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RESEARCH ARTICLE

BIRTH WEIGHT, CATCH UP GROWTH AND ITS EFFECT ON COGNITION IN CHILDREN  
AGED 5 TO 6 YEARS

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ABSTRACT

Cognitive assessment is a formal assessment of a child's abilities in a range of areas, such as verbal and non-verbal skills, memory and speed of processing. A Child may be assessed for concerns about their school performance or for any specific disorders. Birth weight is associated with cognition and educational attainment across the full birth weight range in the normal population. The objective of this study was to assess the effect of birth weight on cognition, as well as the effect of catch up growth on cognition among term born small for gestational age (SGA) children at 5 to 6 years of age. Seventy one healthy children, of whom forty four appropriate for gestational age (AGA), twenty one SGA and six large for gestational age (LGA) born, were selected from different private schools. Data on birth weight, obstetric history and parental demographic factors were obtained from parents of the children. NIMHANS neuropsychological battery for children was used to assess motor speed, attention, memory, speech and visuospatial function. Children born LGA performed poorer in tests of attention, and memory where the difference was statistically significant ( $P=0.002$ ), while those born SGA scored lower in tests for speech when compared to children born AGA ( $P=0.002$ ). Among term born SGA children, those who did not have a catch up growth, had significantly lower scores for motor speed of left hand ( $P=0.037$ ), speech ( $P=0.038$ ), and memory i.e reverse digit span (0.004) and picture recall (0.042). This study showed that children born LGA performed poor in tests of memory and attention while those born SGA scored low in tests of speech.

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INTRODUCTION

Birth weight of an infant is the single most important determinant of its chances of survival, healthy growth and development (Green-Abatte, 1986). Birth weight of a child depends on many factors like maternal factors (malnutrition, physical activity during pregnancy, chronic maternal diseases, smoking, maternal prepregnancy BMI, maternal age during pregnancy, parity and birth spacing), socioeconomic status, parental education and other environmental factors. The average birth weight of infants is lower in many developing countries than in developed countries, which is largely attributed to maternal malnutrition (Park, 2013). Nutrients and growth factors are important for development of brain during fetal and early postnatal life. The developing brain between 24 and 42 weeks of gestation is particularly vulnerable to nutritional insults because of the rapid trajectory of several neurologic processes, including synapse formation

and myelination. But as the young brains are plastic, this results in remarkable brain repair after replenishment of nutrients (Georgieff, 2007). Alarming, the trend for SGA in urban area has been increasing, and this has been reportedly attributed to an elevated biomarker of stress (C-reactive protein) during pregnancy (Ernst *et al.*, 2011). Incidence of LGA babies is about 1-10% of all deliveries. This can be caused by genetic factors as well as maternal conditions, such as obesity or diabetes (most common) (Medscape, 2014). Birth weight is associated with cognitive and educational attainment across the full birth weight range in normal population independently of social background. However, the extent to which birth weight reflects fetal growth and/or is a marker of subsequent size, is still not clear (Chaudhari *et al.*, 2004). Socioeconomic status (SES) has been an important contributor in determining the birth weight of the child. It has significant implications for the access to and use of primary health care services (Bacharach and Baumeister, 1998). Although long-term developmental changes in children have been discussed by different authors, but its emergence at preschool age is less well documented. As cognitive assessment at such an early age could enable clinicians to identify and treat children with

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developmental disorders, as well as, alert parents regarding the potential difficulties their child might experience, prior to the start of elementary school. This study was undertaken to assess the effect of birth weight on cognition, as well as the effect of catch up growth on cognition among term born small for gestational age (SGA) children at 5 to 6 years of age.

