ABSTRACT

After defining the difference between pain and nociception, the author likens that binomial to another featured in the international debate on analytical psychotherapy – subjectivity and pre-subjectivity. He places the focus of comparison of those binomials during the period of the primary object relationship – the first 500 days of a person’s life, from conception to weaning.

A wide range of factors – anatomical, physiological, hormonal, and cytochemical – are given, supporting the hypothesis that awareness of pain is not necessary for marks to be incised in the implicit memory of the bodily unconscious as a basis for possible relational suffering.

Keywords: Nociception, pain, primary object relationship, intercorporeity, implicit memory

In evolutionary terms, pain represents a form of sensorial intelligence that is fundamental for survival – a symptom indicating a threat attacking health and full vitality. Pain is a sensorial experience in which it is important to distinguish between nociception and pain.

The term nociception refers to neuronal events that occur when a damaging stimulus comes into contact with any part of our organism where nociceptors are present. Nociceptors (from the Latin noxa, meaning damage) are the unmyelinated ending of sensory neurons, which signal tissue damage through the skin, muscles, joints, and visceral sensations (Wikipedia).

Pain means becoming aware of nociceptive information so that information from the thalamic nuclei is integrated into the limbic and cortical areas (Zimmermann, 1997). No complex living system, however primitive, is without a means to signal harmful events, nor without the capacity for self-medication with endogenous opiates (endorphins, enkephalins) to relieve pain. (This holds true from insects to crustaceans and birds to mammals.)

Each species has its own means of transmission, such as vocalizations, olfactory communication, or visual messages, as in the case of human facial expression.

As for all forms of communication, intensity can vary, as for whispered, quiet, or shouted verbalizations, for example.

Nociception and pain have therefore represented part of bodily-analogical communication ever since the very beginnings of the evolution of living systems. Even in humans, life has surprising characteristics from conception onwards. A dialogue begins between mother and child, which is spelled out in hormonal
messages such as “allowing the little one to pass,” and “not rejecting them as extraneous,” thus “being able to welcome them in the womb.”

The dialogue between mother and child is analogical, presubjective, and intercorporeal, being made up of the language of the biochemical exchanges that accompany the evolution of the little one “from the embryonic state to becoming a fetus and then a newborn baby” in the various stages of the primary object relationship. It is a journey that takes place in three stages over 500 days, moving from conception to implantation (the autogenous stage), from the seventh day to birth (the tropho-umbilical stage), and, finally, from birth until weaning (the oro-labial stage). This journey is structural and structuring, and these 500 days will be fundamental for building the personality on various levels. (Ferri G. & Cimini G., 2012)

**Pre-Subjectivity and Subjectivity**

The distinction between nociception and pain can be associated with the distinction between pre-subjectivity and subjectivity, which is a widely discussed topic in international psychotherapy.

*Without having a mind capable of subjectivity, we would have no way of knowing that we exist and even less chance of knowing who we are or what we are thinking...* (Damasio, 2012, p. 14). *There is no dichotomy between the Self-object and the Self-subject, which is founded on the Self-object...* (Damasio, 2012, p. 21). The self-subject originated from the self-object at a very clear turning point in biological evolution – the upright stance with bipedal deambulation. The I subject, and its field of consciousness, progressively emerge from the functional prevalence of the neopallium (neocortex) over previous brains (reptilian complex and limbic system). This emergence occurs during ontogenesis, from weaning onwards, because of increasing neuronal pyramidalization, with myelination and striated muscular dominance, which represents an increase in the complexity of motor circuits. (Ferri G., 2017)

As well as the association between nociception and pain, and between pre-subjectivity and subjectivity, another similar distinction emerges between implicit and explicit memory.

This topic has been widely researched in neuroscience. The hippocampus handles the selection and codification of information in explicit memory. It is part of the limbic system and is not mature before the age of two, which means that memories connected to explicit memory cannot be formed before that time. Along the arrow of evolutionary and evolutive time, the hippocampus overlies the earlier systemic organization of implicit memory, which is related to the amygdala.

