Giriş

1b

To be happy, from Newborn Infant's Perspective*

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This is from the perspective of infant, their feelings are configurated by the pain concept.

Subjective considerations are commonly configurated in order to evaluate the individual situation. In this Unit, the sight from the newborn infant is recognized, under the perception of aching and pain assessments. Touching, skin to skin, kangaroo method by holding tightly, breastfeeding is more than it is done, not really a comfort but, a place of heaven for the newborn infant.

The most comfortable, physiological all the happiness hormones are directly effective position is, mother's contact by breastfeeding. Thus, mother must be also in situation and position at comfortable, physically and mentally and be at love effect, concept to the infant.

Outline

To be happy, from Newborn Infants Perspective

AIM: The feeling of preterm infants, have to be in happy considerations, at least no pain or other stress factors, thus, arbitrarily and unavoidably due to ventilation and other medical approach it is inevitable. From baby's perspective, these considerations are indicated at this Unit.

Grounding Aspects: The hormones at happiness and pain and their effect on human body discussed and the importance at the infants, thus, is taken in consideration.

Introduction: Under the pain estimation scales, the reactions and physiological response to the pain is taken at the based scientific concept, for the evaluation of infant's perspective on happiness and pain.

Proceeding: General Considerations; Touch, skin to skin contact, breast feeding and mother's milk, not only sugar, just holding as kangaroo method is more important for pain relief or even lessening of pain at the newborn infants, even at the preterm infant, even by holding his/her hand, thus, this indicates us, the act to the preterm infants, is not as for humanistic and ethical considerations, but also for the physiological grounding for the pain declining and diminishing.

Notions and Conclusion: The love of mother to infant's is more than social and psychiatric notion, it is more physiological positive manner to the newborn infant, thus, be a native Right of the infant.

The best love affairs of the other to the newborn infant is breastfeeding, by heart, not by obligatory.
Key Words: Hormones for happiness (Dopamine, Endorphin, Oxytocin, Serotonin) and pain (sex hormones, emotions, genes, reactions), and actions of this hormones, Pain and Happiness at Neonatology Period

Özet

Mutlu Bebek Olmak, Onların Bakış Açısı ile

Amaç: Yenidoğan bebeklerin, özellikle prematüre bebeklerin duyularının olduğu, özellikle ağrı açısından korunmaları, mutlu olmaları için önemli bir zorunlu yaklaşım ötesinde, bebeğin algısı boyutu ile bu konu irdelenmektedir.

Dayanaklar/Kaynaklar (Materyal ve Metot): Mutluluk ve ağrı sırasında oluşan hormonlar temelinde, bunların fizyolojik etkileri boyutunda yenidoğanlarda etkileşim bakılmıştır

Giriş, Genel Yaklaşım: Dokunma, cilt, cilt teması, emzirme, anne sütü almak, şeker tek başına olmadan, bebeği kucakta Kanguru metodu ile tutmak, ağrının azalması ve önlenmesi ötesinde, insancıl ve etik yaklaşım olarak öngörülen bir boyut olmaktadır.

Yaklaşım, Başlıca boyutlar: Bebeğin emzirmesi konusunda her bebeğe ve anneye özgü yaklaşım ve geliştirmenin sağlanması ile bunun etkin uygulanabilir olması açısından yaklaşım gereklidir. Teorik olmanın ötesinde uygulanabilir boyuta getirilmelidir.

Yorum ve Sonuç: Annenin bebeğine olan sevgisi, sosyal ve psikiyatrik yaklaşımdan öte, fizyolojik oluşturduğu olumlu yanları ile dikkate alınmalı ve bebeğin doğal hakkı olarak görülmelidir.

Anahtar Kelimeler: Mutluluk ve ağrıda etkili olan hormonlar, Neonatoloji Dönemi

Baby

Each baby has some sensational receptions, especially pain, thus, the reaction is not so specific and be not so sure on the evidence based. Therefore, we cannot directly consider the perception of senses of the newborns, but, considering on the for estimation of the pain, there are some scales are constructed and used in Neonatology Units.