## MATERIALS AND METHODS

Seventy one children, of whom forty four AGA, 21 SGA and 6 LGA born were selected from private schools in Bengaluru. Approval and clearance from the institutional ethics committee was obtained before starting the study. Subjects with a birth weight of 2500 to 3999 grams were taken as AGA, birth weight < 2500 grams were taken as SGA and birth weight  $\geq$  4000 grams were taken as LGA. Children born LGA to mothers with gestational diabetes, who did not have any behavioural problems were included in the study. Children born preterm, with any neurodevelopmental disorder and those born to mothers who were hypothyroid or were on treatment during pregnancy were excluded from the study. All children aged 5 to 6 years irrespective of exclusion criteria of the selected school were tested to avoid ethical issues however their data was not included in the study. Written informed consent was obtained from the parents of the subjects. Data on parental age, educational status and occupation; order of the child; obstetric history and number of years of schoolings was obtained from parents of each child. Post natal growth was assessed by anthropometric indices which included recording height of the child for age and weight for age. BMI was calculated using the formula weight divided by height squared (kilograms per meters squared), with reference to the growth standards of 2007 WHO growth reference tables, provided separately for girls and boys (World Health Organisation, 2014). Temperament profile (Uma Hirisave *et al.*, 2011) was given to the teachers of children and asked to encircle the most appropriate description that fits the child. Only children with good temperament were included in the study.

### Cognitive assessment

NIMHANS neuropsychological battery of tests was administered, which is developed as a psychometric instrument for comprehensive neuropsychological assessment of children in the age range of 5–15 years (Uma Hirisave *et al.*, 2011 and Kar *et al.*, 2004). The battery has been standardized on a normative sample of 400 children. The test retest reliability coefficients of the various tests in the battery range from .53 to .82 that indicates a fairly good test retest reliability of the battery. All neuropsychological tests were individually administered to children in their familiar surroundings and in the presence of their teacher or parents. Total duration of the test was about 20 to 25 minutes. Two rest pauses of 5 minutes each were given during the entire course of tests.

These tests included:

### Motor speed

1) *Finger tapping test* (Jobbágy *et al.*, 2005): The subject is asked to tap the mounting key on a finger-tapping instrument

as rapidly as possible using the index finger of the preferred hand. A comparable set of measurements is then obtained with the non-preferred hand. Five trials are given for each hand, with each trial lasting for 10 seconds. This test takes about 1 minute. Average number of taps for each hand comprises the score.

### Attention

2) *Color cancellation test* (Uma Hirisave *et al.*, 2011): A measure of visual scanning/selective attention. It consists of 150 circles in red, blue, yellow, black and grey. The participant is required to cancel only the yellow and red circles as fast as they can. Number of circles/dots missed or errors made are also noted down. Time taken in seconds to complete the test comprised the score.

### Expressive speech

Expressive speech test (Foy and Mann, 2012) is administered to rule out any speech related deficits. It is assessed in a question answer form.

3) *Repetitive speech*: This is done to test the clarity of pronunciation of words & sounds. The subject is asked to repeat an increasing series of 3 to 4 simple sounds & word. Ex: sounds like 'ra, cha, ba, sa'; words like 'sun, cat, train, school'

4) *Nominative speech*: i) *Object naming*: Subject is asked to name 5 objects out of 10 pictured objects ii) *Categorical naming*: Subject is presented with a set of 5 words belonging to same category, and asked to give one word which defines the set. Ex: lion, tiger, elephant, monkey = animals iii) *One word naming*: Subject is presented with simple description and asked to name what it is. Ex: what is it that tells time = clock. The test takes 5 minutes. Each correct item is given a score of 1, and a summated score is obtained.

### Visuospatial function

5) *Visual discrimination*: A measure of visuoperceptual ability, like the child's ability to match shapes and geometric forms (Kapur *et al.*, 1991 and Krajewski and Schneider, 2009). Here the subject has to identify the odd figure out of the 4 figures on the card. This test takes 5 minute. Sum of the correct responses constitute the score.

### Memory

6) *Digit span* (Banken, 1985): The subject is asked to repeat numbers in the same order, as the examiner reads. The numbers are read at the rate of one/sec. Ex: 3, 7, 6. Highest number of digits repeated correctly is the score.