It is clear that the field of consciousness of the neopallium, with its new capability of three-dimensional vision, introduces the localization of objects in space and time, in before and after, and in where and when. In other words, it permits the traceability of memories on the arrow of time, as well as their recall in subjectivity. It is likely that the enormous quantity of information generated by the complexity of motor circuits and by stereoscopic, three-dimensional vision leads to the development of the new central depository – the hippocampus.

Returning to nociception in pre-subjectivity, there are two initial questions:

- Is it possible, etiologically and epigenetically, to consider nociception to be significant in terms of relational suffering during the time of the primary object relationship?
- Can relational suffering represent a platform that predisposes a certain type of phenotypical expression or particular relational trait patterns in the future personality?

Contemporary Reichian analysis (an international school of body psychotherapy) establishes an unconscious at the time of implicit memory, in relational-intercorporeal pre-subjectivity, which marks the individual, peripherally and centrally, in very precise relational areas.

I would like to suggest some indicators from the fetus that reinforce this hypothesis. The fetus experiences nociception.

**Anatomical Indicators**

The fetus has sensorial capacity from the first few weeks of its existence onwards. First, it has touch; secondly, hearing, taste, smell; and then sight.

- Cutaneous receptors for sensitivity indeed appear in the perioral area at seven weeks; they spread then over the rest of the face, onto the palms of the hands, and onto the soles of the feet at 11 weeks, on the trunk and the proximal part of the limbs at 15 weeks, and over the whole of the cutaneous and mucous surfaces by 20 weeks.
- The fetus’ heart begins beating on the 16th day of life.
- The most important part of the brain for pain perception is the thalamus, which forms from eight to 12 weeks.
- The thalamic-spinal pain pathways are formed between the seventh and 20th weeks.
- The thalamic-cortical connection is established between the 17th and 26th weeks.
- Myelination of neurons is already occurring in the 22nd week.
- The limbic anterior cingulate gyrus, which is responsible not only for the fetus’ nociceptive capacity, but also for relational suffering, begins to form during the 26th week (Cesari E. et al., 2011).
How can we fail to associate Porges’ polyvagal theory, which indicates that the maturation of the ventral vagal circuit occurs in human mammals only during the final period before birth and the first year of life – with times that belong to the primary object relationship? Isn’t this a fundamental circuit for the activation of affiliation behavior and reciprocal affectivity? (Porges, 2014)

Physiological and Hormonal Indicators

- From the 16th week onwards, if the fetus finds itself under stress (hypoxemia, hemorrhage, reduction in uterine blood flow), it is able to redistribute its own hematic flow, protecting organs like the myocardium and brain, and regulating vasoconstriction in certain regions, such as in the splanchnic, cutaneous, and renal areas.
- The fetus already has a motor reaction to being pricked with a needle after eight weeks of life.
- After the intrahepatic vein is punctured to take a sample of fetal blood, plasmatic cortisol and beta-endorphin levels increase from two to six times, compared to cordocentesis in which the fetus is not pierced (Giannakoulopoulos, 1994).

These responses do not occur if analgesic opioids are administered. Some authors (Fitzgerald, 1985; Lee, 2005 in Cesari E. et al., 2011) claim that these responses do not indicate fetal pain-nociception but, rather, are reflexes. However, these affirmations are associated with an unthinkable negation of the unconscious in the body!

Cytochemical Indicators

- Substance P (a substance that is a pain mediator) has been shown to be present in the fetus from 8 to 10 weeks onwards and encephalin (a neurotransmitter in the endorphin family) from 12 to 14 weeks onwards.
- The μ (Mu) and κ (Kappa) morphine receptors are present in the spinal cord at very early stages of development, while the δ (Delta) receptors appear later (Cesari et al., 2011).

Memory of Intrauterine Suffering

At 25 weeks, the fetus in the womb can respond to the acoustic stimulus of the mother’s voice, and at birth, they recognize, through a sort of memory, the acoustic stimuli they heard before birth.

