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TILAK A. VENKOBA RAO ORATION AWARD

RESEARCH IN PSYCHIATRIC GENETICS IN INDIA[1]

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Mr. Chairman, Respected Colleagues, Ladies and Gentlemen, I feel specially privileged to be selected for the First TILAK ORATION on Biological Psychiatry by the Indian Psychiatric Society. I am deeply aware of the honour and thank you all for the same.

The present oration is devoted to young age in more than one way. It is notable that a personal loss of the family of Prof. A. Venkoba Rao, I am referring to the untimely demise of Tilak, has been the starting point for the oration. Tilak was only 26 years old, no age to see ones own creator, when fate snatched him away from the mortal world. It has been a very thoughtful gesture on the part of the family to consider someone young to deliver an oration every year.

I have chosen the topic of 'RESEARCH IN PSYCHIATRIC GENETICS IN INDIA' for the oration. As I mentioned earlier, the oration being for those less than 40 years, it is natural that I should draw material from sources other than my own research work for the oration. Around 10 years of experience in the profession is too short a time to have done enough personal work to be the sole subject of the oration. In view of this, I ask your indulgence to be with me in the next 45 minutes as (i) I share with you the excitement of my own research efforts in psychiatric genetics, (ii) review the Indian literature for comprehensive understanding of the topic and lastly, suggest a few areas for future research in this area.

Of the aetiological studies of mental disorders, genetic studies have been important since the beginning of the Century. The initial efforts were to sort out the 'NATURE-NURTURE' controversy. Following the twin studies and more recently from the adoption studies, the focus of attention has moved from the either-or approach to one of the mechanism of interaction of the genetic predisposition and environmental influences (Slater and Cowie, 1971).

The methods used for genetic research in psychiatry have been, (i) twin studies, (ii) family studies, (iii) adoption studies, (v) population studies (especially for mental handicap) and (v) study of genetically determined characteristics like blood groups and dermatoglyphics.

At the beginning of the broad survey of work, it is appropriate to point out that genetic research had received very low priority in India. A recent major review of the area brought out as two volumes titled MEDICAL GEENTICS IN INDIA (Verma and Puri, 1978) contains very little reference to mental disorders other than mental handicap. There have been no twin studies, no adoption studies in the Country. Only a limited number of family studies have been undertaken in functional psychosis. The method of population screening has been widely employed for the study of mental handicap. This limited work in this area of psychiatric research, in contrast to what is happening in the West, is largely due to limited professional training as well

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as the limited facilities for genetic work. Thus, even those who have studied problems in this area, efforts have been to choose simple methods like blood group, family study and dermatoglyphics as research tools.

Historically, one of the first reports that I was able to trace was a report by Narayanam (1952). He studied the prevalence of congenital defects of the external ear and found that it was present in 78% of the Institutionalised patients in contrast to only 2% in the general population. The next significant report is a report on Mongolism from Bangalore (Verghese and Murthi Rao, 1961) in 1961. In the last two decades, there have been more than 100 reports in the published literature. They vary from single case reports to well planned prospective studies, the former being the most common. My attempt is to share with you the collected knowledge and suggest future avenues for work.

My personal interest in this area of work was stimulated by Prof. Rose Chacko, of C. M. C. Vellore in 1971 when I was having my first experience in Psychiatry. We began an initial study with schizophrenics but this data was never published. I recall with gratitude the guidance provided by Prof. Chacko which was the foundation on which future work was carried out. At PGI, Chandigarh, under the guidance of Prof. Wig I took up the subject of DERMATOGLYPHICS IN SCHIZOPHRENIA for my M. D. Thesis work. This choice of the topic was partly due to my earlier exposure and I must admit, partly due to my initial difficulties with Hindustani and Punjabi language spoken by patients. I thought looking at hands of patients was easier than doing follow-up or phenomenological work which was the area of interest at that time in the department. It is ironic that, in less than three years my focus of research took me right into the community which made me lose my fears of talking in the local languages.