7) *Picture recall* (Uma Hirisave *et al.*, 2011): Subject is shown a row of pictures. After which the pictures are covered and the subject is asked to recall what he/she saw in the saw order.

Each picture correctly recalled is given a score of one. This entire test for memory takes about 5 minutes.

## Statistical analysis

The results are presented as mean  $\pm$  SD (standard deviation). The significance of any difference was tested with t- test, ANOVA followed by Bonferroni multiple comparisons and Chi square test wherever appropriate. Differences were considered statistically significant for P values  $< 0.05$ .

## RESULTS

The mean birth weight for children born AGA, SGA and LGA was 3.06, 2.10 and 4.05 respectively (Table 1). There was no difference amid the groups when maternal age during pregnancy, maternal education, paternal education and number of years of schooling was considered.

Hence these confounding variables had no effect on birth weight. Cognitive parameters among the three groups was compared as in Table 2. In this study we found that for test of attention, the time taken (in seconds) was greater in LGA and SGA when each was compared to AGA but the difference was not statistically significant. Number of colored dots/circle missed was higher in LGA and lower in SGA when compared to AGA, but this difference was not significant. The errors done by children in LGA were significantly higher than those in AGA (P=0.005) (Figure 1&2). While LGA and SGA attained lower scores for speech than AGA, the difference was significant only for SGA (P=0.002) (Figure 3). No such difference was found in visuospatial function and digit span (both forward and reverse).

**Table 1. Comparison of birth weight among the three groups (ANOVA followed by Bonferroni multiple comparisons)**

Group	Mean(kgs)	SD <sup>+</sup>	SE <sup>+</sup> of Mean	95% CI <sup>+</sup> for Mean		F	P-Value	Sig Diff Between
				Lower Bound	Upper Bound			
AGA (n=44)	3.06	0.37	0.06	2.95	3.17	105.918	<0.001*	AGA vs SGA (P<0.001)
SGA (n=21)	2.10	0.26	0.06	1.99	2.22			AGA vs LGA (P<0.001)
LGA (n=6)	4.05	0.08	0.03	3.96	4.14			S GA vs LGA (P<0.001)

\* Denotes significant difference (P<0.05) <sup>+</sup> SD –standard deviation, SE- standard error, CI – confidence interval  
AGA- Appropriate for gestational age, SGA- Small for gestational age, LGA- Large for gestational age

**Table 2. Comparison of cognitive functions among the three groups (ANOVA followed by Bonferroni Multiple Comparisons)**

