences, hyperactivity and attack[6].

In conclusion, exposure to low-level lead can have adverse effects on neurobehaviors of preschool children. The study of childhood lead poisoning in our country should be emphasised.

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