In general, 5 senses, we commonly considering; sight, smell, hear, touch, and taste.

There are others to be mentioned as; mechanical perceptions, heat, cold, stretching of the legs, etc. Interior perceptions as; tension, distension, defecation, urination etc.

Receptors can be grouped under three, as; a) chemoreceptors, as noticeable at taste, b) photoreceptors, as light at the retina, c) mechanical receptors/baroreceptors, as dryness of the skin, tension of the body, etc.

Comment

The newborns, even the preterm infants noticed the receptors but not so specialized and localized them. General behavioral and habitual reactions can be noticed and be taken as an indicator of the pain or comfort.

Thus, the main concept, to be cool, rest and happy. Pain is also reciprocally configurated endogen secretion of endorphin, dopamine and other ones, to overcome the pain/stress. The best is skin to skin touch, holding as kangaroo method, breastfeeding and face to face contact. All living organism, required humanity acts, love and empathy based respect. Even nonliving ones, as, not to hit the ball in anger, just a gentle, controlled kick or hit.

To be love and be loved is the main ethical considerations as not to do any harm, primum non nocere, means, not to behave as a human may also considered s harmful and non-respectful behavior/act.

NOTE (From PhD Thesis): The validity and reliability of the Neonatal Pain/Agitation, Sedation Scale (N-PASS), in Eskişehir, Turkey. A Turkish adaptation of the Neonatal Pain/Agitation, Sedation Scale (N-PASS) and its validity and reliability. Ayfer Açıkgöz, Z. Çiğdem, S. Yıldız, C. Demirüstü, M. Yarar, M. A. Akşit.

In order to measure the pain, there are no reliable and easily performed physiological and biochemical tests. The behavioral attitudes are mainly used for pain assessment. Several measurement scales are indicated, however for neonatal period the verdicts must have adapted to newborn infants.

However, neonates cannot verbally express their feelings about pain, and the assessment of pain is very difficult in this age group. There are no physiological or chemical tests to measure pain, and therefore pain is generally evaluated by observing behavioral changes. There are several pain assessment scales that are currently available; however, the need to use a different pain scale for infants with different characteristics complicates the adoption of the routine use of pain scales in neonatal intensive care units.

Neonatal Pain, Agitation and Sedation Scale (N-PASS), one of the currently available pain scales, can be used on full-term and preterm infants. The scale measures both acute and chronic pain and can easily be applied to all infants whether they are on respiratory support or not. N-PASS was developed by Pat Hummel and his colleagues in 2003 and was revised on October 2, 2009. N-PASS consists of two sections that measure the sedation levels and pain levels of infants. The scale has five sub-parameters that include crying and irritability, behavioral state, facial expression, body tension with hand and feet and vital signs. Scores of 0 to +2 points are assigned for the evaluation of pain, and scores of 0 to -2 points are assigned for the evaluation of sedation in each behavioral and physiological criterion. If the infant was born before 30 weeks of gestation, +1 is added to the total score for the evaluation of pain. The total pain score ranges from 0 to +11, and the total sedation score ranges from 0 to +10. A high score indicates that the pain is severe. The aim of pain treatment is to maintain the score at or below 3. The standard score for infants, in terms of the sedation evaluation, changes according to the desired sedation level. If there is no sign of sedation in the infant, 0 points are assigned, which reaction to these points does not mean inadequate. Slight sedation usually results in scores between -2 and -5 points, and deep sedation usually results in scores between -5 and -10 points. The average time spent implementing the scale is 1 minute.

The measurement/estimation of the sense, indicating as pain

There are some measurement methods, considering the pain measurement and let the newborns be comfortable and be safe at the medical procedures.

We cannot sure on the newborn infants, thus, the physiological changes are indicating they feel as same as the adults. Therefore, painkillers are required also for them, thus not as people demand.