The fetus not only also notices prosodic variation in the voice, but also physical activity and the mother’s heart rate.

I would add that the taste of the amniotic fluid translates the taste of the intrauterine primary object relationship, which I defined a few years ago as being a “mirror-taste.” Jacobsen’s vomeronasal organ had resolved the question arising from psychopathological certainties: “How could the unborn child know about the taste of the relationship in a liquid environment and in which they were not breathing?” (Ferri, 2017)

By injecting sweet or bitter substances into the amniotic fluid after the 24th week of gestation, a preference of the fetuses for sweetness and an aversion to bitter tastes was observed. In the first case, they swallowed double the amount of amniotic fluid, and their facial expressions showed pleasure, whereas in the second case, their facial expressions showed disgust, and they immediately stopped drinking.

During the embryonic-fetus period, the vomeronasal organ, which is located above the incisors, transduces odorous substances in liquid solution into flavor, and permits the fetus to recognize the flavor of the relationship with the mother. This organ, which is also present in fish, normally atrophies in humans after birth.

The fetus in the uterus at 20 weeks can experience more intense nociception compared to a newborn child or an adult. The fetus has a greater density of nerve receptors, their skin is not very thick, and they have not yet developed the descending neuronal circuit, which will attenuate pain as it develops after birth.

Various studies have shown the dangerous effects of maternal depression during pregnancy on the child’s mental development. Prolonged, constant rejection of the child by the mother is an example of significant fetal relational suffering. Another example is that of children born to women who have not yet elaborated their grief after a previous miscarriage or abortion. These children can develop the replacement child syndrome in which they report living with the perception of being a substitute (Sabbadini., 2008).

More generally, maternal stress, such as anxiety while waiting for the results of a karyotype test, adapting to a new psycho-emotionally unbearable situation, losing a loved one, or trauma from a fall, for example, can be dangerous because they occur in a critical phase during which the brain is still “plastic and flexible.” A given genotype can express different phenotypes according to the environmental influences it experiences.

Although the discovery of transgenerational epigenetic effects for mammals is relatively recent, transgenerational epigenetic effects in nature have long been rec-
In the 1st phase of the primary object relationship, which lasts until weaning, the last port of call (D’Udine).

**Nociception in Newborn Babies**

Birth is the first great separation. It is the dividing line between the first and second phases of the primary object relationship. It involves moving from water to air, from amniotic fluid to epidermic contact, from dark to light, from the uterus to the breast, from inside to outside, from the umbilical cord and placenta to the lips and nipple, and from the sixth relational bodily level – the umbilical-abdominal area – to the second relational bodily level – the mouth.

The seven relational body levels are the places in the body that carry the imprints and peripherally incised tracings from object relationships during the time of the evolutionary stages. (Ferri, 2020)

In reality, threats of potential separation can occur even during pregnancy. However, these are very different from separations, and is confirmed by the fact they stimulate production of the noradrenergic (NA) alarm neuromediators. Potential separation during gestation is not merely equivalent to loss, which usually causes serotoninergic depletion, but represents real, vital alarm. In this regard, 5HT is the neuromodulator that plays the greatest role in nociception and pain. Depletion of 5HT, in fact, increases pain, including relational pain, while an increase in 5HT lowers the perception of pain, again also for relational pain, improving mood. (McGuire & Troisi, 2003)

At birth, we move into the analytical time of the orolabial stage, which lasts until weaning, the last port of call for the primary object relationship!

**Oxytocin**

Oxytocin is the hormone that causes mother-child attachment. It is the chemical messenger that is essential to initiate labor and permit birth by stimulating contractions of the smooth muscle tissue in the uterus. Oxytocin then stimulates cells in the lactiferous ducts in the breast, causing contraction of muscle cells and the secretion of milk, all as a response to the stimulus of breastfeeding.

