## Impaired Picture Sequencing Ability in Children with Premature Birth

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**Background:** Children born preterm are at increased risk for executive dysfunction, which affects learning outcomes. Picture sequencing ability is considered as executive function (EF) that requires skills in working memory and organizing the pictures. Children born preterm might have difficulties in these skills. The present study aimed to develop practical Picture Sequencing test (PS test) and examine the sequencing ability in preterm children comparing with term children.

*Material and Method:* The PS test was developed to assess the child's ability to arrange pictures into a sequence. It consisted of three conditions, which were daily activities, social interaction routines, and feeling expressions. Each story had four cartoon styles cards. The child had to rearrange picture cards into the correct sequence positions. Thirty preterm children aged five to six years with gestational ages of  $\leq 32$  weeks and birth weights of < 1,500 grams, and thirty-five term children matched age, gender, child's education, parental education, and socioeconomic status were performed the PS test. The total scores were compared between the preterm group and the term group.

**Results:** The PS test scores on the daily activities domain of the preterm and term group were 18 and 25 (p = 0.03), respectively. The scores on the social interaction routines domain of the preterm and term group were 20 and 28 (p = 0.01) and the scores on the feeling expression domain were 18.5 and 25 (p = 0.03), respectively. There was no significant correlation between perinatal complications and the PS test scores.

**Conclusion:** The preterm children with IQs in the average range showed impairment in sequencing ability compared with the term children. The results underline the need for follow-up care with more comprehensive assessment of EF.

Keywords: Preterm infants, Executive function (EF), Sequencing ability

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The increase in survival rates of children born preterm with less major physical and mental disabilities has raised concern about long-term cognitive outcomes, academic achievement, and behavioral problems<sup>(1)</sup>. Premature children are at increased risks for cognitive impairment, academic underachievement, and behavioral problems, which includes executive dysfunction when they are compared with term children<sup>(2-5)</sup>. Infants, who were very preterm, who experience perinatal complications including periventricular leukomalacia or cerebral white matter injury, are at risk to have major deleterious effects on subsequent brain development at the prefrontal cortex area<sup>(6)</sup>, which may result in deficits in executive function (EF)<sup>(7)</sup>. Poorer performances on various tasks of EF in children born preterm compared with children born at term have been previously documented<sup>(7-10)</sup>.

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Sequencing ability is a part of planning ability in EF. The sequencing ability refers to the organization of previous knowledge, reasoning, and sequencing a situation to approach a destination goal that plays an important role in school performance and academic achievement<sup>(11)</sup>. The picture sequencing task requires manipulation tasks in which the subject needs to compare pictures held in working memory in order to select the correct response from a number of competing elements<sup>(12)</sup>. A fMRI study showed that event sequencing ability required activation in the dorsolateral prefrontal cortex and globus pallidus internal part<sup>(13)</sup>, which are the areas where very preterm children might have injury. This results in difficulties for the neural representations of the pictures to be maintained. The very preterm children might not cognitively reorganize images in order to sequence pictures. The present study aimed to develop a simple and practical assessment of sequencing ability that could help assess easily in clinical settings and examine the sequencing ability in preterm children compared with term children.

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# Material and Method *Ethical approval*

The study had the approval of the Mahidol University Ethics Committees. All families recruited to the study were provided informed consent to participate, and the research was conducted in accordance with the ethical standards outlined of the Helsinki Declaration.

#### Study design

A cross sectional study was conducted.

#### **Participants**

Sixty-five, five to six years old, children were recruited into the study. The first group consisted of 30 children who were born at Ramathibodi Hospital, Bangkok, Thailand, between 2005 and 2006, with gestational ages of  $\leq 32$  weeks and birth weights of <1,500 grams. No children had major disability such as cerebral palsy (CP), intellectual disabilities (Intelligence Quotient, IQ <70), deafness, or blindness. Because some very preterm participants did not continue follow-up at the Very Low Birth Weight Clinic, Ramathibodi Hospital, the participants who did were viewed as convenient participants. However, we interviewed by telephone for basic characteristic data and reviewed their medical records for those who did not continue follow-up. We found no statistically significant difference in basic characteristics and neonatal complications between the missing group and the participating preterm group. The second group comprised of 35 typically developing children who were born with gestational age >37 weeks and birth weights >2,500 grams, with no perinatal complications. The full term comparison children were matched for age, gender, education, parental education, and socioeconomic status with the preterm group.

