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SCOPE OF *BRAHMI* IN GROWTH AND DEVELOPMENT OF INFANTS

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ABSTRACT

Introduction: A strong foundation for lifelong physical and mental health can be laid by maximizing the growth and development (G&D) of an infant, especially that of brain, because CNS plays a dominant role in unifying the whole organism as the infant develops and moves from one cycle of growth to next. In *Ayurveda*, *Medhya dravyas* are primarily indicated for improving the functions of brain, apart from having a myriad of other useful effects. *Brahmi* (*Bacopa monnieri* Linn) is one such drug widely recommended in *Ayurveda* for promoting G & D of children, but paucity exists regarding scientific studies supporting such a use in infancy. **Aims and Objectives:** To assess the effect of *Brahmi* on G & D of infants. **Materials and Methods:** Randomized controlled clinical trial was done on 34 newborns, divided into two groups- Group A (receiving *Brahmi* syrup orally twice daily in dose of 8 mg dry extract/kg/dose) and Group B (control group). Anthropometrical assessment of growth was done at monthly intervals, developmental assessment by Gesell developmental schedule (at 4, 16, 28 weeks) and the first appearance of social smile was noted, and the results were statistically analyzed. **Results:** Albeit the babies of both groups mostly demonstrated results 'within normal limit; those of Group A often showed a general trend of having G & D on the earlier side of normal range. **Conclusion:** *Ayurvedic Medhya* drugs as *Brahmi* can play a promising role in maximizing the G&D within inherent genetic potential, and the early infantile period appears to be the best period for introducing them.

KEYWORDS: *Bacopa monnieri* Linn, *Brahmi*, Brain, Growth and Development, Infants, Neonates.

INTRODUCTION

Children's health is a nation's wealth, as a sound body and mind enhance the capacity of children to develop a wide range of competencies that are necessary to become contributing members of a successful society.[1,2] Science tells us that meeting the developmental needs of young children is as much about building a strong foundation for lifelong physical and mental health as it is about enhancing readiness to succeed in school.[3] It has also been clearly observed that environmental influences during the early postnatal life can significantly affect the pace and pattern of G & D.[4] Hence all attempts must be made to ensure transformation of an infant to his/her healthiest possible adulthood.

During first two years of life, both mental and physical growth is rapid. Human brain has 100 billion neurons at birth, with each neuron developing an average of 15,000 synapses by the age of three year.[5] The seat of all sensorimotor pathways, central nervous system (CNS), is the central force which becomes dominant and unifies the whole organism, as the infant develops and moves from one cycle of growth to next. Thus, both development (neurological maturity), as well as growth (physical maturity) is dependent upon maturation and myelination of CNS.[6] Hence it can be inferred that, for ensuring transformation of an infant to his/her healthiest possible adulthood, healthiest possible G & D of brain should be ensured.

There is growing evidence that certain standardized natural products have reproducible neurocognitive effects in humans, possibly because of their inherent poly-pharmacological properties. Herbal extracts may contain multiple active components which, in concert, may influence numerous neuronal, metabolic and hormonal systems involved in behavioural processes.[7] Ancient *Ayurvedic* literatures have profuse description of *Medhya dravyas*, the class of drugs used primarily for improving the functions of brain. But, apart from the traditional use in mental development, some *Ayurvedic medhya dravyas* may also be used to facilitate physical growth in children. *Bacopa monniera*, known as *Brahmi* is one such drug which has been frequently recommended in *Ayurvedic* classics for promoting G & D of children.[8] Animal studies have shown it to be an antioxidant,[9] memory enhancer, [10] antidepressant,[11] and to reduce the concentrations of beta-amyloid in a mouse model of Alzheimer's disease.[12] Human studies reveal consistent cognitive enhancement as a result of *Brahmi* administration across young, old and impaired adult populations.[13] The most robust effects of *Brahmi* are on memory performance, including positive effects on learning and consolidation of target stimuli,[14] delayed recall,[15] total learning,[16] visual retention of

information,[17] and working memory.[18] There is also evidence that it can improve the speed of information processing in both the inspection time task and rapid visual information processing.[18,14,19] *Brahmi* is thus perhaps one of the most scientifically studied in terms of mechanisms of action, but paucity exists regarding those specifically supporting its use for promoting G & D in infancy. Hence, *Brahmi* was selected specially selected for this study on assessment of effects of oral administration of *Brahmi* on G & D of infants.