FUNDAMENTALS OF DERMATOGLYPHICS

The palms and soles of all primates bear ridged skin. This includes man. The function of the ridged skin is apparently associated with the prehensile use of hands, feet and tails. In man the entire palmar surface of the hands and fingers and of the plantar surfaces of the feet and toes are ridged. The STUDY OF THE RIDGED SKIN IS CALLED DERMATOGLYPHICS. Until 1926, there was no specific term for the study of dermal ridges. It was in that year that Cummins and Midlo, proposed the word Dermatoglyphics (derived from derma-skin, and glyphe-carve).

Dermal ridges have various notable characteristics which make them important, not only in personal identification but also in human biology for the following reasons : (i) unlike lost human traits dermal ridges and configurations are formed and not affected developmentally by age, (ii) throughout post-natal life they are not affected by the environment, (iii) detail structure of the individual ridges are extremely variable, and (iv) although the patterns formed by the ridges vary in size, shape and detailed structure, they can be classified into several main types.

FORMATION OF DERMATOGLYPHICS

Ridges develop in relation to the volar pads. The volar pads are evident at about the 6th week of gestation and reach their maximal size by the 12th to the 13th week. At this time, patches of elevated ridges become evident and grow and coalesce as the volar pads regress. By the fourth month the epidermal ridges are well developed but

the process is probably not complete before the sixth month. The epidermal ridges form in a cranio-caudal manner. Once completed, the ridges remain unchanged except in size for life in terms of the detail structure of the ridges or the ridge patterns. The effect of Environmental factors can be only in the uterus at the time of ridge formation. Thus the patterns that characterise an individual are determined with finality at birth.

The analysis of the finger and palm prints is carried out both qualitatively and quantitatively. These are presented in detail by Penrose (1968), Cummins and Midlo (1961) and Cherill (1954). Similarly the process of taking a print is simple.

The inheritance of these patterns and quantitative characteristics are not fully understood. On the basis of the current knowledge it can be said that the total ridge count has a greater clarity in terms of hereditability, followed by 'atd' angle and the patterns in the fingers and palms in that order. This limitation in the mode of transmission is one of the limitations of its use in research work. Some of the hypotheses suggested for the mode of inheritance or control of expression are: (i) dominance is almost absent, (ii) it is a multifactorial character in which the genes are additive, (iii) there is no indication of sex-linked inheritance and (iv) the contribution from environmental factors is very little.

STUDIES IN SCHIZOPHRENIA

The research work we undertook at Chandigarh was the study of 240 schizophrenics using standard diagnostic criteria and comparison with a control population (200) of the same ethnicity. There were 120 patients of each sex and 100 persons of each sex in the controls. Efforts were made not to include those with other familiar illnesses in both the groups. More details of the process of patient choice, subcategorisation and analysis of prints is presented elsewhere (Srinivasa Murthy and Wig, 1977a).

The study showed that there were differences between the normals and schizophrenics in the qualitative and quantitative features. Further it was noted that there were differences between the four sub-categories of schizophrenia studied. Further analysis showed that among the schizophrenic patients, those with family history of schizophrenia and those without, were different in the pattern distribution (Srinivasa Murthy and Wig, 1977b). There was an accentuation of the difference between the normals and schizophrenics in the group with a positive family history.

Review of literature relating to 28 studies in India and abroad has been published recently (Balgir and Srinivasa Murthy, 1982).

STUDIES IN AFFECTIVE DISORDERS

The next series of studies were carried out in regard to affective disorders. Mr. Balgir, an anthropologist was chiefly involved in this phase of study (Balgir, 1982).

The sample of the study consisted 175 MDP patients (100 Males and 75 females) and 200 normal controls. Standard diagnostic criteria were used both for the diagnosis of affective psychoses and the subcategorisation into unipolar (UP) and bipolar (BP) patients. The findings showed that the MDP and normals differed in a number of dermatoglyphic characteristics (Balgir et al., 1978). Further, it was noted that the UP and BP were also significantly different from each other.

