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# Neonatal Psychoneuroimmunology: Emergence, Scope and Perspectives

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**Keywords:** developmental neonatology; psychoneuroimmunology

**Abstract:** Interdisciplinary Neonatology investigates and cares for at-risk babies, including risk for developmental disabilities. Psychoneuroimmunology seeks to unravel relationships amongst behavioural, neural, endocrine, and immune processes, and their mutual role in maintaining health and treating disease.

This article presents an integrative approach to the emergence, scope and perspectives of a new sub-discipline i.e. Developmental Neonatal Psychoneuroimmunology. The Equilibrium Model (ThEM) proposed by Adamson-Macedo (1991) will be used as a way of representing coactions; within this frame, Gottlieb's experiential canalization (1991b) contributes explanation of how the psychoneuroimmunological development of the preterm neonate can be facilitated.

**Zusammenfassung:** *Neonatologische Psychoneuroimmunologie: Entstehung, Anwendungsfeld und Perspektiven.* Die interdisziplinäre Neonatologie erforscht Risikokinder einschließlich möglicher Entwicklungsbehinderungen und ist gleichzeitig um ihre bessere Versorgung bemüht. Psychoneuroimmunologie bemüht sich um die Aufklärung der Beziehungen zwischen verhaltensmäßigen, neuralen, endokrinen und immunologischen Prozessen und ihrer wechselseitigen Rolle bei der Aufrechterhaltung von Gesundheit und bei der Behandlung von Krankheit.

Dieser Artikel stellt ein integratives Vorgehen bei der Entwicklung, dem möglichen Anwendungsfeld und den Perspektiven einer neuen Subdisziplin, und zwar der entwicklungsneonatologischen Psychoneuroimmunologie dar. Das von Adamson-Macedo (1991) entwickelte Equilibrium-Modell wird als Weg zur Darstellung von Koaktionen verschiedener organismischer Ebenen verwandt; innerhalb dieses Rahmens ist Gottliebs Konzept der „Kanalisation des Erlebens" (1991b) hilfreich für die Erleichterung der psychoneuroimmunologischen Entwicklung des frühgeborenen Kindes.

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## Introduction

As a sub-discipline of Medicine, Neonatology investigates and cares for at-risk babies, including risk for developmental disabilities; it has increasingly become interdisciplinary. Being born too early, and sometimes too small, is a stressful life event, and it can be predicted that prematurity results in distress to the infant, the parents and the caregivers (McIntosh 1989).

The experiences of the neonate in intensive care can also be painful and this has become a focus of considerable research; studies have been accumulating which indicate that the neonate is capable of displaying reliable non-verbal responses to painful stimuli (Grunau et al. 1990; Craig et al. 1993; Sparshott 1989). Other studies have reported possible impairments of the immune and endocrine systems where pain has not been treated (Aynsley-Green et al. 1985; Anand 1987, 1990). Wolke (1987) has also discussed the detrimental developmental effects of neonatal intensive care on preterm infants.

Despite the successes of both medical and environmental advances in controlling infection in the newborn baby, Neonatal Units continue as stressful environments and infection continues to cause neonatal mortality. Infections in general, and particularly gut infections such as necrotizing enterocolitis (NEC), as well as severe neonatal complications such as asphyxia, respiratory distress syndrome (RDS), cerebral haemorrhage, and cardiac failure are frequently associated with impairment of the immune systems of neonates. Such impairments have been reported, examples being Wright et al. (1975) and Shigeoka et al. (1981).

That the environments of preterm infants are highly stressful is well documented and such neonates, albeit resilient, are prone to infections which may compromise growth, development, well-being and survival. As Whitelaw (1990) pointed out "Despite the continued development of new antibiotics with increased ranges of activity and spiralling prices, sepsis – either acquired from the mother intrapartum or acquired nosocomially from invasive procedures – remains a serious problem in preterm infants ... infants born at less than 32 weeks' gestation have clinically important immunoglobulin deficiency ... " (p. 347). The author reported on 4 randomised trials using Immunoglobulin G (IgG) replacement intravenously in preterm infants at risk of sepsis. Two of out of those four trials provided evidence that such prophylaxis could reduce septicaemia in infants weighing $< 1500$ g.

Haque et al. (1988) reported on the use of IgM-enriched intravenous immunoglobulin (5 mL/kg/d) therapy in a group of preterm infants with their first episode of neonatal sepsis in conjunction with antibiotics; the immunotherapy consisted of 250 mg of protein, 30 mg of IgM, 30 mg of Immunoglobulina A (IgA), and 190 mg of IgG. Mortality in this group was of 3.3% (1/30) against 20% (6/30) in the control group which received only antibiotic therapy.

It is known that IgA is the second most abundant Ig in serum and is the predominant one in the gastrointestinal and respiratory tracts and in human colostrum and breast milk. Secretory IgA seems to be uniquely suited for functioning in the secretions of the respiratory and gastrointestinal tracts. Albeit controversial, studies are showing that secretory immunoglobulin A (sIgA) can be isolated as early as three days after birth (Friedman et al. 1993).