MATERIALS AND METHODS

Sample Design

This randomized, controlled clinical trial was conducted upon the newborns delivered in patient department of *Kaumarabhritya/ Bal Roga*, Institute of Medical Sciences, Banaras Hindu University. This study started with the birth of the baby and continued till a maximum period of eight months age. The total numbers of follow ups were variable for each case, as despite the all efforts to ensure their timely follow up, some parents failed to present their babies in time and this tendency was observed more often as the baby grew older. Hence, for initial observations, a larger number of samples were available.

Inclusion criteria

- Healthy newborns (full term, appropriate for gestational age, without any perinatal complications, timely breastfed, etc).
- Their mothers were healthy, both ante- and post- natally (till the period of study).

Exclusion criteria

- Infant criteria: Pre or post term, twins, with any kind of pre- or peri- or post- natal complications, those receiving any medications other than *Brahmi* syrup.
- Maternal criteria: Infection(s) during pregnancy, any significant medical disorders (e.g., preeclampsia), use of any drug known to have impact upon the G & D of newborn.

Grouping of the sample

On the basis of above criteria, a total of 34 newborns were included in this study and divided randomly into following two groups

Group A (n=16) = Infants given *Brahmi* syrup

Group B (n=18) = Control group (Infants not given any medication)

Preparation of *Brahmi* syrup

Kwatha (decoction) of fresh *Brahmi panchanga* (all the parts of plant) was prepared as per the method described in *Sharangadhara Samhita*.[20] Dry extract of this *Kwatha* was obtained and *Brahmi* syrup was prepared from it in a concentration of 250 mg/ml, by the standard method of syrup preparation. This syrup was dispensed via dropper bottles.

Dose and administration

Brahmi syrup was administered orally to infants right after their birth and continued until the end of the study. It was given in a dose of 8mg/kg/dose, twice daily (once in morning & evening) after feed.

Assessment of drug response

In both these groups, following assessments were made:-

- 'Growth' was assessed at monthly intervals by anthropometrical evaluation.
- 'Development' was assessed at 4, 16, 28 weeks by Gesell's developmental schedule.
- 'First appearance of social smile' was observed to have occurred before 4 wks /between 4 to 6 wks /after 6 weeks.

Statistical analysis

A cross-sectional and longitudinal analysis of the collected data was done. Anthropometry was analyzed by way of mean, standard deviation paired't' test, intergroup-one way ANOVA F-test, multiple comparison test (least significant difference test) and percentile charts. Various parameters of Gesell developmental examination and first social smile were analyzed by chi-square test and percentages. A total of 23 variables and many sub variables were studied, but only the most remarkable ones are being given and discussed here. The results of ANOVA F-test, multiple comparison test have been given at the bottom of respective tables and during discussion.

OBSERVATIONS AND RESULTS

The gathered observations showed that albeit the babies of both groups mostly demonstrated 'within normal limit' findings of anthropometry, Gesell's developmental scale and social smile; those of Gp A often showed a general trend of having G & D on the earlier side of normal range. The overall G & D in both groups expectedly remained within normal range because for this study only healthy babies were selected. Infants of Group A also demonstrated an overall reduction in morbidity, which could be attributed to the

antibacterial,[21] antifungal, anti-diarrheal,[22] immunomodulatory and stress reliever properties of *Brahmi*.

Anthropometry

Weight [Table 1]: Comparison of the data of present study with the mean, standard deviation and selected centile of weight for age from birth to 8 months at 50th percentile,[23] showed that the treated group achieved the weight at 5th month, while the control group belonged to less than 25th percentile. At 6th and 7th month, the weight gain was found more significant in Group A in which achieved weight was near to 75th percentile, whereas control group had not achieved the weight mentioned at 50th percentile (near to 25th percentile).

Head Circumference [Table 1]: Inter group comparison of gain in head circumference in between subsequent months of both groups suggest that the gain in head circumference was highly significant in Gp A, but not in Gp B between the 5th and 6th month Although the ANOVA test has shown the insignificant 'P' value in both the groups.