In another smaller study with a sample of 60 neurotic depressives, differences were noted among the normals

and neurotic depressives. However, the neurotic depressives and affective psychosis did not differ in the dermatoglyphic characteristics. As pointed the sample size of neurotic was small and this needs to be studied further before firm conclusions can be drawn.

COMPARISON OF MDP AND SCHIZOPHRENIA

An attempt was made to compare 240 schizophrenics and 120 MDP. The results showed that the male MDP differed significantly with male schizophrenics in the finger patterns and palmar patterns. On quantitative analysis, difference was noted in the 'atd' angle with the MDP group showing larger 'atd' angle (Balgir et al., 1980).

To-date no large scale studies of MDP have been undertaken outside the Chandigarh centre. The only other report is that of Narayanan and Mallikarjuniah (1980) from Bangalore with a smaller sample.

At this point it will be worthwhile looking at the reasons for different results by different investigators. Methodological problems arise by not being rigid about (i) diagnosis, (ii) sex distribution, (iii) homogeneity of the sample, (iv) adequacy of the controls, (v) type of analysis undertaken and the statistical treatment of the data (Reviewed in detail by Balgir and Srinivasa Murthy, 1982).

OTHER GENETIC RESEARCH IN SCHIZOPHRENIA

Approaches studying the genetics of schizophrenia in India other than dermatoglyphics is an area for future work. There is a single report each of chromosomal study in schizophrenics (Chatterjee and Basu, 1980) and morbidity of disorders in relatives of schizophrenics (Sethi et al., 1980). In both the studies it was noted that there is more morbidity in the families and individuals as compared to the control population. This needs to be studied in greater depth.

Two interesting reports have been recently reported about the schizo-affective psychoses as a different diagnostic entity. The Patiala report (Gurmeet Singh and Sachdeva, 1982) found this group to be closer to MDP than schizophrenia while the Manipal report (Raju and Mani, 1982) consider it as a separate entity.

Other genetic research issues in schizophrenia as to the relevance of genetic factors in relation to phenomenology, course and outcome, response to physical methods of treatment and association of cerebral abnormalities are the areas not studied to-date.

OTHER GENETIC RESEARCH IN AFFECTIVE DISORDERS

There is general recognition from different parts of the world that affective psychoses can be divided at least into two major subgroups, namely the unipolar and the bipolar groups (UP and BP).

The first attempt to examine this issue in the Indian setting was made at Madurai (Venkoba Rao, 1973, 1974). In a family study of 101 endogenous depressives, it was reported that there were no differences between the first attack depressives, recurrent depressives and BP group. A similar report was the result of the research work of Chopra (1975) from Ranchi. This was in strong contrast to the reported differences from Western centres. Some of the reasons for such negative reports were probably due to the sample characteristics and other aspects of the study (Srinivasa Murthy, 1975). These negative reports have not been supported by studies from Patiala (Gurmeet Singh and Agarwal, 1980) and

Chandigarh (Gupta and Srinivasa Murthy, 1980). Both these groups report that the affective psychosis consists of two entities namely UP and BP. Further differences were noted in the blood group distribution (Gurmeet Singh et al, 1979). The BP group show greater frequency of O blood group. The issue is still open. Another interesting attempt was made to study the lithium prophylaxis and genetic aspects (Ghosh et al., 1977). It was noted that positive family history was related to better response to lithium therapy.

An interesting controversy, with genetic implications, exists in the country. I am referring here to the reported differences in the prevalence of affective disorders in the North and South India. It is reported that affective disorders are more in North (Gurmeet Singh, 1979, Raju, 1979). However, the conclusions are largely based on hospital based data. This again is an interesting area for genetic work and multi-ethnicity in the country can provide rich material for work.

GENETIC STUDIES OF MENTAL RETARDATION

A large number of publications relate to the genetic disorders causing mental retardation. The research in this area falls into four groups: (i) case reports, (ii) systematic surveys of patients for inborn errors of metabolism, (iii) studies to elucidate other genetic theories and causation, (iv) chromosomal disorders, especially relating to Mongolism.

