Maternal endocrine situation and fetal behaviour: possible correlation mechanisms
Propiomelacortin - ß-endorphin - Cortisol

Giorlandino C.*, Vizzone A., Gentili P.*, Arduini D.**

Clinica Ostetrica e Ginecologica, Università Tor Vergata, Roma, Italy
*Centro Medico Artemisia, Roma, Italy
**Clinica Ostetrica e Ginecologica, Università Cattolica S. Cuore, Roma, Italy

It has been known for a long time (Prechtl,1974) that the fetus - as the pregnancy comes to an end - acquires a behaviour similar to that of the newborn.

Moreover,the cardiotocographic studies (Timor-Trish et al,1978,Romanini et al,1983),associated with the ultrasonic ones (Nijhuis et al,1982,Arduini et al,1985) have broadly demonstrated the existence of circadian rhythms concerning the major fetal movements (FM) (Patrick et al,1982),the respiratory movements (Patrick et al,1980)and the variability of the fetal cardiac frequency (Visser et al,1982).

Although different hypoteses were formulated to explain these attitudes, it should be added that the existence of endocrine and behavoural biorhythms has been evidenced experi= mentally.

The fetus, in particular,represents from this point of view a very special model, given that a large part of its behaviour may be determined and/or affected by the maternal endocrine mechanosms.

Some experimental data do prove, in fact, the hypothesis that both these systems are interactive:

1) The fetal activity index features a daily distribution similar to the one of E_3 (Patrick et al,1982)
2) Plasmatic E_3 (fetal derivation)shows a biorhythm which is exatly the inverse of that of cortisol in the mother (Patrick et al,1980);
3) The administration of cortisonics to the mother before the 38th week of pregnancy leads to a loss in thecir= cadian variations and to a considerable increase of the activity index (Arduini et al,1985)
4) Maternal stress causes an initial condition of fetal hyperactivity which is then followed by a fetal hypo= activity phase (Ianniruberto,1981).

Such experimental premises lead to two hypotheses and considerations:

- Fetal behaviour is affected by the maternal neuro= endocrine modifications.
- Cortisol is at least one of the regulation and inter= action factors.

It must of course be said that although the encephalus activity is extremely sensitive to the endocrine environment

(Ettigi et al,1978), the latter is also conditioned by numerous other factors.

We know that in the case of Cushing's disease adults are usually depressed, but on the other hand, in the exogenous cushingoid there is usually euphoria. It may be thus hypothe= sized that the activating mechanism does not lie in cortisol itself, but in some other point of the hypothalamus-hypophysis-suprarene axisis.

Neuroregulatory control mechanisms both neurotransmit-ters and neuromodulators such as DOPA and 5HTprobably do play a role in this; DOPA and 5HT affect the tone of the Corti=cotropin-Realizing Factor (CRF) and Proprio-Melano-Cortin (POMC).

Further proof of the fact the cortisol mechanism is only partially responsible for fetal behaviour is, as previously stated, the clear contradiction constitued by the increase in fetal movement during the administration of cortisonics or under stress conditions and, on the other hand, fetal behaviour under basal conditions, a behaviour which is characterized by a decrease in activity during morning hours (when cortisol contents in the mother are high) and an increase in activity at night (when cortisol contents in the mother are low).

Therefore when cortisol is administred and it rises quickly (stress) a fetal activity increase is observed which can be explained in the diagram illustred in fig.1. It shows at the end a reduction in the ß-endorphin and thus an activity disinibition.

Such mechanism is of absolutely no use in explaining the opposite behaviour in basal conditions.

The state of immobility could be at least partially explained by the increase of endorphins.Experimentally,in fact, the iniection of 5OH-triptamine into the brain of sheep fetuses produces a state of restful sleep (Jouvet,1967)and also increases the ACTH, hence also the POMC and ß-endorphins. However, it's difficult to say whether such restful sleep mechanism only accompaines the endogenous morphine in-crease or is the consequence of it.

ß-endorphin increases progressively in fetal blood dur-ing the whole pregnancy period Wardlaw,1979), reaching at the end of gestation, values about four times higher than those found in normal adults Facchinetti,1982).

Experimental data on sheep demonstrate there is an association between hypoxia and fetal distress and ß-endorphin (Wardlaw,1981) but it is not certain whether ß-endorphin is the cause of a reduction in fetal movement or whether it only accompaines such a reduction as a conséquence of asfixia.