Comparative Pain Scale (Wikipedia)

- No pain
- Minor Pain
  - Very Mild: mosquito bites, but itching is remarkable and differs
  - Discomforting: two fingers pressing the cheeks, noticeable touch
  - Tolerable: injections of the medicine
- Moderate Pain
  - Distressing: toothache, thus, tolerable ones
  - Very Distressing: sprained ankle, foot, hand
  - Intense: migraine headache
- Severe Pain

- Very intense: spasm of colon, changing the positions and required analgesics
- Utterly horrible: child bearing, personality changes
- Excruciating unbearable: pain killer must be given
- Unimaginable unspeakable: nearly out of mind, cause of pain

Neonatal Infant Pain Scale (NIPS)

In this scale, the common arguing verdicts are indicated below. The scoring for each parameter is from 0 to 2 points. 7 points indicates as normal, four or less are specified the pain.

1. Facial expression: relaxed or contracted
2. Crying: none/absent, mumbling/incoherent or vigorous
3. Breathing: relaxed, differs
4. Arms: relaxed or flexed/stretched
5. Legs: relaxed or flexed/stretched
6. Alertness: calm/sleeping, or uncomfortable

Neonatal Pain/Agitation, Sedation Scale (N-PASS)

Assessment of the Pain Criteria at N-PASS:

- **Crying / Irritability**

-2 → No response to painful stimuli, e.g.:
- No cry with needle sticks
- No reaction to ETT or nares suctioning
- No response to care giving

-1 → Moans, sighs, or cries (audible or silent) minimally to painful stimuli,
e.g. needle sticks, ETT or nares suctioning, care giving

0 → Not irritable – appropriate crying
- Cries briefly with normal stimuli
- Easily consoled
- Normal for gestational age

+1 → Infant is irritable/crying at intervals – but can be consoled
1. If intubated – intermittent silent cry

+2 → Any of the following:
- Cry is high-pitched
- Infant cries inconsolably
- If intubated – silent continuous cry
- **Behavior / State**

-2 → Does not arouse or react to any stimuli:
1. Eyes continually shut or open
2. No spontaneous movement

-1 → Little spontaneous movement, arouses briefly and/or minimally to any stimuli:
- ✓ Opens eyes briefly
- ✓ Reacts to suctioning
- ✓ Withdraws to pain

0 → Behavior and state are gestational age appropriate

+1 → Any of the following:
- ❖ Restless, squirming
- ❖ Awakens frequently/easily with minimal or no stimuli

+2 → Any of the following:
- Kicking
- Arching
- Constantly awake
- No movement or minimal arousal with stimulation (inappropriate for gestational age or clinical situation, i.e. post-operative)
- ***Facial Expression***

-2 → Any of the following:
- Mouth is lax
- Drooling
- No facial expression at rest or with stimuli

-1 → Minimal facial expression with stimuli

0 → Face is relaxed at rest but not lax normal expression with stimuli

+1 → Any pain face expression observed intermittently

+2 → Any pain face expression is continual

- ***Extremities / Tone***

-2 → Any of the following:

1) No palmar or planter grasp can be elicited
2) Flaccid tone

-1 → Any of the following:

- Weak palmar or planter grasp can be elicited
- Decreased tone

0 → Relaxed hands and feet – normal palmar or sole grasp elicited – appropriate tone for gestational age

+1 → Intermittent (<30 seconds duration) observation of toes and/or hands as clenched or fingers splayed

- Body is *not* tense

+2 → Any of the following:

1. Frequent (≥30 seconds duration) observation of toes and/or hands as clenched, or fingers splayed
2. Body is tense/stiff

5) Vital Signs: HR, BP, RR, & O_2 Saturations

-2 → Any of the following:

- No variability in vital signs with stimuli
- Hypoventilation
- Apnea
- Ventilated infant – no spontaneous respiratory effort

-1 → Vital signs show little variability with stimuli – less than 10% from baseline