CASE REPORTS

Nearly all major types of metabolic disorders have been reported from different parts of the country. Though there are regional concentration of the reported cases, there is at present not sufficient evidence to see regional differences. It is noted that centres start reporting cases when they look for them and have the facility to investigate the cases.

The cases reported are of phenylketonuria (Chandra *et al.*, 1968, Joshua *et al*, 1968), Hartnup's disease (Srikantia *et al*, 1964, Rao *et al*, 1970, Nair and Rao, 1971, Somasundaram and Papakumari, 1973), homocystinuria (Verma and Sinclair, 1970, Verma *et al*, 1974, Narayanan *et al*, 1978), alkaptonuria (Verma, 1968, Chitra *et al*, 1976) Hurlers disease (Narayanan *et al*, 1971), tyrosinosis (Jaiswal, 1973) histidenemia (Rao et al, 1974) cystinosis (Sunderavalli *et al*, 1975) In addition other hereditary disorders like tuberous sclerosis has been reported by Somasundaram (1968) and Vyas *et al.* (1978).

SURVEYS FOR INBORN ERRORS OF METABOLISM

A number of such studies are available in the country. Surveys for phenylketonuria have been conducted by Centerwall and Ittyerah (1966), Punekar (1968), Sharada and Polassa (1968), Joshua (1973), Rao *et al.* (1973) and Bharucha (1977). Of the studies, the studies at NIMHANS, Bangalore are representative of the knowledge from these surveys. A comprehensive survey of inborn errors of metabolism associated with mental handicap involving 2000 children was carried out. All the children were below 12 years of age. Authors found 50 (2.5%) to have one or other inborn errors of metabolism. The most common of these was PKU (44%) followed by Hurler's syndrome (24%) (Rao, Narayanan, and Subash, 1981). What is interesting is the observation of the authors that all of them had consanguinously related parents and in many of them consanguinity was present in earlier generations as well.

The remarkable aspect of the inborn errors is that the Bangalore centre accounts for 67% of cases reported from the Indian subcontinent. Further, 75% of the cases originate from Karnataka. This concentration of cases needs further study as opined by the authors-namely, (i) has the high rate of consanguinity contributed substantially to the number of homozygotes for this autosomal recessive disorder ? Is the relatively high frequency due to comprehensive biochemical monitoring of an at-risk population ? Is there a particularly high risk group in the population ? Has the PKU gene any heterozygote advantage in the local population ? Definite answers to these questions need to be found based on systematic chemical screening of the newborn (Rao. *et al*, 1981).

CONSANGUINITY

Consanguinity and mental handicap raises important public health questions. Repeatedly investigators have found among the parents of the mentally retaded a greater frequency of this inbreeding. In Rao *et al's* study (1981) refeired earlier, all inborn errors occurred from these types of marriages. Similar reports have come from Vellore (Centrewall, 1965, Centrewall and Centrewall, 1966), Delhi (Sinclair, 1972), Bangalore (Narayanan and Rao, 1978) and Tirupati (Indira Bai and Sastry, 1978). What is reported is indicative of a greater association of mental retardation in consanguineous marriages. There are reports of familial mental retardation being more is also there.

On the face of it, the issue looks clear and the evidence convincing. However, the issue is more complicated. In a series of reports in Medical Genetics in India (Verma and Puri, 1978) this issue has been discussed. Rao (1978) from Vellore studied prospectively, 6169 non-consanguineous and 5459 consanguineous marriages and found congenital malformations not to be significantly different in the two groups. Puri *et al.* (1978) from Pondicherry studied 3206 children in a similar survey and found that there was enhanced frequency of autosomal recessive disorders in consanguineous marriages, especially those families practicing it in two or more generations. In terms of mental retardation, there was significantly increased risk seen in groups other than Brahmins. Disorders noted were primary microcepaly, icthyosis congenita, Hurlers syndrome, albinism, Laurence-Moon Beidl syndrome and Mongolism. The increased risk was estimated as 1½ to 2 times over non-consanguineous marriages.