The acknowledgment by the medical professsion that very preterm infants have a pronounced, prolonged deficiency of immunoglobulin thereby putting them at increased risk of bacterial sepsis is encouraging. Further encouragement is drawn from the literature on Developmental Comparative Immunology which analyses the shift in the 1950s towards a more satisfactory definition of immunity by Burnet i.e. “the distinction by the body between self and non-self” rather than only seeing immunity as the resistance of the body to disease. As Ratcliffe (1989) pointed out “. . . the folly is apparent of examining immunity in isolation and not taking into account its interaction with other systems of the body, as well as the influence of environmental factors such as stress. Understanding the relationships between the various organic and psychological systems of the preterm infant is however uncharted waters to all professionals involved in the care of such vulnerable yet resilient population.

New propositions which challenge established beliefs are always controversial if not side lined. However, as O’Leary pointed out the evidence that emotional factors are related to immune function has been accumulating for some years but in adults; studies investigating the psychoneuroimmunologic (PNI) relationships in children is almost non-existent (1991, 1990).

Developmental psychoneuroimmunology, as a new interdisciplinary field, is presently opening new avenues of enquiry within which Psychology can make an important contribution. The emergent discipline seeks to understand the complex interrelationships of behavioural, neural, endocrine, and immune processes, and their consequential role in the maintenance of health and treatment of disease. Scientific investigations which accept that the preterm infant is a self-regulating and coactive being and seek to unravel such relationships as occur whilst the preterms are lying in their incubators are beginning to appear (Adamson-Macedo 1996a; Hayes et al. 1996).

A century ago, Preyer (1888) emphasised that the fundamental activities of the mind, as they later become manifest, do originate before birth; this approach remains uncontested and Karmiloff-Smith (1995) recently stated “Cognitive development, starts in the womb. During the final 3 months of intrauterine life, the foetus is capable of extracting invariant patterns across the complex auditory input that is filtered through the amniotic fluid”. From the second trimester of pregnancy until three years of age, the brain itself is vulnerable (physically and behaviourally) to environmental modifications (Gupta 1989).

For any developmental age, evidence continues to accumulate that the time spent in the womb is critical for normal development and function of the mind. In preterm cases, the abrupt interruption of womb experiences can be terminal for a few, whereas for others their normal rate of growth and development can be jeopardised. The recent emergence of Neonatal Psychology (Adamson-Macedo 1996b, 1997) indicates that the time has come for psychology to make an effective contribution to both the theory and the care of the preterm neonate.

This paper presents an integrative approach in order to explain the emergence, scope and perspectives of a new sub-discipline i.e. Developmental Neonatal Psychoneuroimmunology. **T**he **E**quilibrium **M**odel (**ThEM**) which was proposed and modified by Adamson-Macedo (1991) will be used as a way of representing coactions; within this frame, Gottlieb’s experiential canalization (1991b) contributes explanation of how the psychoneuroimmunological development of the preterm neonate may be *facilitated*.

## Emergence

During the past decade, developmental psychology has witnessed a renaissance of interest in the study of the relations between genes and behaviour. Corresponding system analysis in developmental psychology include rationales and theories which have been called ecological (Bronfenbrenner 1979), transactional (Dewey and Bentley 1949; Sameroff 1983), contextual (Lerner and Kaufman 1985), interactive (Johnston 1987; Magnusson 1988), probabilistic epigenetic (Gottlieb 1970, 1992), individual-sociological (Valsiner 1987), and structural-behavioral (Horowitz 1987).

As defined by Gottlieb, epigenesis is probabilistic, and his particular system view of development sees the individual as an "emergent, coactional, hierarchical system." This definition of epigenesis declares that "individual development is characterized by an increase of complexity of organization, i.e., the emergence of new structural and functional properties and competencies – at all levels of analysis (molecular, subcellular, cellular, organismic) as a consequence of horizontal and vertical coactions among its parts, including organism – environment coactions (Gottlieb 1992 op cit.).

Horizontal coactions are those which occur at the same level, e.g,. gene to gene, cell to cell; vertical coactions occur at different levels, e.g., gene-cytoplasm, behavioural activity-nervous system, and are reciprocal in that they can influence each other in either direction. Thus the sensory experience of a developing organism affects the differentiation of its nerve cells such as that the more experience produces the more differentiation and vice-versa. The more highly-differentiated nervous system permits a greater degree of behavioural competency and the less differentiated nervous system permits a lesser degree of behavioural competency.

Following William James definition of Psychology and Gottlieb's system's approach to development, Adamson-Macedo (1996b) defined Neonatal Psychology as "the scientific study of the phenomena of mental life and the behaviour of the preterm neonate as an emergent, coactional, hierarchical system."

The preterm infant is here viewed as a functioning interactive organism which imply that s/he has self-regulatory abilities. Self-regulation is a "dynamic process of adaptive functioning operating through a large number of individually distinct mechanisms which may be hierarchically arranged or classified" (Walcher and Peters 1971, pp. 232). This dynamic process of adaptive functioning occur amongst the various systems (e.g. Gottlieb 1993) of the infant born too early.

Adaptive change ranges from self-regulation at the cellular level (Rosenzweig 1971) to issues of child/care-giver communications; thus Krauss (1971) recognised that self-regulatory principles are general characteristics common from the genome up to psychological behaviors and "... to be found in both organic and cognitive behaviours." Other relevant viewpoints are those of Greenspan (1979) on self-regulation relating to structure, Vygotsky (1962, 1978) on function, Gedo (1979) on developmental aim for a particular phase, Lichtenberg (1983) and Stern (1985) on relational processes, and Emde (1988) on biopsychological principles.