#### Procedure

We developed a Picture Sequencing test (PS test) and used it to measure the sequencing ability. The child's education, maternal education, family income, perinatal and postnatal complications, which may influence performance on EF, were recorded. The IQ test was administered to all participants. Children's IQ was measured by using the Wechsler Intelligence Scale for Children Third Edition (WISC-III)<sup>(14)</sup> for children older than six years old and by the Stanford-Binet Intelligence Scale: Fourth edition (Stanford-Binet IV)<sup>(15)</sup> for children aged  $\leq 6$  years old. Subsequently, the PS test required participants to

order the series of four pictures and were scored by the developmental and behavioral pediatrician (KJ). In order to familiarize participants with the test, three practices preceded the experimental session. The stories were presented in the same fixed order for every participant. The assessment lasted for approximately 30 minutes. No participants failed to complete the assessment session. Once the participants completed each sequence, the order of cards and time employed were recorded.

#### Measures

#### The picture sequencing test (PS test)

The PS test assessed the child's ability to arrange pictures into a sequence. The test consisted of three domains, which were daily activities, social interaction routines, and feeling expressions. There were six different stories for each domain (see example of picture stories content in Appendix 1 and example of picture stories in Appendix 2). The pictures were cartoon styles that were drawn on white 12.5x12.5 centimeters cards. Each story had four pictures that were placed in the same fixed incorrect order. The child had to rearrange picture cards into the correct sequence positions. The sequence of the first and the last picture cards were important and they might lead to an error on the third and the fourth cards arrangement. Therefore, a sequence scored two points each if the first and the last card were positioned correctly and one point each for the second and the third cards being positioned correctly. The total score was six in each story and totaled 36 in each condition.

#### Intelligence test

The Stanford-Binet Intelligence Scale: Fourth edition (Stanford-Binet IV) was administered to assess the intellectual abilities of children between ages of two years to six years. The Stanford-Binet IV was translated to Thai and adapted to use in Thailand by qualified psychologists.

The Wechsler Intelligence Scale for Children Third Edition (WISC-III) was used to provide the IQ score for children aged older than six years. The test was translated to Thai and adapted to use in Thailand by qualified psychologists.

#### Statistical analyses

All data were analyzed by using SPSS version 17.0 (SPSS, Chicago, IL, USA). Chi-square tests of significance were used for bivariate analysis

of discrete variables and unpaired t-tests were used for continuous variables (age, birth weight and IQ scores). The Mann-Whitney U test was used to compare the preterm group and the term group differences on the PS score. The Spearman's rank-order correlation was used to study the correlation between neonatal complications and performance on the PS test. The significance threshold for all analyses was set at p<0.05.

#### Results

Table 1 shows the basic characteristics for the preterm group and the term group. There were no group differences for age, sex, gestational age, children's education, parental education, and family income. Mean birth weight of the preterm group was  $1,155\pm239$  grams and the term group was  $3,216\pm451$  grams.

Regarding the IQ scores, there was no statistically difference between the preterm and term groups (p = 0.23). The mean IQ score (SD) was 94.9 (12.2) in the preterm group and was 98.7 (12.6) in the term group. All of the children in both groups had IQ scores within the normal range, offering reassurance that they were an average ability samples. Significant differences between the preterm group and the term

group were found on the sequencing ability in all three domains. The PS test scores on the daily activities domain of the preterm and term group were 18 and 25 (p = 0.03), respectively. The scores on the social interaction routines domain of the preterm and term group were 20 and 28 (p = 0.01) and the scores on the feeling expression domain were 18.5 and 25 (p = 0.03), respectively (Table 2). There was no statistically difference between the preterm and term groups in term of time they completed the PS test.

It is possible that adverse perinatal complications affected performance on sequencing abilities. The Spearman's correlation was applied to test the impact of perinatal complications on the PS scores of the preterm group. We found no correlation between neonatal complications including birth asphyxia, respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), retinopathy of prematurity (ROP) and patent ductus arteriosus (PDA), and the PS scores (Table 3).

#### Discussion

The present study developed the picture sequencing test and assessed the sequencing ability in the preterm children aged five to six years compared

 Table 1. Basic characteristics of the preterm and term comparison group

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Characteristics	Preterm group $(n = 30)$	Term group $(n = 35)$	<i>p</i> -value
Age (months), mean (SD)	73.73 (7.39)	71.80 (6.07)	0.25
Sex, n (% male)	17 (56.7)	18 (51.4)	0.67
Birth weight (grams), mean (SD)	1,155 (239)	3,216 (451)	0.004
Children's education, n (%) No education Kindergarten Primary school	2 (6.7) 17 (56.7) 11 (36.7)	0 (0) 20 (57.1) 15 (42.9)	0.29
Parental education > Bachelor, n (%)	17 (56.7)	21 (60.0)	0.87
Family income >30,000 baht*/month, n (%)	14 (46.6)	16 (45.7)	0.87
* 1 US\$ = 30 baht			