Table 1: Weight, Head circumference & CHL (Crown to heel length) [unshaded areas represent absolute values, whereas shaded areas represent the change]

	Weight		Head circumference		CHL	
Follow-ups	**Mean & SD**		**Mean & SD**		**Mean & SD**	
	Group A	**Group B**	**Group A**	**Group B**	**Group A**	**Group B**
a. At birth	2.94 ± 0.43 (n=16)	2.96 ± 0.39 (n=18)	34.19 ± 1.65 (n=16)	34.33 ± 1.32 (n=18)	10.40 ± 1.51 (n=16)	9.97 ± 0.80 (n=18)
b. 1 month	4.00 ± 0.55 (n=16)	3.94 ± 0.52 (n=16)	36.29 ± 1.64 (n=16)	35.66 ± 1.33 (n=16)	10.76 ± 1.01 (n=16)	10.46 ± 0.75 (n=16)
c. 1 month – birth (paired 't' test)	1.06 ± 0.40 t = 10.55 p < 0.001 (HS)	1.00 ± 0.21 t = 18.83 p < 0.001 (HS)	2.11 ± 0.55 t = 15.47 p < 0.001(HS)	1.52 ± 0.52 t = 11.79 p < 0.001 (HS)	0.36 ± 0.95 t = 1.53 p > 0.05 (NS)	0.50 ± 0.19 t = 10.35 p < 0.00 1(HS)
d. 2 month – 1 month (paired 't' test)	1.08 ± 0.36 t = 12.07 p < 0.001 (HS)	1.02 ± 0.16 t = 22.21 p<0.001 (HS)	1.08 ± 0.36 t = 12.07 p < 0.001 (HS)	1.02 ± 0.16 t = 22.21 p < 0.001 (HS)	0.42 ± 0.22 t = 7.73 p < 0.001 (HS)	0.52 ± 0.15 t = 11.72 p < 0.001 (HS)
e. 2 month	5.08 ± 0.58 (n=16)	5.04 ± 0.51 (n=14)	38.14 ± 1.59 (n=16)	38.05 ± 1.40 (n=14)	11.18 ± 0.92 (n=16)	11.04 ± 0.72 (n=14)
f. 3 month	6.13 ± 0.65 (n=16)	5.94 ± 0.67 (n=14)	40.13 ± 1.54 (n=16)	39.87 ± 1.46 (n=14)	59.38 ± 2.53 (n=14)	11.41 ± 0.65 (n=14)
g. 3 month – 2 month (paired 't' test)	1.05 ± 0.23 t = 18.66 p < 0.001 (HS)	0.97 ± 1.16 t = 19.94 p < 0.001 (HS)	1.99 ± 0.30 t = 26.82 p < 0.001 (HS)	1.96 ± 0.17 t = 38.55 p < 0.001 (HS)	0.63 ± 0.36 t = 7.01 p < 0.001 (HS)	0.42 ± 0.17 t = 8.06 p < 0.001 (HS)