Self-regulatory constructs are now being used in many sub-disciplines of Psychology, e.g., health psychology/behavioural medicine, and experimental psychology. However, interest in seeking to unravel relationships amongst the various organic and psychological systems is not new; the literature yields several examples of both animal and human studies, which sought to elucidate e.g. the role of early sensory stimulation on self-regulation, or lack of the same.

## Scope

For the past 5 decades many comparative studies have tried to investigate the role of environmental factors e.g. sensory stimulation on self-regulation.

Both animal and human studies have attempted to elucidate the role of early stimulation on self-regulation; for the purpose of presenting the scope of the emergent sub-discipline of neonatal psychoneuroimmunology, the following selection concentrates on handling, tactile-kinaesthetic, and tactile modes of stimulation only. This investigative route has provided major evidence, since tactile sensibility is present in the foetus as early as 7.5 weeks gestational age (Hooker 1969); this category moreover is the one to which the author's own work consistently belongs.

### *Animal Studies*

In the 1950s and 1960s, Levine, Denenberg and associates used handling as the medium for investigating the consequences of such stimulation in infancy. 'Handling' was defined as simply placing the pups separately into a can containing shavings and leaving them alone for 3 minutes; they were then placed back onto the tray which belonged to the maternity cage. The young pups were not fondled or caressed during their manipulation, and the amount of touching which they received was minimal.

Levine et al. established behavioural factors, e.g., avoidance learning, discrimination learning, exploratory behaviour and physiological changes; the last included body weight, resistance to leukemia virus, and ability to survive terminal stress (see Denenberg 1967, 1969; Levine 1962; Newton and Levine 1968). These various authors concluded that the emotional reactivity, or 'emotionality', of rats was significantly reduced by these early handling experiences.

This was followed by enquiry into the existence, or not, of any correlated changes at the physiological level. They anticipated that changes in emotional reactivity would implicate the adrenal gland, and ultimately, the complete hypothalamic-pituitary-adrenal axis. Levine and Denenberg were able to demonstrate that animals handled in infancy gave a significantly lower adrenocortical response to mild novel stimuli than non-handled controls, whilst a greater corticosterone response appeared to a distinctly noxious stimulus such as electric shock. A relationship exists between behavioural measures of emotional reactivity and the response of the adrenal cortex, and an analogy suggests that corticosterone might be involved in mediating the effects of stimulation in infancy.

In 1979, Evoniuk and colleagues suggested an enzymatic-hormonal mechanism as the mediator of physical benefits associated with tactile programmes. More recently Schanberg and Field (1987) found that the release of growth hormone and protein in rat pups are regulated by a specific form of tactile stimulation, i.e., brush stroking.

*Human Studies*

Scott and Richards (1979) found that an increase in growth rate of preterm infants by using a simple enhancement of the baby's environment, known as 'nursing the baby with lambswool'. Speculation regarding the mediators was that babies were calmer than their control counterparts, and hence the release of stress hormones could have been less.

Rausch (1981) suggested that increased fluid intake would account for greater weight gain in infants given supplemental tactile stimulation, but others, e.g., Scafidi et al. (1990) did not find such a link.

Amongst other results, Macedo (1984) found that preterms increased their growth rate as a consequence of tactile stimulation, the medium in this case being a unimodal (gentle/*light* stroking only) procedure. At that time, two mediators were postulated:

(i) that systematic gentle and *light* stroking affects the infants' metabolism indirectly through glandular action and hormones, or by cortical or sub-cortical loci acting through the hypothalamus and in the adenophypophesis. Stroking accelerates the synthesis and liberation of important hormones which promote growth [somatotropic (SH), adrenocorticotropic (ACTH) and the thyrotropic and gonadotropic (TSH).

(ii) Systematic gentle and light stroking affects digestion and fat absorption. Since the treated infants showed better performance in sucking, it was hypothesised that lingual lipase could be the catalyst of hydrolysis of dietary fat in the stomach. Hamosh (1983) reported on the function of lingual lipase in both digestion and fat absorption as of major importance in physiological and pathological conditions associated with pancreatic insufficiency, as occurs in prematurity.

Since the infants who received systematic gentle and *light* stroking appeared to be less susceptible to infection than their control counterparts, a new hypothesis was generated i.e. stroking was decreasing the secretion of stress hormones and strengthening the immune system of infants born early.

More recently Acolet et al. (1993) found that cortisol concentrations decreased consistently after (their) particular tactile stimulation programme (massage). Massage programmes have an interpretative problem in that they involve a variety of intra-modal operations; within such overall stimuli it is not possible to determine the contribution of the individual physical operations, e.g., kneading, rubbing, stroking, and/or lifting of arms and legs. Adamson-Macedo and Attree (1994) have discussed the differences between massage and stroking.

De Roiste and Bushnell (1995) measured stomach lipase concentration, i.e., lingual and gastric lipase before and after tactile stimulation; they also measured gastric pH in order to determine the effect of tactile stimulation on hydrochloric acid (HCI) concentration. Overall results suggested that gentle/*light* stroking improves gastro-intestinal functioning in preterms and that "better digestion and greater nutrient absorption is facilitated by stroking prior to feeds".