These contrasting reports call for futher work in the community. The implications and future areas for work has been suggested by Vasalu (1978) and Malhotra (1978). Malhotra (1978) summarises the situation as follows : to date about 10 studies have been conducted in evaluating effects of inbreeding. The results obtained are to some extent contradictory. While Sanghvi, Rao, Jacob and Jayabal found no significant differences in malformation rates, Dronamraju and Meera Khan, Centrewall and Centrewall, Kumar *et al*, Murty and Janice, Basu and Rao and Mukharjee reported high frequency of congenital malformations and total morbidity. Most of these studies were retrospective in nature except that of Rao (1976) and were hospital based. The contradictory results obtained may be due to (i) difference in ethinicity of the groups, (ii) the parameters considered and the variability in definitions, and (iii) due to lack of non-inbred controls. Thus this area remains open for future work.

MONGOLISM

Reports of characteristics of Mongol children have been made from different parts of the country. One of the earliest reports was from Verghese and Murti Rao (1961). These have been followed by reports from Andhra Pradesh (Rao *et al*, 1973), Madras (Rafi and Marimuthu, 1977), Somasundram and Papakumari, 1978). The one comment to which I want to draw your attention relates to the maternal age of the mongols. Verma and Singh (1975) found Mongol children being born to mothers of older age group, while Rao *et al.* (1973) and Somasundaram and Papakumari (1978) found the mothers to be young. This raises the question whether the maternal age is less important in India, or it is due to poor age recording. This again is an area for community based sample and rigorous methodology.

SUMMARY AND CONCLUSIONS

The current review of the genetic research at Chandigarh in which I was personally associated and the other reports point to large lacunae in our understanding of genetic aspects of mental disorders in India. The review has also brought forth the need for further work in this area. There are many areas for study of major public health importance. Some of them are specially part of our need like inbreeding effects on mental handicap and others are of universal importance. I would like to suggest FOUR major areas for future work, namely,

(i) Studies of inbreeding and mental retardation

(ii) studies of disputed diagnostic syndromes like hysterical psychosis, schizo-affective schizophronia,

(iii) In ter-regional differences in prevalence of different mental disorders,

(iv) genetic studies relating to course, outcome and therapeutic response in major mental disorders.

I would like to end this oration, recalling with gratitude the opportunity provided by the Indian Psychiatric Society and specially Prof. Venkoba Rao and family for this encouragement to young mental health professionals. I hope the future work will throw light in areas of darkness in our understanding of mental disorders and aspects of mental health.

THANK YOU, again.

BIBLIOGRAPHY

Author's Publications on Psychiatric Genetics

SRINIVASA MURTHY, R., GHOSH, A., AND KAUL, S. (1974). Dermatoglyphics in Manic Depressive Psychosis. *Bulletin of PGI.*, **8** : 74-76.

SRINIVASA MURTHY, R. (1975). Unipolar and Bipolar depression : Are they different? (Lto Editor) *Indian J. Psychiatry*, **17** : 159-160.

SRINIVASA MURTHY, R. AND WIG, N. N. (1977). Dermatoglyphics in Schizophrenia-relevance of family history. *Brit. J. Psychiat.*, **130** : 56-58.

GHOSH, A., WIG, N. N. AND SRINIVASA MURTHY, R. (1977). Prophylactic value of lithium in MDP-genetic aspects. *Indian J. Psychiat.*, **19** : 73-76.

SRINVASA MURTHY, R., AND WIG, N. N. (1977). Dermatoglyphic study of male schizophrenics. *Indian J. Psychiat.*, **19** : 48-51.

BALGIR, R. S., GHOSH, A., SRINIVASA MURTHY, R. AND WIG, N. N. (1978). Dermatoglyphics in MDP. *Indian J. Psychiat.*, **20** : 384-389.

BALGIR, R. S., GHOSH, A. AND SRINIVASA MURTHY, R. (1978). Qualitative dermatoglyphics in depressive neurosis. *Bulletin P.G.I.*, **12**: 187-191.