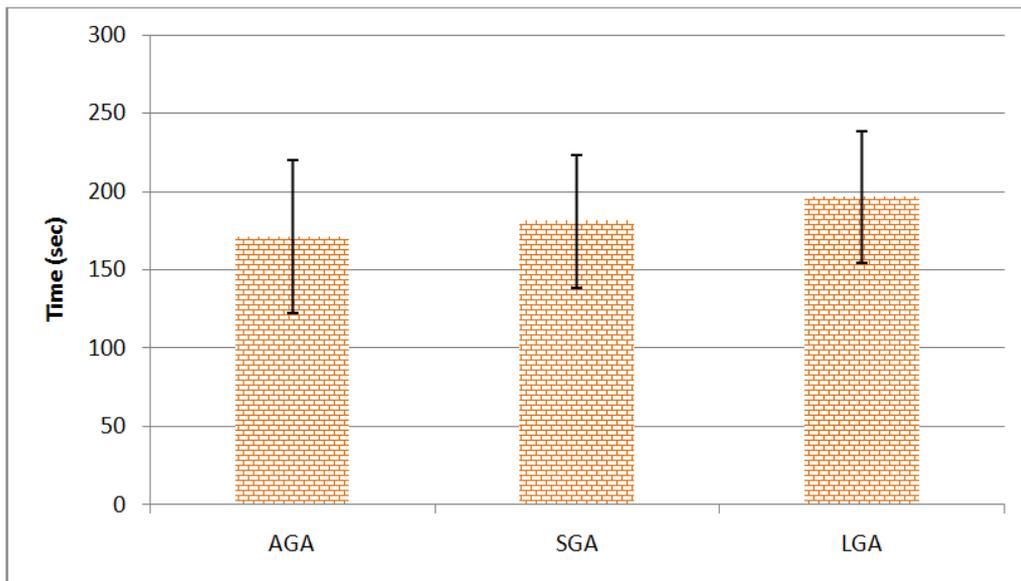
Parameters	Group	Mean	S D	SE of Mean	F	P-Value	Significant difference
Motor Speed (Right)	AGA	24.59	3.37	0.51	1.708	0.189	
	SGA	25.67	2.15	0.47			
	LGA	27.17	7.60	3.10			
Motor Speed (Left)	AGA	21.93	2.98	0.45	0.257	0.774	
	SGA	22.43	2.54	0.55			
	LGA	22.67	6.19	2.53			
Attention (time- secs)	AGA	171.41	48.92	7.38	0.917	0.404	
	SGA	181.14	42.54	9.28			
	LGA	196.50	42.14	17.20			
Missed	AGA	3.43	4.31	0.65	0.148	0.863	
	SGA	3.00	2.55	0.56			
	LGA	3.83	3.19	1.30			
Errors	AGA	0.34	1.10	0.17	5.317	0.007*	AGA vs LGA (P=0.005)
	SGA	0.62	1.43	0.31			
	LGA	2.33	2.88	1.17			
Speech	AGA	19.32	1.09	0.17	6.482	0.003*	AGA vs SGA (P=0.002)
	SGA	17.38	3.07	0.67			
	LGA	18.67	2.80	1.15			
Visuospatial function	AGA	9.98	0.15	0.02	1.357	0.264	
	SGA	9.95	0.22	0.05			
	LGA	9.83	0.41	0.17			
Memory (DS-F)	AGA	5.23	0.83	0.13	0.637	0.532	
	SGA	5.24	0.77	0.17			
	LGA	4.83	0.98	0.40			
Memory (DS -R)	AGA	1.50	1.11	0.17	0.914	0.406	
	SGA	1.19	1.25	0.27			
	LGA	1.83	0.98	0.40			
Memory (Picture Recall)	AGA				7.153	0.002*	AGA vs LGA (P=0.001)
	SGA	14.30	2.24	0.34			
	LGA	13.62	1.36	0.30			
		11.00	2.28	0.93			

\* Denotes significant difference (P<0.05), DS- F= Digit span Forward, DS- R= Digit span Reverse

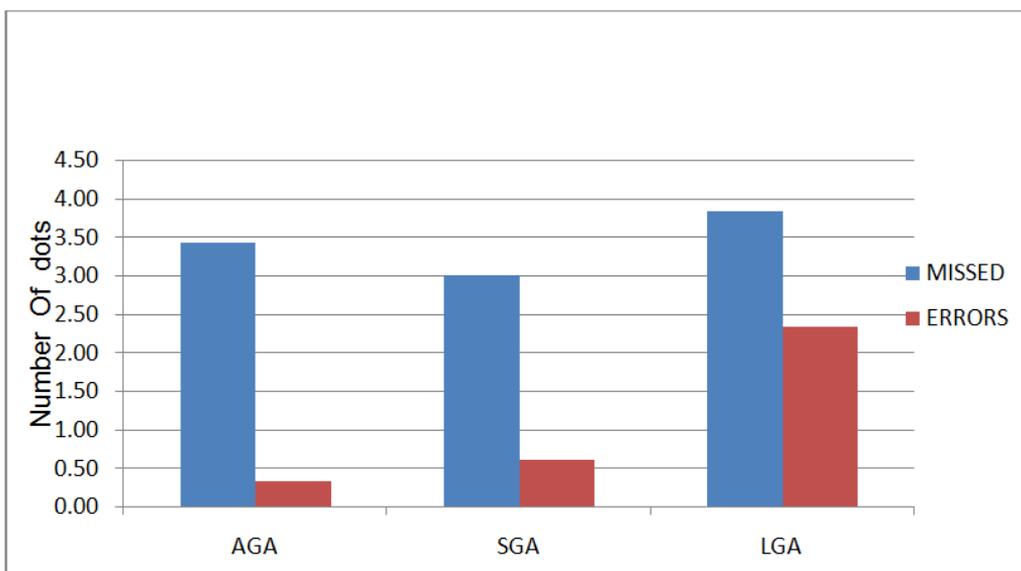
**Table 3. Comparison of cognitive scores between Normal and Underweight Children in SGA group**