Hayes, Adamson-Macedo and Perera (1996) and Hayes (1966) using a counterbalanced pre-test/post-test design, measured secretory Immunoglobulin A (sIgA) of unstimulated saliva of very/extremely low birthweight ranging from 0.65 to 1420 g (Mean = 0.99 g; SD 0.02), thirty-five (M = 17; F = 18) ventilated preterm infants whilst lying alone in their incubators compared with when they received TAC-TIC therapy, version-3. Saliva samples were obtained very gently using a small sterile flexible plastic filament attached to a sterile 5ml syringe.

An enzyme-linked immunosorbant assay, ELISA which was adapted from Atkinson et al. 1990 was used to ascertain secretory Immonoglobulin A (sIgA) concentrations; Sigma chemicals were used (Poole, Dorset, U.K.). All standards and samples were run in duplicate. Gestation age ranged from 25 to 30 weeks (Mean = 27; SD = 27). Apgar Scores at 1 minute ranged from 1–9 (Mean = 5; SD = 2.4) and at 5 minutes from 2–10 (Mean = 8; SD = 2.3) Twenty one (60%) were born by spontaneous vaginal delivery, eleven (31.4%) emergency caesarean section (EMCS) and three (18.5%) by elective caesarean section (ELCS).

Criteria for recruitment were, as follows:

* birthweight < 1500 g
* gestation age < 32 weeks
* mechanical ventilation required for a minimum of three days either continuous positive airways pressure (CPAP) via nasal prongs or endotracheal intubation and full mechanical ventilation (IPPV).
* less than seven days postnatal age

All infants were receiving only intravenous parenteral nutrition (TPN). Thirty one (88.5%) suffered respiratory distress syndrome. Thirty three (94.4) received surfactant therapy after delivery and twenty three (65.7%) received morphine as a sedative agent at the time of the study. There were 8 (22.8) infants with confirmed cases of sepsis. A one-way repeated measures ANOVA indicated that sIgA concentrations (135 sessions) were significantly higher after TAC-TIC therapy ($F = 5.03$; $df = 1$; $p < 0.05$) but not after spontaneous activities (129 sessions). The results suggest that beneficial vertical coactions i.e. the sensory nurturing *light* stroking or TAC-TIC and the secretory immune system thereby facilitating the development of the immune system.

Smith and Taubman (1993) stated that saliva contains essentially no IgA at birth but secretory immune responses to oral and non-oral microbial antigens emerge early in life. Recent publication by Hanson et al. (1996) confirmed that "… serum IgA develops slowly, but secretory IgA antibodies, measured as Escherichia coli antibodies in saliva, can reach adult levels in only a few weeks under heavy microbial exposure …"

The infants studied by Hayes were under stress. Stress and emotions have been known for some time to be associated with substantial physiological changes, including activation of the sympathetic adrenal-medullary (SAM) system, the hypothalamic-pituitary-adrenocortical (HPAC) system, and other endocrine systems (see O'Leary 1990, p. 365). Frankenhauser 1983 described SAM and HPAC as the effort and distress systems, respectively.

Activation of the adrenocortical system often accompanies chronic stress, however changes in sIgA were observed and recorded only after 3 minutes of TAC-TIC; this short time may suggest that it is activating SAM. As O'Leary pointed out several mechanisms of sympathetic influence on immune function have been elucidated e.g. the release of catecholamines. Adamson-Macedo and Carson (1997) suspect that it might be an opioid activation i.e. beta-endorphin which is released from the pituitary acting by decreasing the secretion of catecholamines.

Schanberg and Field (op cit.) found that the release of growth hormone and protein in rat pups is regulated by a specific form of tactile stimulation, i.e., brush stroking, and that body weight was regulated by tactile-kinesthetic stimulation in human preterm neonates.

Although the studies above have been investigating the role of self-regulation on the various systems of animals and humans, the immune system of the preterm neonate has been one of which only recently has been attracting interest of health professionals including psychologists and health (developmental) psychologists particularly.

Scientific investigations directed towards unravelling the relationships of the various organic and psychological systems with the immune processes of the preterm neonate did not appear until recently (Hayes et al. 1996 and Adamson-Macedo 1996a op cit.).

## Perspectives

Neonatal Psychoneuroimmunology is systemic and the preterm infant is viewed as an emergent, coactional, hierarchical system. Gottlieb's probabilistic epigenetic system development theory is the one favoured here, and provides the theoretical rationale to **T**he **E**quilibrium **M**odel (**ThEM**); **ThEM** is the frame which represents the on-going coactions amongst the various systems of the incubated preterm infant whilst either lying alone or receiving tactile nurturing in the form of TAC-TIC therapy (Macedo op cit.).

Any new sub-discipline requires a perspective; the one proposed here is that of *system development* based on Gottlieb's experiential canalization, on this basis, **ThEM** may be represented either geometrically or as space equations.