0 → Vital signs and/or oxygen saturations are within normal limits with normal variability – or normal for gestational age

+1 → Any of the following:

- HR, RR, and/or BP are 10-20% above baseline
- With care/stimuli infant desaturates minimally to moderately (SaO_2 76-85%) and recovers quickly (within 2 minutes)

+2 → Any of the following:

1) HR, RR, and/or BP are > 20% above baseline
2) With care/stimuli infant desaturates severely (SaO_2<75%) and recovers slowly (> 2 minutes)
3) Infant is out of synchrony with the ventilator –fighting the ventilator

Table 1b/1: N-PASS Scale © Hummel & Puchalski (*Rev. 8/14/01)* Loyola University Health System, Loyola University Chicago, 2000

Assessment Criteria	Sedation		Normal	Pain / Agitation	
	-2	-1	0	1	2
Crying Irritability	No cry with painful stimuli	Moans or cries minimally with painful stimuli	Appropriate crying Not irritable	Irritable or crying at intervals Consolable	High-pitched or silent - continuous cry Inconsolable
Behavior State	No arousal to any stimuli No spontaneous movement	Arouses minimally to stimuli Little spontaneous movement	Appropriate for gestational age	Restless, squirming Awakens frequently	Arching, kicking Constantly awake or Arouses minimally / no movement (not sedated)
Facial Expression	Mouth is lax No expression	Minimal expression with stimuli	Relaxed Appropriate	Any pain expression intermittent	Any pain expression continual
Extremities Tone	No grasp reflexes Flaccid tone	Weak grasp reflex ↓ muscle tone	Relaxed hands and feet Normal tone	Intermittent clenched toes, fists or finger splay Body is not tense	Continual clenched toes, fists, or finger splay Body is tense
Vital Signs HR, RR, BP, SaO_2	No variability with stimuli Hypoventilation or apnea	< 10% variability from baseline with stimuli	Within baseline or normal for gestational age	↑ 10-20% from baseline SaO_2 76-85% with stimulation – quick ↑	↑ > 20% from baseline $SaO_2 \leq 75\%$ with stimulation – slow ↑ Out of sync with vent

Comment

The newborn infants, as living organism, directly have a reaction, especially to pain.

It must be mentioned for the contrary reaction, as a happy child syndrome, as we noticed. The smiling and sleeping, thus, in clam and cool way, with spontaneous movements.

Pleasure confirmed Hormones

The mostly mentioned hormones, secreted in happiness conditions are;

- Dopamine:

- Endorphin:
- Oxytocin:
- Serotonin:

Dopamine

MacDonald, Mhairi G.; Seshia, Mary M. Avery's Neonatology: Pathophysiology and Management of the Newborn (Avery's Neonatology Pathophysiology and Management of the Newborn)

Dopamine is an adrenergic agent with variable and unpredictable effects in the developing human. In animal models, dopamine improves renal and mesenteric blood flow at low doses, increases myocardial contractility via β-adrenergic effects at moderate doses, and has predominantly vasoconstrictive α-adrenergic effects at higher doses. In preterm neonates, there have been few studies on pharmacodynamics (PD), making this progression less clear. There is variability between individual neonates in response to dopamine at similar doses. When exposed to dopamine at doses of 6 to 8 mcg/ kg/ min, some neonates demonstrate an increase in LVO with a modest increase in MBP, whereas others demonstrated a reduction in LVO with a larger increase in MBP. This likely represents a difference in the balance of inotropic versus vasoconstrictive effect between individuals (99), which is independent of dose. The unpredictability of these effects is a concern. Caution should be used with dopamine in immature patients,

In contrast, dobutamine, a synthetic catecholamine with predominantly β-adrenergic activity, has been shown to increase CO by augmenting stroke volume and may be more effective at improving systemic blood flow (100,101). Dopamine has been consistently identified as superior to dobutamine at increasing blood pressure. Echocardiographic studies consistently suggest that the predominant mechanism is via peripheral vasoconstriction by documenting increases in blood pressure with little change in LVO (99) or SVC flow. In a blinded, randomized trial, SVC flow increased by 35% in infants receiving dobutamine as compared to a 1% decrease in infants receiving dopamine (100). PBF was also significantly higher in dobutamine-treated patients, suggesting it to be more advantageous as the primary agent in PPHN.