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Characteristics	Preterm group $(n = 30)$	Term group $(n = 35)$	<i>p</i> -value
IQ scores, mean (SD)	94.9 (12.2)	98.7 (12.6)	0.23
Picture sequencing scores, median (range)			
Daily activities	18 (0-36)	25 (0-36)	0.03
Social interaction routines	20 (0-36)	28 (0-36)	0.01
Feeling expressions	18.5 (0-36)	25 (0-36)	0.03

Neonatal complications	Preterm group $(n = 30)$	Correlation coefficient (r)	<i>p</i> -value
Birth asphyxia (%)	3 (10.0)	-0.15	0.17
Respiratory distress syndrome (RDS) (%)	24 (80.0)	0.04	0.06
Necrotizing enterocolitis (NEC) (%)	6 (20.0)	-0.19	0.29
Intraventricular hemorrhage (IVH) (%)	7 (23.4)	-0.02	0.31
Retinopathy of prematurity (ROP) (%)	3 (10.0)	0.10	0.93
Patent ductus arteriosus (PDA) (%)	18 (60.0)	-0.02	0.08

Table 3. The correlation between neonatal complications and the PS test scores

with the term children. The results showed significant impairment in picture sequencing ability in preterm children when they were compared with term children, even though the IQ score in preterm group were in normal range and not different from the term group. The results are consistent with previous studies that preterm children had executive dysfunction on various tasks measuring  $EF^{(7,8,16-18)}$ . The study demonstrated that there was no correlation between the sequencing ability and IQ. This is consistent with previous studies in preterm that the EF performance was independent of IQ level<sup>[(17,19-21)</sup>.

In the previous research, the environmental aspects such as maternal education and socioeconomic status were associated with  $EF^{(22,23)}$ . The strength of the present study was to consider these factors and enrolled comparable participants in both groups in terms of child's education, parental education, and family income. The study found poorer performance on sequencing ability in the preterm group. However, some environmental factors such as parenting style, educational resources, and family function might be associated with the performance<sup>(24)</sup>, which the authors did not study.

From the present study, the authors could not postulate that the deficit in sequencing ability could be linked to later learning or behavioral outcomes. In addition, the authors still questioned to what extent this deficit persists over time or whether the preterm children may catch up later. However, a few studies showed deficit in EF have been linked to later learning, attention or behavioral problems<sup>(25,26)</sup>. Such EF assessments may provide means of early detection of problems, to which preterm children are prone, and followed-up studies are required to evaluate long-term adverse effects.

Sequencing ability is regulated by the dorsolateral prefrontal cortex<sup>(27)</sup>. The deficit in sequencing ability in preterm children may associate with the adverse effects of perinatal complications that

lead to abnormal prefrontal cortex during the period of brain development<sup>(28)</sup>. However, the study could not conclude that prefrontal cortex injury might be the cause of impaired sequencing ability. The present study found no significant correlation between perinatal complications and sequencing ability performance. This might relate to the fact that in the study, the incidence of IVH was low and all had IVH grade I-II. It might not be the perinatal complications of preterm that result in executive dysfunctions, but rather preterm birth itself<sup>(29,30)</sup>.

However, limitations of the present study have to be addressed. First, the validity and reliability of the picture sequencing test has not been assessed and the test does not fully cover the comprehensive range of EF. There has been a very limited use of standardized executive function assessments in Thailand. Thus, it is necessary to find the EF task that can assess executive dysfunction in preterm children in order to provide an intervention to help preterm children overcome their executive dysfunction. Second, the results represented one hospital center; therefore, these were not a representative sequencing ability of all the preterm population. Further study in other centers using a large sample size should be conducted.

In fact, the sequencing ability function has emerged during this age and proceeds through development during the school age-years. The sequencing ability impairment in the preterm group supports remediation programs tailored to children to help them overcome their impairments.

#### Conclusion

The present results indicated that, the preterm group with IQs in the average range showed impairment in sequencing ability compared with the term group. The findings underline the need for early detection of executive dysfunction and initiating the development of interventions to children of this population.

#### What is already known on this topic?

Premature children are at increased risks for cognitive impairment, academic underachievement, and behavioral problems, which includes executive dysfunction, when they are compared with term children. Poorer performances on various tasks of EF in children born preterm compared with children born at term have been previously documented.

#### What this study adds?

Sequencing ability is a part of planning ability in EF. The present study aimed to develop a simple and practical assessment of sequencing ability, which could be assessed easily in clinical settings, and examine the sequencing ability in preterm children compared with term children. Early detection of the EF impairments leads to early intervention that results in better long-term outcome.

#### Authors' contributions

Chuthapisith J made substantial contributions to conception and design of the study and interpretation of data as well as being involved in drafting and finalizing the manuscript. Jantarapagdee K was involved in study planning, data collection, data analysis, and interpretation, and in manuscript preparation. Roongpraiwan R and Nunnarumit P were involved in study planning and data interpretation. All authors read and approved the final version of the manuscript for publication.