### *The Equilibrium Model*

#### Origin and Representation

The choices to be made of a particular sensory stimulation and its timing are critical; they are certainly not simple due to the controversy which surrounds intersensory perception. Yet these factors maintain and enhance function integration, and support growth and development (Turkewitz and Devenny 1993; Lickliter 1993). The hypothesis consequently adopted was that an appropriate intervention, when offered to the infant at an optimum time should induce beneficial coactions:

* horizontally, between the infant's sensory system, and the system of sensory-stimulation which is adopted;
* vertically, between the sensory stimulation-Neuro-behavioural (NB) immunological (IM), and endocrinological/physiological (E/P) systems.

Three theories currently prevail to explain the phenomenon of intermodal perception. Two of these are Integration (Birch and Lefford 1963, 1967; Blank and Bridger 1964; Bryant 1974) which asserts that the senses are independent at birth, and Differentiation or Invariant detection (Gibson 1969; Bower 1974)

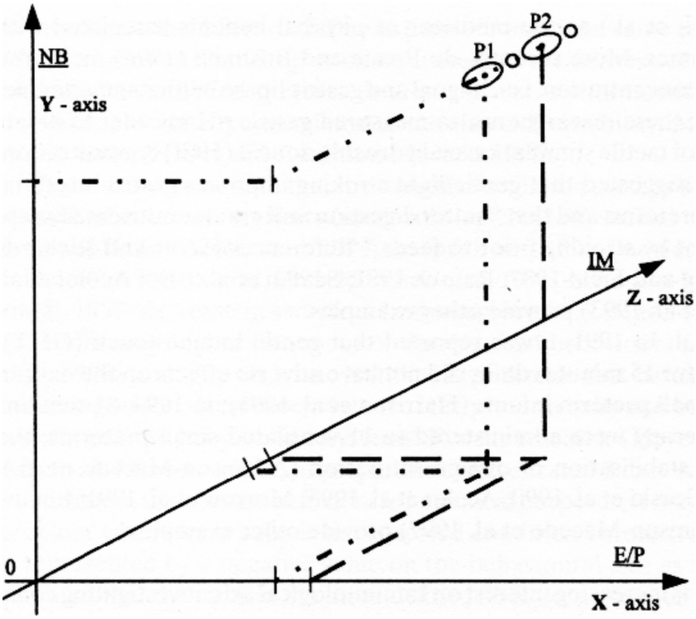


**Fig. 1.** The **E**quilibrium **M**odel (**ThEM**) (Macedo 1984; Adamson-Macedo 1988, 1991, 1995, 1996).

which advocates that the senses are unified at birth. The third is the Intensity hypothesis (Schneirla 1959, 1965; Turkewitz et al. 1983), which draws elements from the previous two theories and is favoured by the author of this paper; it defends the proposition that multimodal relations can be detected early in development and that, with experience, infants can discern characteristics of stimulation ranging from the quantitative such as size, brightness, loudness, duration, or rate of stimulation, to the qualitative such as rhythm, melody, texture or shape.

Representations of the beneficial coactions promoting temporary equilibrium are made on orthogonal axes. For example, should the sense of touch be the appropriate stimulation for the ventilated preterm, the vertical coactions expected in consequence would be beneficial, i.e., the behavioural system would organise itself, the physiological system would stabilise, the endocrinological system would be balanced, and the immunological system would be 'enhanced'. It is thus helpful to display **NB**, **IM**, and **E/P** three-dimensionally, as shown notionally in Figure 1 where 1 and P2 only represents different positions of the baby in relation to each one of the axes.

Phenomena represented on these axes have been separately tested by using the sense of touch but with different types of stimuli such as handling, rubbing, massage, gentle human touch (GHT) or the gentle/*light* and systematic stroking known as TAC-TIC therapy. For infants born preterm, examples of studies which demonstrate the occurrence of positive horizontal and/or vertical coactions are given below:

* **E/P** axis:
  (a) Endocrinological: In 1979, an enzymatic-hormonal mechanism was sug-

gested (Evoniuk et al.) as the mediator of physical benefits associated with tactile programmes. More recently, de Roiste and Bushnell (1996) measured stomach lipase concentration, i.e., lingual and gastric lipase before and after tactile stimulation; these researchers also measured gastric pH in order to determine the effect of tactile stimulation on hydrochloric acid (HCI) concentration. Overall results suggested that gentle/light stroking improves gastro-intestinal functioning in preterms and that "better digestion and greater nutrient absorption is facilitated by stroking prior to feeds." References (Scott and Richards 1979; Schanberg and Field 1987; Rausch 1981; Scafidi et al. 1990; Acolet et al. 1993; Berezin et al. 1993) provide other examples.

(b) Physiological: In 1991, it was reported that gentle human touch (GHT), when provided for 15 minutes daily, did not have adverse effects on the oxygen saturation of small preterm infants (Harrison et al. 1991); in 1994, 81 sessions of TAC-TIC therapy were administered to 11 ventilated small preterms; the results showed stabilisation of oxygen saturation (Adamson-Macedo et al.). References of Gorski et al. 1990; Acolet et al. 1993; Morrow et al. 1991; Leeuw et al. 1991; Adamson-Macedo et al. 1997) provide other examples.