BALGIR, R. S. SRINIVASA MURTHY, R., AND WIG, N. N. (1978). A comparative study of dermatoglyphics in depressive neurosis and MDP. *Acta Anthropogenetica*, **2** : 33-40.

GUPTA, S., AND SRINIVASA MURTHY, R. (1980). Genetic study of MDP. *Indian J. Psychol. Med.*, **3** : 41-44.

BALGIR, R. S. SRINIVASA MURTHY, R. AND WIG, N. N. (1980). Maniv depressive psychosis and schizophrenia. *Brit. J. Psychiat.*, **138** : 558-561.

BLAGIR, R. S., AND SRINIVASA MURTHY, R. (1982) Dermatoglyphics of Schizophrenia—A review. *Indian J. Psychiat.*, **24** : 242-257.

SRINIVASA MURTHY, R. (1975). Dermatoglyphics in Schizophrenia. M. D. Thesis, PGIMER, Chandigarh, 1975.

Source References

SLATER, E. AND COWIE, V. (1971). The Genetics of Mental Disorders., OUP, London.

VERMA, I. C. AND PURI, R. K. (1978). Medical Genetics in India. Vol. I and II. Auroma Publishers. & Pondicherry. 1978.

NIMH. (1980). Behavioural Genetics. By Patricia Mc Broom, NIMH. Washington.

BALGIR, R. S. (1982). Dermatoglyphic studies in affective disorders : An appraisal. *Biological Psychiatry*, **17** : 69-82.

CHERILL, F. R. (1954). The Finger Print system at Scotland Yard. London, HMSO.

CUMMINS, H. AND MIDLO, C. (1961). Finger Prints, palms and soles. An introduction to dermatoglyphics. Dover. New York.

PENROSE, L. S. (1968). Memorandum on Dermatoglyphic Nomenclature. Ed. Bergsma, D. Birth Defects Original Article Series. Vol. IV No. 3 The National Foundation-March of Dimes. New York.

Other Dermatoglyphic studies from India

BISWAS, P. C. AND BARDHAN, A. (1966). *Anthropologist*, **13** : 1.

BALI, R. S. (1971). Palmar creases and schizophrenia. In International Symposium of Human Genetics. Waltair. India.

DASGUPTA, I., DASGUPTA, D., AND BALASUBRAMANIAM, M. (1973). *Indian. J. Psychiat.*, **15** : 104.

AGARWAL, S. S. *et al.*, (1975). *Indian J. Psychiat.*, **17** : 244.

GUPTA, A. K., *et al.*, (1977). J. Ass. Phys. India, **25** : 757.

AGARWAL, S. S. *et al.*, (1978). *Indian J. Psychiat.*, **20** : 52.

BALGIR, R. S. (1978). *Acta Anthropologinat.* **2** : 11.

DASGUPTA, I. (1978). In Verma, I.C. and Puri, R. K. Ref. No. 13.

ESWARIAH, G. (1978). *Indian J. Psychiat.*, **20** : 349.

KURIEN, J. C. *et al.*, (1978). In Verma, J. C. and Puri. R. K. Ref. No. 13.

KARMAKAR, B. AND MALHOTRA K. C. (1980). Palmar dermatoglyphics in Schizophrenia. International Symposium on Dermatoglyphics. Feb. 18-23 1980;. Panjabi Univ. Patiala, India.

NARAYANAN, H. S., AND MALLIKARJUNIAH, M. (1980). MDP and dermatoglyhphics pattern. International symposium on Dermatoglyphics. Feb. 18-23 1980. Panjabi Univ. Patiala, India.

BALGIR, R. S. (1981). Polymorphism of Simian crease in MDP. Spectra Anthropological Progress. **3** : 11.

PONNUDURAI, R. (1981). *Ann. Natl. Acad. Med. Sci.*, **17** : 21.

Genetics of Schizophrenia

SETHI, B. B. *et al.*, (1980). *Indian J. Psychiat.*, **22** : 217.