Comment

Autonomous nervous system can be considered as sympathetic, parasympathetic, or alfa, beta and gamma, or cAMP mediated and cGMP mediated systems, or noradrenaline, adrenaline and catecholamine effective assemblies.

Dopamine is double effect ones, small amount dilates, dose save the tonus, more makes construction, considered as alfa and beta receptors mediator.

Happiness and pain must be on reflection of such mediators, because transmitting the messages. Especially Dopamin scare at the preterm infants and be very helpful for the stabilization and bearing in mind the physiological autonomic functions can be established.

Figure 1b/1: There are eight dopaminergic pathways, but the four major ones are at the above (http://reliawire.com/dopamine-pathways/)

Dopaminergic pathways. http://psychology.wikia.com/wiki/Dopaminergic_pathways

… There are eight dopaminergic pathways, but the four major ones are, illustrated as Figure 1b/2:

- Mesolimbic pathway, transmits dopamine from the ventral tegmental area (VTA-the midbrain) to the nucleus accumbens (the limbic system)

Mesolimbic dopamine release was once thought to be the primary mediator of pleasure, but is now believed to have only a minor role in pleasure perception.

- Mesocortical pathway, transmits dopamine from the VTA to the frontal cortex. Malfunctions of the Mesocortical pathway are associated with schizophrenia.
- Nigrostriatal pathway, transmits dopamine from the substantia nigra to the striatum, and associated with motor control, and degeneration of this pathway is related to Parkinson's disease.
- Tuberoinfundibular pathway, transmits dopamine from the hypothalamus to the pituitary gland, thus, influences the secretion of certain hormones, including prolactin.

Endorphin

MacDonald, Mhairi G.; Seshia, Mary M. Avery's Neonatology: Pathophysiology and Management of the Newborn (Avery's Neonatology Pathophysiology and Management of the Newborn)

Labor Pain: Implications for the Fetus Neural pathways and neurochemical systems involved in pain perception are functional from mid-gestation and are well developed by the third trimester. Gitau et al. (34) conducted a parallel study of the fetal and maternal hormonal responses to fetal blood transfusion. They confirmed that the fetus mounts a hypothalamic– pituitary–

adrenal response to transfusion via the intrahepatic vein, which involves piercing the fetal trunk, but not to transfusion in the umbilical vein at the placental cord insertion, which has no sensory innervation. The rise in fetal cortisol and endorphin occurred independently of the maternal reaction. Pretreatment of the fetus with fentanyl for this same procedure attenuated the rise in β-endorphin (35). Hormonal stress responses do not provide a direct index of pain. While it is true that a rise in cortisol and endorphin is seen as a consequence of painful stimuli in children, other nonpainful situations (e.g., exercise) are also associated with an increase in the levels of these hormones. Nonetheless, the editorial review of Fisk's fentanyl pretreatment study suggests that fetal analgesia should be given during invasive in utero procedures (36). At present, there is no literature on fetal "pain" during labor or delivery.

Endorphins and Emotions. http://science.howstuffworks.com/life/endorphins.htm

Endorphins block pain, but they're also responsible for our feelings of pleasure. It's widely believed that these feelings of pleasure exist to let us know when we've had enough of a good thing -- like food, sex or even companionship -- and also to encourage us to go after that good thing in order to feel the associated pleasure.