Oxytocin is, therefore, the key hormone for this evolutionary window, in which specific patterns of relational suffering can be imprinted from the transitions between stages, onto what will become the multistory building of the individual personality.

In the presence of symptoms of psychotic depression, which are extremely painful from a relational perspective and are found in egocentric, persecutory, self-referral situations often correlating analytically with this evolutionary period, administering an oxytocin spray results an easing of the clinical picture.

- It increases the amount of time spent observing the ocular region and improves the ability to recognize facial expressions.
- It reduces the degree of arousal when confronted by threatening visual stimuli.
- It reduces the possibility that positive or neutral facial expressions are erroneously perceived as negative (Pallanti, 2015).

**Neurophysiological and Neurovegetative Indicators in Newborn Babies**

Until the 1980s, surgery was performed on infants without any kind of analgesic. Only in 1987 did Anand demonstrate that cardiac surgery on newborn babies was followed by a significant increase in adrenaline and cortisol values, and that these parameters did not increase when opioid analgesics were used.

It was believed that the lack of myelination of the nociceptive fibers prevented the newborn infant from experiencing pain, and that the cells in the dorsal horns of the spinal cord, which transfer sensorial information from the periphery to the higher centers, did not respond to nociceptive impulses before the second week after birth!

Using an MRI, in newborn babies aged from one to seven days, 18 of the 20 regions of the brain associated with pain were illuminated. These were the same 18 of 20 regions that were illuminated in adults, but with greater sensitivity (Salter, 2018). It should be remembered that the density of nociceptors is greater, and the presence of substance P is higher in newborn babies than in adults.

In newborn babies, invasive procedures (tracheal aspiration, mechanical ventilation, and venous sampling) cause crying, tachycardia, diaphragmatic contraction, and sudden, violent motor responses.

With regard to venous sampling, Bellieni’s study on sensorial saturation is illuminating. This technique produces a reduction in pain and sometimes works as a real analgesic for newborn babies (Bellieni, 2007). It is based on the concept that a painful stimulus can be contrasted to other sensorial stimuli such as touch, taste, smell, and the sound of the voice talking (3T). The study was performed on four groups of newborn infants, all requiring venous sampling.

- In the 1st group, the sample was simply taken.
- In the 2nd group, a 10% glucose solution was given orally by cannula during the sampling.

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In the 3rd group, the glucose was given before the sampling.

In the 4th group, a nurse gave the babies the glucose solution during the sampling, allowing them to suck it from a pipette while *stroking them and talking to them*.

In the 1st group, there was crying and prolonged motor agitation.

In the 2nd and 3rd groups, there was only crying, but less prolonged.

In the 4th group, utilizing sensorial saturation, the babies did not cry, and were not agitated during the sampling.

The importance of the relationship in neonatal suffering is evident from this study in terms of epidermic contact (gentle stroking), visual stimuli (including joyous eyes), and prosody (a kind, warm voice). Again, how can we fail to remember Porges’ ventral–vagal circuit and his accurate neologism *neuroception* – the capacity of the infant to evaluate their environment as being safe or dangerous? (Porges, 2014)

**Conclusion**

Experiencing pain during the first 500 days of life, during the time of the primary object relationship in which the pain circuits are highly plastic and still maturing, can influence the physiological development of the central nervous system, the hypothalamus, the pituitary gland, the adrenal gland axis, and the immune system. This can produce long-term vulnerability to inflammatory disease, psychodynamic difficulties, and psychiatric disorders.

*It is not essential to be aware or conscious of pain for it to alter the development of these systems, and cause difficulties and disorders!*

From a psychopathological and psychotherapeutic perspective, this means that pre-subjective, nociceptive imprints from the person’s life story, received during the primary object relationship evolutionary stages and stage transitions, can represent a platform for disturbances and for beyond-threshold relational patterns. By extending this “temporal” observational perspective to include intrauterine life, the current psychopathological nosography could be revisited, and research in psychotherapy could make a significant contribution towards improving therapeutic, psychocorporeal, and psychopharmacological appropriateness.

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