CHATTERJEE, S. B. AND BASU, S. K. (1980). *Indian J. Psychiat.*, **22** : 142.

GURMEET SINGH AND SACHDEVA, J. S. (1982). *Indian J. Psychiat.*, **24** : 42.

RAJU, S. S., AND MANI, A. J. (1982). *Indian J. Psychiat.*, **24** : 49.

Genetics of affective disorders

VENKOBA RAO, A. (1973). *Brit. J. Psychiat.*, **121** : 601.

VENKOBA RAO, A. (1974). *Indian J. Psychiat.*, **16** : 189.

CHOPRA, H. D. (1975). *Brit. J. Psychiat.*, **126** : 191.

GHOSH, A. *et al.* (1977). *Indian J. Psychiat.*, **19** : 73.

GURMEET SINGH *et al.* (1979). *Indian J. Psychiat.*, **21** : 81.

GURMEET SINGH. (1979). *Indian J. Psychiat.*, (corres.) P. X-XII.

RAJU, S. S. (1979). *Indian J. Psychiat.*, **21** : 176.

GUPTA, S. AND SRINIVASA MURTHY, R. (1980) Ind. J. Psychol. Ned., **3** : 41.

GURMEET SINGH AND AGARWAL, M. L. (1980). *Indian J. Psychiat.*, **22** : 39.

Mental Retadation : Case Reports

SRIKANTIA, S. G. *et al.* (1961). *Brit. Med. J.*, **i**, 282.

CHANDRA, P. *et al.* (1968). *Indian Pediatr.*, **5** : 77.

JOOSHUA, G. E. *et al.* (1968). *Indian Pediatr.*, **5** : 362.

SOMASUNDARAM, O. (1968). *Indian J. Psychiat.*, **10** : 142.

VERMA, I. U. (1968). *Indian J. Pediat.*, **35** : 394.

VERMA, I. C. AND SINCLAIR, S. (1970). *Indian J. Psychiat.*, **37** : 263.

RAO, B. S. S. *et al.* (1970). *Indian Pediatr.* **7** : 6.

NAIR, K. P. B. AND RAO, B. S. S. S. (1971). *Indian J. Pediatr.*, **38** : 357.

NATAYANAN, H. S. *et al.* (1971). *Trans. A.I.I. M.H.*, **11** : 73.

REDDY, V. *et al.*, (1972). *Indian Pediatr.*, **10** : 629.

JAISWAL, R. B. (1973). *Indian Pediatr.*, **10** : 243.

SOMASUNDARAM, O. AND PAPAKUMARI, M. (1973). *Indian Pediatr.*, **10** : 455.
RAO, B. S. S. S. *et al.* (1974). *Indian J. Pediat.*, **40** : 311.
RAO, G. P. (1974). *Indian Pediatr.*, **11** : 585.
VERMA, I. C. *et al.* (1974). *Indian Pediatr.*, **11** : 753.
SUNDERVALLI, N. *et al.* (1975). *Indian Pediatr.*, **12** : 355.
CHITRA, D. P. *et al.* (1976). *Pediat. Clin. India.* **11** : 211.
NARAYANAN H. S. AND RAO, B. S. S. S. (1978). *Indian J. Psychiat.*, **20** : 98.
VYAS, B. K. *et al.* (1978). *Indian J. Psychiat.*, **20** : 281.
MANCHANDA, R. AND AGNIHOTRI, S. S. (1979). *Indian J. Psychiat.*, **21** : 288.