… There are at least 20 different kinds of endorphins, and one kind, beta-endorphins, are stronger than morphine and have been shown to play a part in everything from alcoholism to diabetes to aging of the brain

… The majority of your emotions (and memories) are processed by your brain's limbic system, which includes the hypothalamus, the region that handles a range of functions from breathing and sexual satisfaction to hunger and emotional response. The limbic system is also rich with opioid receptors. When endorphins reach the opioid receptors of the highly emotional limbic system, and -- if everything is working normally -- you experience pleasure and a sense of satisfaction.

… Neurotransmitters play a key role in the function of the central nervous system and can either prompt or suppress the further signaling of nearby neurons.

… Endorphins are produced as a response to certain stimuli, especially stress, fear or pain. They originate in various parts of your body -- the pituitary gland, your spinal cord and throughout other parts of your brain and nervous system -- and interact mainly with receptors in cells found in regions of the brain responsible for blocking pain and controlling emotion.

... It's been theorized that problems with endorphin production or the binding process may be responsible for clinical depression or sudden shifts in emotions. Some people who engage in self-hurting behaviors may do so in part to feel the feelings of euphoria and emotional isolation that can -- for them -- be prompted by controlled amounts of self-inflicted pain.

… Endorphins may also be responsible for heightened states of rage or anxiety. If your endorphins overdo their job or the hypothalamus misreads the endorphin cue, you could be flooded with "fight-or-flight" hormones at the slightest hint of trouble or worry.

… Endorphins affect us like codeine or morphine do, but without the addiction. Regular users of opiates generally aren't models of emotional stability, and steady, controlled endorphin release is something of a pipe dream. Making matters worse, some of us have brains that act like ambitious drug dealers, and others of us only dabble now and then. This variation can help explain why one person reacts differently from another to the same stimulus.

… Endorphins are produced throughout your body and requested by the hypothalamus, but what else besides stress and pain triggers the release of endorphins are; a) … Exercise, b) … Meditation or controlled-breathing exercises, c) … Childbirth -- Giving birth to a child is clearly a subcategory of both pain and stress, d) Alcohol -- Light to moderate drinking stimulates endorphins, but heavy drinking doesn't, e) Chili peppers -- Capsaicin, which puts the burn in chilies, also triggers the body to release some fire-quenching endorphins, f) Bodywork -- Both acupuncture and massage therapy trigger your inner drug dealer, g) Ultraviolet light -- This may explain why some users of tanning beds achieve

Comment

The newborn infants for adaptation and to be accepted the ventilation, some opiate compounds are using nowadays. For reducing the pain, the endorphins may not so satisfactorily have produced and be required.

Oxytocin

MacDonald, Mhairi G.; Seshia, Mary M. Avery's Neonatology: Pathophysiology and Management of the Newborn (Avery's Neonatology Pathophysiology and Management of the Newborn)

Vasopressin or antidiuretic hormone (ADH) and oxytocin are the two-major posterior pituitary endocrine hormones. Oxytocin has no known function in the neonate although ADH helps to regulate intravascular volume and osmolality. ADH is synthesized in the supraoptic and periventricular nuclei of the hypothalamus by 12 weeks of gestation. It is bound to neurophysin and is transported along the neuro-hypophyseal tract to the posterior pituitary, where it is stored and released as necessary. ADH increases the permeability of the collecting tubules of the kidney to water and urea. Its secretion is stimulated by hyperosmolar states and volume depletion and inhibited by volume overload. The two main disorders of ADH secretion are DI and SIADH.

dilute, with an average osmolality less than 200 mOsm/ kg. Higher osmolality in utero may result from obstructive urinary tract disease, poor tubular reabsorption of sodium, administration of oxytocin or indomethacin to the mother, or intrauterine asphyxia. Urine produced after birth usually is isotonic or hypertonic, probably as a result of increased release of oxytocin and ADH.