In this respect it should be noted that Chermick(1982) has proved that the administration of Naloxone(the specific antagonist to ß-endorphin) improves the conditions of rabbit fetuses made hypoxic experimentally, and it increases their Apgar score at birth.
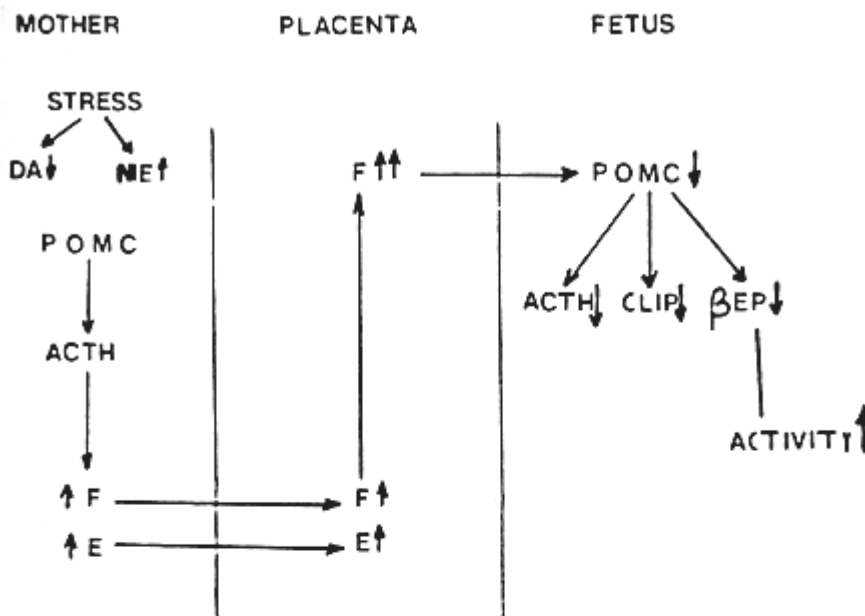
Fig.1 - A maternal stress determines an increase
(NE) and reduction (DA) of neuroendocrine media-
tors,that produces an increase of POMC peptides.
The increase of ACTH stimulates cortisol (F) and
cortison (E) production. Those hormones cross
throgh the placenta where E is converted in F.The
F inibites fetal POMC owing a reduction of fetal
ACTH,fetal CLIP and fetal ßEP. The reduction of
ßEP realases an increase of fetal activity.It
seems so explained the old clinical impression
that a maternal stress creates a strong activity
in the fetus.NE=Nor-epinephrine;DA=dopamine;
POMC=Propio-melano-cortin;CLIP=corticoid liberator
intermediate peptide;ßEP=ßendorphin.

Whatever the etiological mechanism might be, one of the
deciding fáctors in fetal activity is no doubt endogenous
morphine.
     Endogenous morphines are produced in particular by the
fetus (Wardlaw,1979), while the mother does not transfer her
own endorphins to the fetus (Csomtos,1979;Goland,1981).
     The placenta would instead provide peptides and ACTH
similar activities and ß-endorphins in the amniotic fluid

(Kriger,1982),though such chorial production cannot be said to play any role in the physiology of the maternal-fetal hypothalamus-hypophysis-suprarene axis.

A particularly important factor is the loss of control of the secretion of cortisol on the part of the fetal suprarene and E_3,after the 36th week of gestation. This loss is probably related to the increase in the fetal suprarene mass which acco= rding to various Authors (Jackson,1909;Spector,1956;Kondo,1959) increases decisively going from 3-5 grams at 35 weeks to 8-10 grams at the end of pregnancy.

The volume increase of the suprarenal mass is however limited to the so called fetal area, a structure typical of intrauterine life, which quickly involutes after birth and which,according to some authors (Silman,1976 and 1978), would be directly controlled by the intermediate hypophysis portion that is also bound to the spontaneously reabsorbed after birth.

On the other hand, although the relation E_3/cortisol cannot be investigated after the 35th-36th week, behavioural biorhythms are not modified by the same.

It is in fact possible that maternal conditioning (via cortisol) continues to be active even when the inhibition on the steroid synthesis of the fetal suprarene is lost. This is probably made possible by the fact that the fetal area does not secrete large quantities of cortisol which could add to the maternal one. It would be quite impossible for this to happen as the fetal suprarene lacks that fundamental enzyma= tic activity constituted by 3ß-HSD (5- 4 isomerase).

In this way the fetal suprarene goes on producing li= mited amounts of cortisol and the cortisol levels in the mother will always be 8 to 10 times higher than those in the fetus (Gibson,1980).

Moreover, althogh the "diffusable cortisol" (that which is linked to the CBG and not conveyed by the albumins) repre= sents the lesser amount of cortisol in the mother, the diffu= sion gradient is always at least 3:1 (Campbell,1977). This proportion stays high till the end of gestation when the corti sol amount in the mother - which is transformed into cortisone in numerous parenchymals (fetal lung and chorion) by means of an 11-dehydrogenase - remains integral due to the decrease in this enzymatic activity and the increase in the opposite activity (11-ketoreductase) which is capable of carryng out the cortisone-cortisol transformation.

On the basis of studies effected on radioisotopes (Beitins,1979), it is calculated that the maternal contribu= tion to the fetal cortisolemia varies at the end from 25% to 50%, and for the cortisonemia it is about 100%.

The fetal suprarene produces instead ever-increasing amounts of DHEA-S which only after passing into the chorial area will find those specific enzymatic activities (3ß-HSD,

sulfatase,aromatase) capable of converting it into progesteron and corticoids.

The above mentioned considerations justify the hypothesis that fetal behaviour is in some respects correlated to the ma= ternal-fetal endocrine condition and that the hypothalamus-hypo physis-suprarene axis of the mother and the fetus are inter= active.

This is only one of the aspects of the complex mechanism which regulates such behaviours and which undoubtedly involves in the process many other glands and controls of the central nervous system.

What today appears as a hypothesis can therefore be considered as just the tip of an iceberg which the present studies on fetal behaviour have brought to light.

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