Cognitive Parameters	BMI at age	n	Mean	Std Dev	SE of Mean	Mean Difference	T	P-Value
Motor Speed – Right	Normal	8	26.25	2.12	0.75	0.942	0.973	0.343
	Underweight	13	25.31	2.18	0.60			
Motor Speed – Left	Normal	8	23.88	2.17	0.77	2.337	2.243	0.037*
	Underweight	13	21.54	2.40	0.67			
Time (sec)	Normal	8	167.00	44.51	15.74	-22.846	-1.209	0.242
	Underweight	13	189.85	40.56	11.25			
Missed	Normal	8	2.00	2.78	0.98	-1.615	-1.448	0.164
	Underweight	13	3.62	2.29	0.64			
Errors	Normal	8	0.00	0.00	0.00	-1.000	-1.617	0.122
	Underweight	13	1.00	1.73	0.48			
Speech	Normal	8	19.13	1.64	0.58	2.817	2.234	0.038*
	Underweight	13	16.31	3.30	0.92			
Visuospatial Function	Normal	8	10.00	0.00	0.00	0.077	0.777	0.447
	Underweight	13	9.92	0.28	0.08			
Digit Span – Forward	Normal	8	5.38	0.92	0.32	0.221	0.631	0.536
	Underweight	13	5.15	0.69	0.19			
Digit Span – Reverse	Normal	8	2.13	1.13	0.40	1.510	3.278	0.004*
	Underweight	13	0.62	0.96	0.27			
Picture Recall	Normal	8	14.38	1.30	0.46	1.221	2.178	0.042*
	Underweight	13	13.15	1.21	0.34			

\* Denotes significant difference (P<0.05)