h. 4 month – 3 month (paired 't' test)	0.74 ± 0.21 t = 13.88 p < 0.001 (HS)	0.55 ± 0.09 t = 19.36 p < 0.001 (HS)	1.09 ± 0.17 t = 25.45 p < 0.001 (HS)	0.95 ± 0.27 t = 11.79 p < 0.001(HS)	0.33 ± 0.11 t = 12.21 p < 0.001 (HS)	0.37 ± 0.30 t = 4.12 p < 0.01 (HS)
i. 4 month	6.87 ± 0.65 (n=16)	6.35 ± 0.66 (n=15)	41.22 ± 1.58 (n=16)	40.69 ± 1.44 (n=15)	12.13 ± 0.96 (n=16)	11.60 ± 0.81 (n=15)
j. 5 month	7.48 ± 0.66 (n=16)	6.84 ± 0.8 (n=12)	42.19 ± 1.51 (n=16)	42.28 ± 1.69 (n=12)	12.45 ± 0.95 (n=16)	11.92 ± 0.91 (n=12)
k. 5 month – 4 month (paired 't' test)	0.61 ± 0.13 t = 18.81 p < 0.001 (HS)	0.56 ± 0.12 t = 15.60 p < 0.001 (HS)	0.97 ± 0.22 t = 18.01 p < 0.001 (HS)	0.87 ± 1.64 t = 1.68 p > 0.05 (NS)	0.32 ± 0.17 t = 7.41 p < 0.001(HS)	0.35 ± 0.16 t = 7.74 p < 0.001 (HS)
l. 6 month – 5 month (paired 't' test)	0.72 ± 0.19 t = 14.41 p < 0.001 (HS)	0.50 ± 0.11 t = 11.46 p < 0.001 (HS)	1.02 ± 0.29 t = 13.70 p < 0.001 (HS)	0.14 ± 2.12 t = 0.18 p > 0.05 (NS)	0.35 ± 0.15 t = 9.39 p < 0.001 (HS)	0.26 ± 0.14 t = 4.87 p < 0.01 (HS)
m. 6 month	8.21 ± 0.72 (n=15)	7.41 ± 0.51 (n=10)	43.22 ± 1.60 (n=15)	42.86 ± 1.41 (n=10)	12.86 ± 0.95 (n=15)	12.05 ± 0.78 (n=10)
n. 7 month	8.77 ± 0.84 (n=9)	7.77 ± 0.37 (n=6)	43.70 ± 1.85 (n=9)	42.86 ± 1.34 (n=5)	13.10 ± 1.14 (n=9)	12.08 ± 0.61 (n=6)
o. 7 month – 6 month (paired 't' test)	0.62 ± 0.10 t = 19.21 p < 0.001 (HS)	0.48 ± 0.12 t = 10.13 p < 0.001 (HS)	0.67 ± 0.13 t = 12.85 p < 0.001 (HS)	0.44 ± 0.11 t = 8.63 p < 0.01 (HS)	0.27 ± 0.18 t = 4.44 p < 0.01 (HS)	0.25 ± 0.12 t = 5.00 p < 0.01 (HS)
p. 8 month – 7 month (paired 't' test)	0.64 ± 0.10 t = 17.43 p < 0.001 (HS)	-	0.63 ± 0.05 t = 30.04 p < 0.001 (HS)	-	0.73 ± 1.88 t = 1.09 p > 0.05 (NS)	-
q. 8 month	9.61 ± 0.75 (n=7)	8.5 ± 0.71 (n=2)	45.25 ± 1.40 (n=6)	44.33 ± 1.53 (n=3)	13.66 ± 0.92 (n=8)	12.70 ± 1.84 (n=2)

Weight: ***Multiple comparison test (MCT) / Least significant different test:***

Gp A vs Gp B: Significant difference (< 0.05).

Head circumference: ***Multiple comparison test (MCT) / Least significant different test:***

Gp A vs Gp B: Significant difference (< 0.05)

CHL: ***Multiple comparison test (MCT) / Least significant different test:***

Gp A vs Gp B: Significant difference (< 0.05).

CHL (Crown to heel length) [Table 1]: Comparison of CHL for age data of present study with the mean, standard deviation and centile of length for age from birth to 8 months at 50th percentile , showed that Gp A achieved the CHL at 3rd, 4th, 5th, month, while control group remained to < 25th percentile. At 6th and 7th month, the gain in CHL was found more

significant in Gp A in which the CHL was achieved beyond the 50th percentile. The control group had not achieved CHL even at 50th percentile (25th percentile), whereas Gp A achieved that at 75th percentile.

Gesell's developmental examination

Prone [Table 2]: At 4 wks, 'crawling movement' in prone position was attained by all infants of Gp A**.** At 16 wks, 41.18% infants had not achieved the 'verge of rolling' in control group. In fact, the infants of *Brahmi* group had achieved almost all of the expected development within due time.

Table 2: Prone.

	Crawling at 4 wks		Verge of Rolling at 16 wks	
	Yes	Yes	Yes	No
Group A (n_4=16) (n_{16}=16)	14 (87.5%)	11 (100%)	15 (93.75%)	1 (6.25%)
Group B (n_4=18) (n_{16}=17)	10 (55.56%)	4 (66.67%)	10 (58.82%)	7 (41.18%)
	χ^2 test = 5.33, p > 0.05 NS		χ^2 test = 17.78 p <0.001 HS	

Standing at 28 wks [Table 3]: Infants of Gp B achieved the 'bounces actively' milestone before 28 weeks, whereas few infants in Gp D (33.33%) had not achieved the same. The children of group B used to bounce vigorously with cheerful mood. However, owing to small sample size, chi square test showed the value to be insignificant.

Table 3: Standing (at 28 wks).