∗ **IM** axis:

Presently, there is increasing interest on Immunological axis: investigating coactions in other organic and psychologic systems; Hayes et al. 1996 showed that secretory Imnmunoglobulin A (sIgA) can be detected during the first week of life of the very small ventilated preterm, and suggested that concentrations of sIgA are greater three minutes after intervention by gentle/*light* stroking, (TAC-TIC). These results referred to a baseline phase (3 mins. before intervention) and a control condition in which the infants undergo spontaneous activities in their incubators.

∗ **NB** axis:

Neuro-behavioural axis: Systematic studies which observe and record both behaviour and behavioural state, prior and during intervention, are rare. In the author's experience, gentle/*light* stroking tends to elicit a greater number of organising rather than disorganising behaviours, and this may indicate that beneficial coactions are occurring (Adamson-Macedo et al. 1994b; Hayes 1996). Constantinou et al. (1997 found that skin-to-skin holding does not interfere with the rest-activity period of low birthweight infants. Other studies show non-beneficial coactions, i.e., disorganised behaviours as a consequence of other kinds of touch intervention (Eckerman and Oehler 1992; Gorski et al. 1990; Harrison et al. 1991). These last results are questionable however since the interventions employed do not appear to be systematic. In any event, the results of different studies are not directly comparable; the area remains controversial, and requires further investigation.

In studying the mediational role of sensory stimulation in promoting beneficial coactions, several variables need to be taken into account; such as Gestational Age (GA), Birthweight (BW), Gender, Behavioural State or morbidity status, as well as quantitative and qualitative dimensions of the sensory stimulatus itself. Systematic and well controlled studies, with large samples, which investigate intra-modal (e.g. deep versus light stroking) variability have not hitherto been carried out. An exploratory study (N = 1) has been recently carried out by Hayes (1996) to investigate the effect of different pressure using the same tactile intervention; results suggested that deep stroking increased the distress of the extremely low birthweight ventilated preterm. It seems that it is paramount to carry out studies which elucidate issues related to intra-modal variability, particularly with the tactile sense (Hayes and Adamson-Macedo 1997b).

There was no evidence that the 'touch' stimulation used by some of the authors above had deleterious effects (medically unaccepted) such as significant increase in cortisol level (Acolet et al. 1993; sharp fall on Tc $PO_2$ (Acolet et al. 1993; Gorski et al. 1990; Morrow et al. 1991; Harrison et al. 1991; Adamson-Macedo et al. 1994a and b, 1997, decrease in secretory Immunoglobulin A (sIgA) (Hayes et al. 1996), or significantly higher frequency of disorganised behaviours (Adamson-Macedo et al. 1994a and b op cit.); one can thus hypothesise that beneficial coactions are occurring within the sensory system of the preterm baby and between the sensory system and the baby's other systems. Recent research (Hayes 1996; Hayes and Adamson-Macedo 1997a, in preparation) have tested 3 axes simultaneously.

Although the above is sufficient for practical purposes, it may create conceptual problem whenever a baby is in distressed condition before treatment, since this is represented by a negative value on the behavioural axis as in Fig. 2. It should be noted that the units in the three defined directions are each arbitrarily chosen; they correspond to the specific and consistent measurements appropriate to the phenomena being measured.

As in Fig. 1 P1, P2 and P3 represent a position of the baby or a group of babies in relation to each of the axes. For example, P3 represents a baby who had a unit of $-3$ in the **Y**-axis; this negative unit implies that the baby had responded to the intervention with more disorganising than organising behaviours. The vertical coaction i.e. of the sensory system with the behavioural system was non-beneficial. If the three axes would show non-beneficial coactions, e.g. a decrease on the unit of the **Z**-axis and a sharp decrease or increase on **X**-axis, it is here suggested that the intervention should be interrupted otherwise it should be continued.

The investigator may require to represent the coactions whenever there are more than 3 variables.

In order to display the 3-dimensional **E**quilibrium **M**odel of Fig. 2, a notation of three-dimensional co-ordinate geometry may be adopted. Thus $Pn = n_1\mathbf{X} + n_2\mathbf{Y} + n_3\mathbf{Z}$, where $n_1$, $n_2$, and $n_3$ simply represent values on the three orthogonal axes **X** (= E/P), **Y** (= NB), and **Z** (= IM); P on Fig. 2 is a point representing the condition of the baby on the diagram, as in Figure 1; $n_1\mathbf{X}$, $n_2\mathbf{Y}$, $n_3\mathbf{Z}$ are not algebraic products, but simply indicate positions or locations $n_1$, $n_2$, $n_3$, appropriate to the measurement regime and scale adopted for each respective axis.

Equation (1) depicts a notional situation in arbitrary units where E/P response $= +3$, Behaviour $= +7$, and Immunological resistance $= +4$:

$$P_1 = 3\mathbf{X} + 7\mathbf{Y} + 4\mathbf{Z} \qquad (1)$$

As a further example, should the baby's behaviour pattern remain at $+7$, but endocrinal/physiological and immunological responses improve by 10% and 5%, respectively, eqn. (1) would then become:

$$P_2 = 3.3\mathbf{X} + 7\mathbf{Y} + 4.2\mathbf{Z} \qquad (2)$$

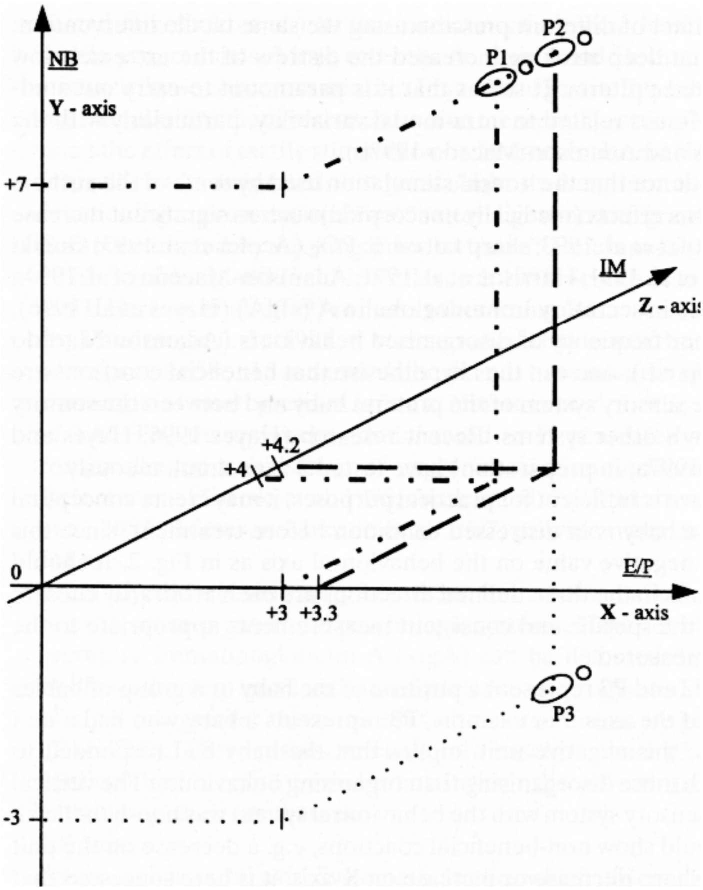


**Fig. 2.** The **E**quilibrium **M**odel (**ThEM**) (Macedo 1984; Adamson-Macedo 1988, 1991, 1995, 1996).

This geometric method of representation in the form of a space equation may be extended felicitously; its superiority is manifest whenever it is desired to represent four or more parameters. For example, data may be forthcoming from specific endocrinal as distinct from endocrinal/physiological measurements. This enables the E/P axis to be divided into two, the **X**-axis being retained for physiological phenomena, P.

The interaction of the endocrine system, E may now be given on a **W**-axis; effectively, there are now four axes in a 4-dimensional space, a situation impossible to represent on orthogonal axes, as well as being conceptually difficult for the human mind. However, by extending the notation adopted above, the conceptual problem disappears and the geometrical representations of Figs. 1 and 2 may be discarded; by adding a fourth term W to represent endocrinal effects E in, say, eqn. (2) and assigning an arbitrary value of +2.5, and substituting the positive value of +7**Y** by a negative one of −3**Y**:

$$P_4 = 2.5\mathbf{W} + 3.3\mathbf{X} - 3\mathbf{Y} + 4.2\mathbf{Z} \qquad (3)$$

It may be noted that this mathematical shorthand also avoids use of suppressed zeros (or origins) in one or more axes whenever the geometrical representation is used, as in Fig. 3: one of the axes (**Z** = IM axis) is drawn, for emphasis, with a suppressed origin. P1 in this example refers to the condition of the baby or group of babies before the beginning of the intervention (3 minutes before). The group of babies displayed a numerical assessment of −3 (**Y**-axis) which indicates that the babies were responding to the environment with more disorganising than organising behaviours. This is considered a non-beneficial vertical coaction i.e. the behavioural system with the environment.

At the same time the **Z** and **X**-axes are assessed and the group of babies' concentration of secretory IgA (**Z**) is of 31 micro-gram per millilitre (μg/ml); their mean Heart Rate (beats/min) was 148. All axes were assessed again after 3 minutes of the intervention; these units were compared were the baseline above represented by P1. As Fig. 3 shows the mean Heart Rate (**X**) did not change, but both axes **Z** and **Y** did; **Z** increased to 44 μg/ml and **Y** became positive or +7. These results are interpreted as an example of beneficial horizontal and vertical coactions; it is expected that such coactions would contribute to improve the quality of life of the preterm infants and facilitate their development.

## Conclusions and Observations

The Model and its representations described here contributes to the requirements stipulated by Munro (1992) who emphasised, "Although it is common to find diverse phenomena included in single formulations (e.g., the linking of immune function to mental effects, or social behaviour to cognition), the nature of the the linkage is typically obscure because, as Harré, Clarke, and de Carlo point out, there is no organizing conceptual framework such as one finds in the physical sciences." (in Munro 1992)

The Model is compatible with Gottlieb's (1991a, 1991b, 1976b, 1993) theory of Experiential Canalization of Behavioral Development; with sociogenesis (Vygotsky 1962, 1987) and with Munro's (1992) proposition of a model of integration rather than reduction in order to explain important phenomena of interest to Psychology; it is supportive of the proposal of Wilson et al. (1992) for an integrative approach to self-regulation.