**Figure 1. Mean Attention time (sec) recorded in the groups**



**Figure 2. Mean Missed and errors recorded for attention in the groups**

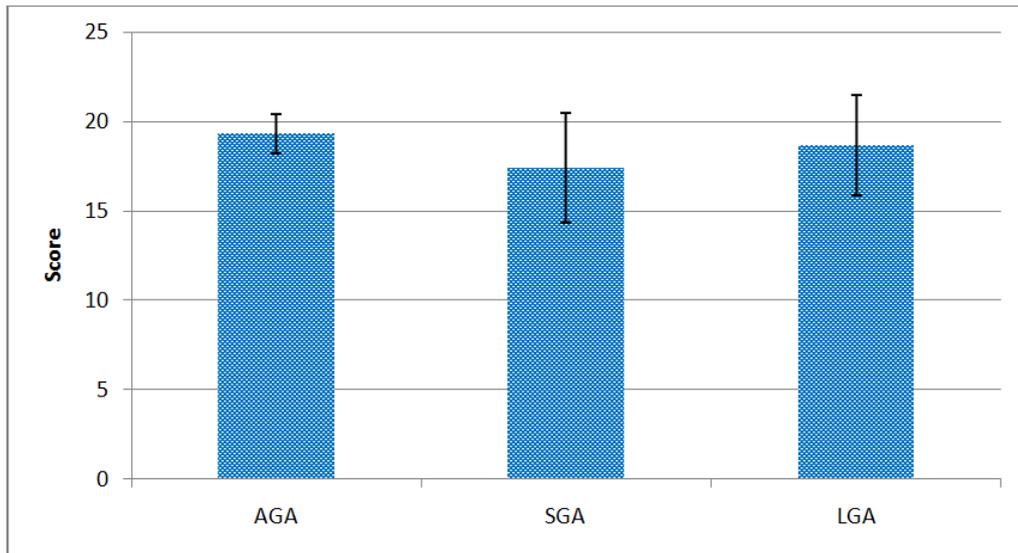


Figure 3. Mean speech scores recorded among the groups

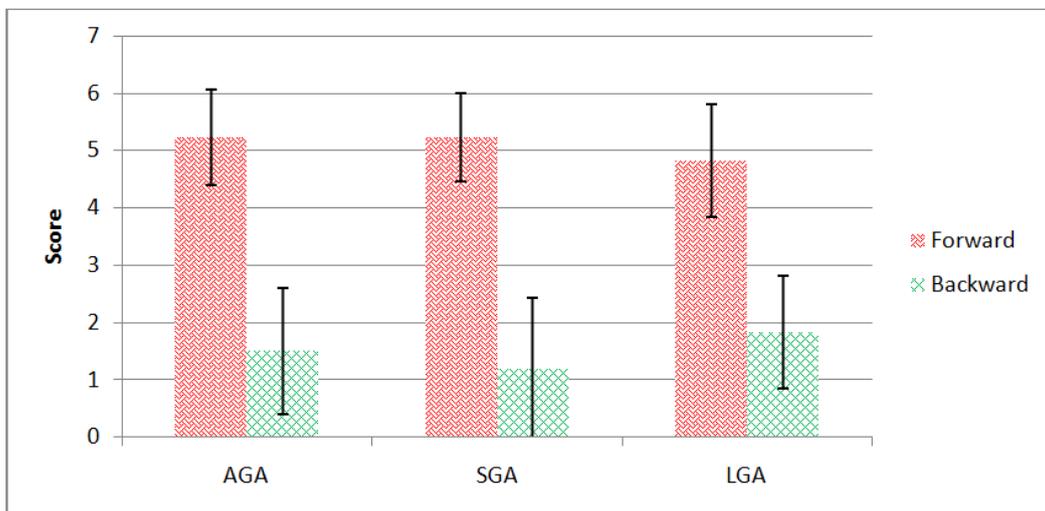


Figure 4. Mean Digit span score (memory) recorded in the groups

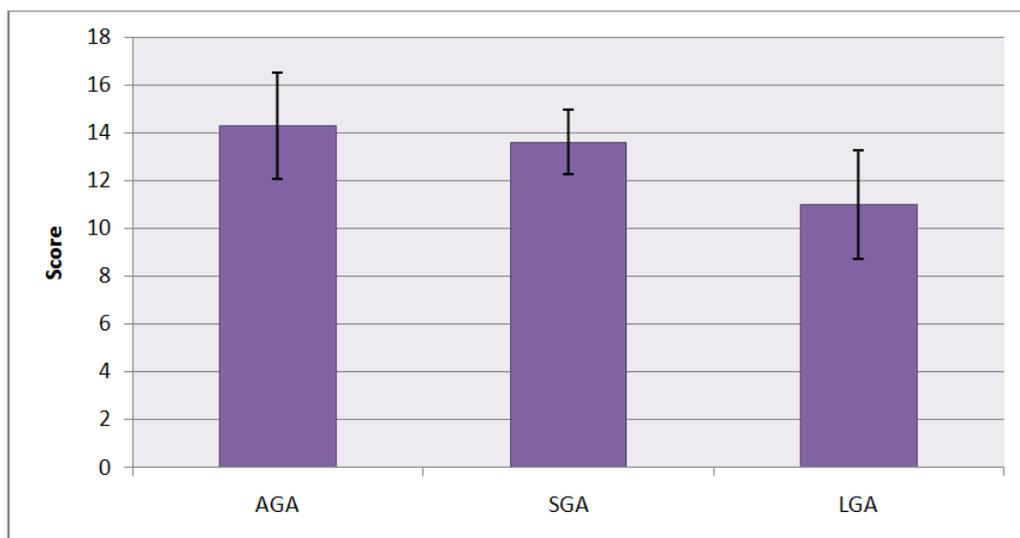


Figure 5. Mean Picture recall score (memory) recorded in the groups

However the ability to recall pictures was lower in both SGA and LGA when compared to AGA, but the difference was statistically significant only with reference to LGA. ( $P=0.001$ ) (Figure 4 & 5). Among the children born SGA, cognition was compared between those who had a catch up growth and attained the normal BMI and those who did not. We found that children who did not attain normal BMI (Still underweight) had significantly lower scores for motor speed of left hand ( $P=0.037$ ), speech ( $P=0.038$ ), & in tests for memory i.e reverse digit span (0.004) and picture recall (0.042) (Table 3).

## DISCUSSION

The size of an infant at birth which is a measure of gestational growth, has been recognized as a biomarker of future risk of morbidity. Both, being born SGA and being born LGA, were associated with increased rates of obesity and metabolic disorder, as well as number of mental disorders including ADHD, autism, anxiety, and depression (Grissom and Reyes, 2013). Maternal under nutrition and anemia are identified with intrauterine growth retardation. Most of the research done is on the effects of low birth weight and cognition in children. Previous research on the effect of birth weight on cognitive development have suggested that birth weight was positively associated with cognition up to the early adulthood, and with likelihood of obtaining advanced educational qualifications, after controlling for social background (Richards *et al.*, 2001). Many authors have reported that associations between body size and cognitive performance are dependent on socioeconomic circumstances and is more apparent in children of developing countries or in economically disadvantaged children of developed countries (Richards *et al.*, 2001; Tanner and Galton, 1966 and Cheung *et al.