Prolonged partial asphyxia was produced either by inducing hypotension in the pregnant monkey with halothane anesthesia or by using intravenous infusion of oxytocin to produce prolonged, frequent uterine contractions. If prolonged partial asphyxia

was maintained for 2 to 4 hours, the fetal monkey could be resuscitated but usually developed extensor posture and seizures. Neuropathology showed a completely different pattern from that resulting from acute total asphyxia, there being widespread injury to the cerebral hemispheres, particularly frontally and occipitally, the watershed areas between the two main cerebral arteries, and no injury to the brainstem and spinal cord. Basal ganglia injury was only seen in fetal monkeys who had experienced prolonged partial asphyxia followed by acute total asphyxia.

Recent development on oxytocin in psychotherapy.

http://www.medicalnewstoday.com/articles/275795.phpIntro

https://www.psychologytoday.com/basics/oxytocin

… Oxytocin activates "social" brain regions in children with autism.

… Oxytocin may also have a role to play in anger management, with research finding that certain polymorphisms of the oxytocin receptor (OXTR) gene are associated with an increased tendency to react more angrily to situations. Specifically, differences in OXTR gene expression appears to affect the regulation of the relationship between alcohol and aggressive behavior.

- Other potential benefits of oxytocin: Recent research has shown that oxytocin increases the release of prostaglandin E2 in cells lining the intestines, which helps encourage repair of intestinal injury and to protect against such injury. This may make oxytocin a useful therapy for preventing chemo-radiotherapy induced intestine injury, as well as a novel and safe treatment for irritable bowel disease (IBD).
- Oxytocin released during sex: In all genders, sexual activity stimulates the release of oxytocin, which has a role in erection and orgasm.
- Some researchers believe oxytocin may play a part in the experience of sexual orgasm.
- Behavioral effects of oxytocin:
    - Oxytocin: the monogamy hormone? This study, published in the journal PNAS in November 2013, examined brain scans of men who had received oxytocin or placebo via a nasal spray. The oxytocin was associated with activation of the men's reward centers in their brains, and with greater feelings of attraction to their partners versus other women in photographs. This followed a very similar study in The Journal of Neuroscience in November 2012: A hormone can help keep men faithful.
    - High oxytocin levels "trigger oversensitivity to emotions of others." Released in January 2014, this study in Emotion found that people receiving oxytocin nasal spray saw facial expression of emotions in others more intensely.
    - Oxytocin makes you feel more extroverted. This 2011 research paper in Psychopharmacology gave results from intranasal oxytocin improving self-perception in social situations, amplifying personality traits such as warmth, trust, altruism and openness.
    - The hormone that allows us to love may also encourage us to lie. This 2014 study found participants given oxytocin were more likely to lie for the benefit of the group.
- Oxytocin as potential psychiatric therapy: oxytocin could help people with disorders such as autism to better understand other people's emotions:
- Oxytocin's effects on emotion: Oxytocin released into the bloodstream affects the uterus and lactation, but its release into defined regions of the brain also affects emotional, cognitive, and social behaviors. The review, by Inga Neumann, states that oxytocin's impact on "pro-social behaviors" and emotional responses contributes to: a) Relaxation, b) Trust, c) Psychological stability, … as also including effects as; on motherly care and aggression, bonding between couples, sexual behavior, social memory… However, another review notes that the hormone does not act alone in the chemistry of love, but is "just one important component of a complex neurochemical system that allows the body to adapt to highly emotive situations." … Brain oxytocin also reduces stress responses, including anxiety - and these anxiolytic effects have been demonstrated in a number of species.

Fast facts on oxytocin: … Oxytocin is a powerful hormone and acts as a neurotransmitter in the brain. It regulates social interaction and sexual reproduction, playing in role in behaviors from maternal-infant bonding and milk release to empathy, generosity, and orgasm. When we hug, or kiss a loved one, oxytocin levels increase; hence, oxytocin is often called "the love hormone." In fact, the hormone plays a huge role in all pair bonding. The hormone is greatly stimulated during sex, birth, and breastfeeding. Oxytocin is the hormone that underlies trust. It is also an antidote to depressive feelings.