Sociogenesis holds that all higher psychological processes, such as learning, cognition, and personality are results of early social interactions. This concept has been recently used in the animal literature (Gottlieb 1993). For example, social induction of malleability in ducklings has been studied; it was found that malleability was absent when ducklings were tactually isolated from one another. These experimental results indicated that tactile contact, even when provided by stuffed ducklings, is the sensory basis of malleability (Gottlieb 1993).

Careful and systematic observations of the incubated infant, which is temporarily his/her natural social ecological context, may lead to the acquisition of new ways of understanding early human development within an integrative perspective. Interdisciplinary complexity of the phenomena of behaviour and mentation requires a systematic approach which recognises the interrelationships between the various non-independent variables; simplistic single stimulus/response models are

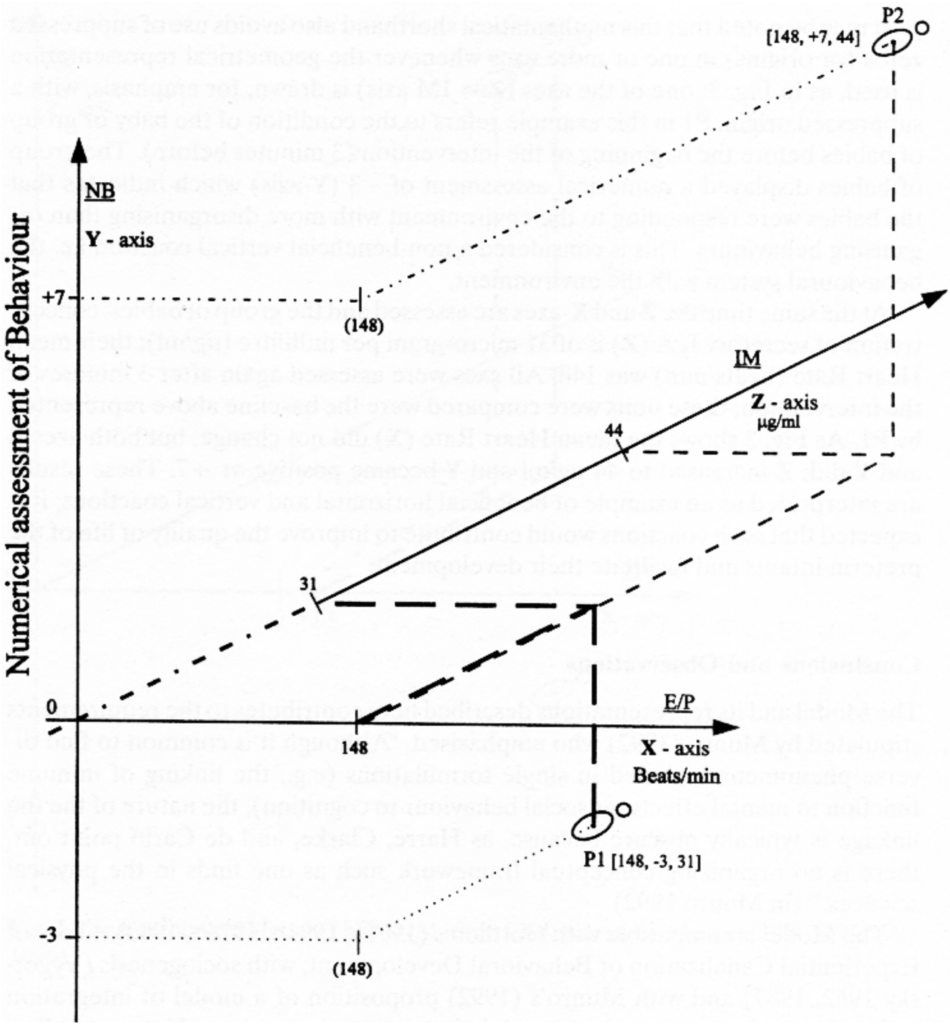


**Fig. 3.** The **E**quilibrium **M**odel (**ThEM**); examples of coactions (suppressed origin on **Z**-axis).

quite insufficient and frequently erroneous. The hypotheses proposed in this paper should be further tested; the Model could be extended to other phenomena such as measures of affect regulation and intersubjective relatedness (Trevarthen and Hubley 1978).

No single branch of neuroscience or of psychology, or other related discipline, can scientifically understand behaviour and mentation; as Bunge (1980) pointed out "... the problem is a multilevel one, and this is because man exists on all levels." To overcome such a difficulty, a system approach is manifestly necessary.

The aim of **T**he **E**quilibrium **M**odel is to establish a display and/or systematic format, as appropriate, for the interactive association of the individual self-regulatory mechanisms of the preterm infant, and so contribute to the theory and practice of Neonatal Psychology. The Model is presently in use and fulfils two important functions:

(i) a method for illustrating self-regulatory phenomena in which the various relationships which contribute to self-regulation become easier to comprehend.
(ii) an experimental framework from which further predictions and postulates may emerge more readily than would otherwise be the case, thereby leading to the design of systematically-formulated experiments, and towards a unified theory of development of the preterm neonate viewed as an emergent, coactional and hierarchical developing system.

Neonatal Developmental Psychoneuroimmunology is here defined as "the scientific study of the complex horizontal and vertical coactions of the phenomena of mental life, behaviour, neural, endocrine and immune processes of the preterm neonate and their consequential role in the facilitation and maintenance of health and treatment of disease".

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