*, 2001). Thus proving that children of parents belonging to the lower socioeconomic status have lesser accessibility to products and health care services, leading to underweight babies who very often turn out to be underweight children. In our study all the children were selected from private schools and most of them belonged to higher socioeconomic class, thus the groups were homogenous with respect to social class. As a result, there was no association between birth weight and SES or parental demographic factors. Such an household provide better care to pregnant women and may also provide more cognitively stimulating growth environments later for the newborn, which may improve child's IQ. Similar observations of lesser influence of the confounding variables were noted by Richards *et al.* (2003) and Sommerfelt *et al.* (2000). In the above study we did not find any significant difference between the motor speed of children and birth weight. While most of the studies done in children born SGA have shown to have more motor problems when compared to children born AGA (Elgen *et al.*, 2003). In another study by Christian *et al.* (2014) the association between preterm birth, SGA and cognition among rural school age children were assessed and found that these children scored lower in finger tapping test.

While this contrasting finding in our study is again because of the homogenous group selected, with higher parental education and only term born children being included. One other reason could be because most of the children in the groups had

minimum of two to three years of schooling or preschool experience, where they are most often exposed to games that required better motor skills. In the present study children born LGA took more time to complete the simple colour cancellation test, used to assess selective attention in children and also the number of coloured dots/circles missed as well the errors committed were significantly higher when compared to AGA group. Thus suggesting that children born LGA had problems in focusing their attention. Even though the time taken and the number of errors made by SGA group was higher when compared to AGA group, this difference was not significant. Many published literatures have shown that over birth weight children were more commonly born to mothers with GDM. Delayed brain maturity is often observed in such LGA children when compared to controls. These children seem to have a higher rate of inattention and/or hyperactivity as observed by various tests and questionnaires (Ornoy, 2005).