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#### Potential conflicts of interest

None.

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Condition	Picture				
		1	2	3	4
1. Daily activities	1.	Walk into bathroom	Put toothpaste on toothbrush	Brushing teeth	Finish brushing
	2.	Preparing food	Table full of food	Eating	Finish eating
	3.	Finish taking a bath	Put on shirt	Put on trousers	Put on socks
2. Social interaction routines	1.	Studying in classroom	Playing with friends after class	Pick up by mother	Goodbye friends
	2.	Playing sand alone	Friend coming	Playing together	Finishing sand castle
	3.	Sitting in a car	Visiting grandparents' home	Greeting grandparents	Talking with grandparents
3. Feeling expressions	1.	Running with a friend	Fall down	Crying	Console by mother
	2.	Playing blocks alone	Destroying block by a friend	Feeling angry	Telling teacher
	3.	Shopping with mother	Want a car	Buying a car	Feeling glad and playing a car

Appendix 1. Examples of picture story contents

Appendix 2. Examples of picture stories



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### การทดสอบความสามารถด้านการเรียงลำดับเหตุการณ์ในเด็กที่มีประวัติคลอดก่อนกำหนด

## จริยา จุฑาภิสิทธิ์, คคนางณ์ จันทรภักดี, รวิวรรณ รุ่งไพรวัลย์, ประชา นันท์นฤมิต

ภูมิหลัง: เด็กที่คลอดก่อนกำหนดมีความเสี่ยงที่จะมีความบกพร่องใน executive function (EF) ซึ่งส่งผลต่อความสามารถ ในการเรียน ความสามารถในการเรียงลำดับเหตุการณ์ (picture sequencing ability) เป็นส่วนหนึ่งของ EF ที่ต้องใช้ความจำ ระยะสั้น (working memory) และความสามารถในการจัดการ (organization ability) เด็กที่คลอดก่อนกำหนดอาจมีความบกพร่อง ในทักษะนี้ได้ การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อพัฒนา แบบทดสอบ picture sequencing test (PS test) และนำมาใช้ประเมิน ความสามารถในการเรียงกำดับเหตุการณ์ในเด็กที่คลอดก่อนกำหนดเปรียบเทียบกับเด็กที่คลอดครบกำหนด

วัสดุและวิธีการ: แบบทดสอบ PS test ถูกพัฒนาขึ้น ซึ่งประกอบไปด้วยเรื่องที่เกี่ยวข้องกับ กิจวัตรประจำวัน การมีปฏิสัมพันธ์ ทางสังคม และการแสดงอารมณ์ แบบทดสอบเป็นภาพวาดการ์ตูน 4 ภาพ ในแต่ละเรื่องและให้เด็กเรียงลำดับให้ถูกต้องตามลำดับ เหตุการณ์ และนำคะแนนที่ได้ในทั้งสองกลุ่มมาเปรียบเทียบกัน กลุ่มศึกษาเป็นเด็กอายุ 5-6 ปี ที่คลอดก่อนอายุครรภ์ 32 สัปดาห์ และน้ำหนักน้อยกว่า 1,500 กรัม จำนวน 30 คน เปรียบเทียบกับเด็กที่คลอดครบกำหนด จำนวน 35 คน ที่มีอายุ เพศ การศึกษา ของเด็ก การศึกษามารดา และเศรษฐฐานะครอบครัว ที่ไม่แตกต่างกันทั้ง 2 กลุ่ม

**ผลการศึกษา:** ค่าเฉลี่ยของคะแนน PS test ในกลุ่มที่คลอดก่อนกำหนดต่ำกว่ากลุ่มที่คลอดครบกำหนดอย่างมีนัยสำคัญทางสถิติ ด้านกิจวัตรประจำวัน เด็กคลอดก่อนกำหนดและคลอดครบกำหนดได้คะแนน 18 และ 25 ตามลำดับ ด้านการมีปฏิสัมพันธ์ทาง สังคมได้คะแนน 20 และ 28 ตามลำดับ สำหรับด้านการแสดงอารมณ์ได้คะแนน 18.5 และ 25 ตามลำดับ สำหรับภาวะแทรกซ้อน หลังคลอดในกลุ่มเด็กคลอดก่อนกำหนด ไม่มีผลต่อคะแนน PS test

สรุป: เด็กคลอดก่อนกำหนดมีความสามารถในการเรียงลำดับเหตุการณ์ต่ำกว่าในเด็กคลอดครบกำหนด เด็กในกลุ่มนี้ควรได้รับการ ติดตามระยะยาวเพื่อส่งเสริมในทักษะที่บกพร่องที่อาจส่งผลต่อการเรียนในระยะยาว