	Bounces actively	
	Yes	No
Group A (n=11)	11 (100%)	0 (0%)
Group B (n= 6)	4 (66.67%)	2 (33.33%)
χ^2 test	χ^2 test = 3.47 p > 0.05 NS	

Dangling ring and Rattle [Table 4]: At 4 wks, the developmental milestone 'regards line of vision' was not achieved by 11.11% of the children of Gp B whereas in Gp A all the infants had achieved it, however the difference is not significant (Chi square=3.32). At 16th week, when 'regards immediately' milestone was observed, the difference was significant as suggested by early recognition and quick response to the object.

Table 4: Dangling Ring and Rattle.

	4 weeks : Regards line of vision only		16 weeks Regards immediately	
	Yes	**No**	**Yes**	**No**
Group A (n_4=16) (n_{16}=16)	16 (100%)	0 (0%)	16 (100%)	0 (0%)
Group B (n_4=18) (n_{16}=17)	16 (88.89%)	2 (11.11%)	13 (76.47%)	4 (23.53%)
χ^2 test	χ^2 test = 3.32 p > 0.05 NS		χ^2 test = 8.57, p < 0.05 S	

Social smile [Table 5]: In this study, first appearance of 'social smile' was also watched for. When observed at 4 weeks, it had been achieved by 31.25% infants of Gp A and none from the Gp B.

Table 5: Social smile.

	By 4 weeks			4-6 weeks			After 6 weeks		
	Total	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**
Group A (n=16)	5 (31.25%)	5 (100%)	0 (0%)	11 (68.75%)	6 (54.55%)	5 (45.45%)	0 (0%)	0 (0%)	0 (0%)
Group B (n=18)	0 (0%)	0 (0%)	0 (0%)	16 (88.89%)	8 (50%)	8 (50%)	2 (11%)	0 (0%)	2 (100%)

DISCUSSION

The class of 'smart drugs' which primarily enhance brain's natural functions are termed as 'Nootropics'. They do so by various methods, such as increasing brain's oxygen supply, increasing glucose utilization, stimulating nerve growth, cleansing the brain of lipofuscin etc.[24] The equivalent class of drugs described in *Ayurvedic* literatures are the *Medhya Dravyas*, which work as *Rasayana* – at the level of *Poshaka rasa* (nutrition)/ *Agni* (metabolism)/ *Srotasa* (body channels). The seat of all sensorimotor pathways, CNS, plays a dominant role in unifying the G&D of an organism and hence *Medhya* drugs can be expected to influence mental development as well as physical growth of an infant, as was apparent from this study with *Brahmi*.

Analysis of anthropometrical results showed that in comparison to untreated group, the growth in *Brahmi* treated group mostly remained towards the higher side of normal ranges of centiles. This suggests that such drugs belikely enhanced the bioavailability of the nutrients at cellular level, thus reflecting the *Rasayana* property of *Brahmi*. This intergroup difference in

growth may in fact become more marked on subsequent follow ups, if drug is administered for prolonged periods.

Analysis of developmental progress in different groups shows that the children of *Brahmi* treated groups had reached almost all the indicated development for 'prone position at 4 and 16 weeks in time, probably because of a minimal effect of stress producing environmental factors or advanced maturation of prefrontal cortex that controls thought, behavior and mood. The children of group A were also seen to 'bounce vigorously' with cheerful mood [Table 3], which may be due to augmentative effect of such drugs on maturation of vestibulospinal spinal fibers, that acts in opposition to rubrospinal system (which maintains the tightly flexed limbs in newborns), resulting in enhanced mobility of limbs. Early recognition and quick response to the objects as 'dangling ring & rattle' [Table 4] suggests an improved early decision making capacity in babies of group A. These findings appear even more significant in the light of the fact that synaptic density increases from birth to eight month of age in visual cortex and to about twelve months of age in frontal cortex.[25] Early appearance of social smile [Table 5] in *Brahmi* treated group could be because of quicker maturational progression of auditory, somatosensory and visual developmental sequences.

CONCLUSION

Ayurvedic Medhya drugs as *Brahmi* can play a promising role in maximizing the G&D within inherent genetic potential, and the early infantile period appears to be the best period for introducing them. Because CNS plays a dominant role in unifying the G&D of an organism and *Ayurvedic Medhya drugs* promote a healthy development of brain, oral administration of drugs as *Brahmi* can not only accelerate mental development, but may also enhance (physical) growth velocity of an infant. However, a detailed study on larger samples is required to affirm these results.

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