Recent evidences show that obesity in pregnancy may be associated with central nervous system problems in the fetus and newborn. A review article suggests that a link may exist between pre-pregnancy overweight and obesity and symptoms of ADHD in children. Relatively little attention has been paid to the biochemical mechanisms that might underlie observed associations. The intrauterine milieu of obese pregnancy is complex but increased levels of oestrogen, cortisol, free fatty acids, pro-inflammatory cytokines and oxidative stress might play a role. Post-natal factors such as obstetric complications, childhood weight and health problems, or even sympathetic nervous system overactivity could also be involved (Kyrou and Tsigos, 2009; Zumoff and Strain, 1994; Ramsay *et al.*, 2002 and Chen and Scholl, 2005). In a follow-up cohort of 397 premature extremely low birth weight (ELBW) (501–1000 g) infants who were matched with normal birth weight control at 8 years and again during young adulthood (22 to 26 years) and found that these children had symptoms of ADHD 15 years later (Kutschera *et al.*, 2002). While such an observation was not found in SGA group of our study, this is because the mean birth weight in this group was 2100 grams and also only term born children were included. Hence all the children had scores which were similar to that of AGA group. Present study showed that both LGA and SGA born children attained lower scores for speech than AGA children but this difference was significant only for SGA born children. No such difference was seen in Visuospatial function of the children among the groups. Previous literatures have observed impaired language development in children born at term with birth weight below the 10<sup>th</sup> percentile for gestational age, assessed at 6 years of age. There were statistically significant differences in language comprehension, total expressive language (vocabulary, structure, content), naming skills and non-words repetition (Puga *et al.*, 2009).

In this study we found that in tests for assessment of memory, there was no significant difference in digit span, both forward and reverse amid the groups. However children born LGA scored lower in picture recall test when compared to AGA, and this difference was statistically significant. While SGA children also scored lower in picture recall test, this difference was not statistically significant. In relation to the present study, one other study investigated 13 infants of mothers with

Gestational diabetes mellitus (GDM) with 16 normal infants and reported that these children demonstrated a deficit in the ability to recall multi-step event sequence when a delay was imposed (Deboer *et al.*, 2005). In a UK based birth cohort, cognitive function was assessed at various ages with birth weight, height adjusted for weight in childhood and adulthood and educational attainment controlling for confounding factors and concluded that birth weight was positively associated with cognition up to the age of 26, and with a likelihood of obtaining advanced educational qualification (Uma Hirisave *et al.*, 2011).

While in contrast to our study, Mysore Parthenon birth cohort (31) concluded that compared to controls, offspring's of GDM scored higher in tests of cognitive assessment, measuring learning, memory, reasoning, attention and concentration, visuospatial and verbal abilities. A recent review has reported that there was no difference in cognitive ability among children born to mothers with or without GDM. However, offspring's of GDM's performed poorer in fine and gross motor functions when compared to controls. Further, this review also reported inverse associations of offspring's intelligence scores, attention, language development, learning, memory-span and mental and psychomotor development with the severity of GDM assessed by glycosylated haemoglobin level and ketonuria, thus suggesting that offspring cognitive performance could be within normal limits in well-controlled GDM (Park, 2013).

### Limitations

Our study had improper distribution of samples in the groups with smaller number of samples forming the LGA group which could have affected the outcome of the study. Most of the data obtained on birth weight, prenatal and postnatal child health was verbally obtained from the parents, thus there could have been a recall bias. Details regarding parental income which tells about the SES of the family could not be obtained as some parents were non compliant.

### Conclusion

Children born LGA had poorer scores in tests of attention and memory when compared to children born AGA. Children born SGA scored lower in tests for speech when compared to children born AGA. Among the children born SGA, children who did not have a catch up growth or those who were still underweight had lower scores for motor speed, speech and memory when compared to children who had a catch up growth and attained the normal BMI. Due to homogeneity among the groups with regard to SES, this confounding factor had no effect on birth weight or cognition. Though our study is by no means exhaustive, it does provide a glimpse into the neurocognitive changes that occur in children with respect to their birth weight. Although the effect of SGA on cognition is well documented, research on the cognitive development in children born LGA is found to be lacking and needs more emphasis. This is because of the increased prevalence of maternal obesity and diabetes which are the two most common causes for children being born LGA. Due to very small sample

size in LGA group in the present study, this effect could not be analyzed.

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