Mental Retardation : Screening Studies

CENTERWALL, W. R. AND ITTYERAH, T. R. (1966). *Lancet.*, ii, 193.
STEVENSON, A. C. *et al.* (1966). *Bull. WHO Supl.* Vol. 34, p. 10.
PUNEKAR, B. D. (1968). *Indian J. Med. Res.*, **56** : 1813.
SHARADA, D. AND POLASSA, A. (1968). *Indian Pediatr.* **5** : 362.
NARAYANAN, H. S. *et al.* (1970). *Trans. A.I.I.M.H.* **10** : 69.
VENKOBA RAO *et al.* (1970). *Indian J. Psychiat.*, **12** : 273.
JOSHUA, G. E. *et al.* (1973). *Indian Pediatr.*, **10** : 243.
RAO, B. S. S. *et al.* (1973). *Indian J. Med. Res.*, **58** : 1953
NARAYANAN, H. S. *et al.* (1973). *Indian J. Pshychiat.* **15** : 143.
JOSHUA, G. E. (1974). *Indian Pediatr.* **11** : 47.
RAO, B. S. S. S. *et al.* (1974). *Indian J. Psychiat.*, **16** : 136
BHARUCHA, N. P. E. (1977). *Indian Pediatr.*, **14** : 395.
RAO, B. S. S., *et al.* (1978). In Verma, I. C. and Puri R. K. *Ref. No.* 13.
RAO, B. S. S. *et al.* (1981). Inborn Errors of Metabolism associated with mental Retardation detected at NIMHANS, Bangalore, India. In *Frontiers of Knowledge in Mental Retardation*—Biomedical aspects Volume II. I.A.SS.M.D. London. p. 273.

Mental Retardation : Consanguinity

CENTERWALL (1965). *Fedestrica Indonesia*, **15** : 906.
CENTERWALL, W. R. AND CENTERWALL, S. A. (1966). *Indian J. Med. Res.* **54** : 1160.
KUMAR, S. *et al.* (1967). *Ann, Human Genet.*, **31** : 141.
RAO, P. S. S. S. *et al.* (1971). *Indian J. Med. Res.* **59** : 294.
SINCLAIR, S. (1972). *Indian J. Med. Res.*, **60** : 1718.
CHAKRABORTY, R. AND CHAKRABORTHI, A. (1975). Proceedings of 2nd Ann. Conf. of Indian Society of Human Genetics, Calcutta, 1975.
PURI, R. K. *et al.* (1977). *Indian J. Med. Res.*, **65** : 859.
RAO, P. S. S. S. (1977). *Ann. Human Genet.* **41** : 87.
CHANDRA, P. AND HARILAL, K. T. (1978). In Verma, I. C. and Puri, R. K. *Ref. no.* 13.
KESAVAN, P. *et al.* (1978). In Verma, I. C. and Puri, R. K. *Ref no.* 13.
Malhotra, K. C. (1978). In Verma, I. C. and Puri, R. K. *Ref no.* 13.
NARAYANAN, H. S. AND RAO, B. S. S. S. (1978). In Verma, I. C. and Puri, R. K. 13.
PURI, R. K. *et al.* (1978). In Verma, I. C. and Puri R. K. *Ref. No.* 13.
RAO, P. S. S. S. (1978). In Verma, I. C. and Puri, R. K., *Ref. no.* 13.
VASALU, T. S. (1978). In Verma, I. C. and Puri R. K. *Ref. no.* 13.
INDIRA BAI, K. AND SASTRY, V. N. (1978). *News Letter FWMR* Feb. 1978.

Mongolism

Verghese, A. AND MURTHY, RAO, D. L. N. (1961). *Trans. A.I.I.M.H.*, **2** : 20.
RAO, S. R. *et al.* (1973). *Indian Pediatr.* **10** : 671.
KUCHERIA, F. (1974). *Indian J. Med., SS.*, **63** : 191.
VERMA, T. C. AND SINGH, M. B. (1975). *Lancet.*, i, 1200.
RAFI, R. S. AND MARIPUTHU, K. M. (1977). Proc. of 2nd Ann. Conf., of Human Genetics, Madras p. 68.
SOMASUNDARAM, O. AND PARAKUMARI, M. (1978). *Ind. J. Psychol. Med.*, **1** : 31.

Miscellaneous

NARAYANAM, P. P. (1952). *Ind. J. Neurol. Psychiat.*, **3** : 247.
GOLECHA, G. R. (1977). *Indian J. Psychiat.*, 19(2)43.