… it plays a more complex role in human behavior than is commonly thought. As a facilitator of bonding among those who share similar characteristics, the hormone fosters distinctions between in-group and out-group members, and sets in motion favoritism toward in-group members and prejudice against those in out-groups. Ongoing research on the hormone is a potent reminder of the complexity of biological and psychological systems.

Here are some key points about oxytocin.

- Oxytocin is a neuropeptide produced in the hypothalamus and secreted by the pituitary gland.
- Oxytocin is released during sex, childbirth and lactation to aid reproductive functions.
- This neuropeptide exerts multiple psychological effects, influencing social behavior and emotion.
- Oxytocin is prescribed for a variety of obstetric and gynecological reasons, including to aid in childbirth.
- High levels of the "love hormone" have been observed in couples in the first six months of a relationship.
- Oxytocin has an anti-anxiety (anxiolytic) effect and may increase romantic attachment and empathy.

- Research shows that oxytocin may have beneficial effects for people with autistic spectrum disorders.
- Oxytocin appears to play a role in protecting the intestine from damage, with potential for use in treatment of irritable bowel disease.

Comment

For ejaculation of the breast milk and even for uterine construction, preventing from uterine atony and bleeding, oxytocin is primary important for mother and secondary to infant.

To overcome the stress and pain of the oxytocin at the newborn infants must be later be more understandable.

Serotonin

MacDonald, Mhairi G.; Seshia, Mary M. Avery's Neonatology: Pathophysiology and Management of the Newborn (Avery's Neonatology Pathophysiology and Management of the Newborn)

Predictable Fetal Toxicity The fetus often responds to drugs with adverse effects predictable from the adult response. Chronic use of opioids, selective serotonin reuptake inhibitors (SSRIs), alcohol, and sedative hypnotics by the mother may produce dependence in the fetus and newborn. This dependence may be manifested after delivery as a neonatal withdrawal syndrome. A less well understood fetal drug toxicity is caused by the use of angiotensin-converting enzyme (ACE) inhibitors during pregnancy. These drugs can result in significant and irreversible renal damage in the fetus and are, therefore, contraindicated in pregnant women. Adverse effects may also be delayed, as in the case of female fetuses exposed to diethylstilbestrol, who may be at increased risk for adenocarcinoma of the vagina after puberty.

Intravenous lipids have been associated with hypoxia, pulmonary hypertension, hyperbilirubinemia, cholestasis, and infection (74). Infants with respiratory disease have minimally lower PaO2 values when given intravenous lipids, most likely because lipids can uncouple hypoxic vasoconstriction. Normally, to optimize ventilation/ perfusion matching, the pulmonary vasculature supplying a poorly oxygenated alveolar area will constrict. This effect is reduced by the infusion of lipids, most likely moderated by serotonin. Trials that have assessed whether early administration of intravenous lipids causes or protects preterm infants from chronic lung disease have had mixed results. Overall, given the profound and early onset of growth failure in infants with severe lung disease, it seems prudent to start lipids early in life.

Serotonin (5-HT) is a widespread neurotransmitter that affects cardiovascular control and modulates activity of the circadian clock. Serotonergic receptors in the brainstem are critical components of respiratory drive. Multiple genes are involved in the control of serotonin synthesis, storage, membrane uptake, and metabolism (17). Polymorphisms have been identified in the promoter region of the 5-HT transporter protein gene located on chromosome 17, and variations in the promoter region of the gene appear to have a role in serotonin membrane uptake and regulation. Several transporter polymorphisms have been described that may occur in greater frequency in SIDS than in control infants, but no data are available related to maturation of breathing control in preterm infants in general or to AOP in particular. Thus, there are no data on the potential role of serotonin-related polymorphisms in determining the extent of clinical manifestations of AOP. However, the greater concordance for AOP among monozygotic twins than same-sex dizygotic twins suggests a genetic contribution (19). These studies illustrate potentially important genetic foundations of neonatal control of breathing. Further work is needed, however, to better understand the developmental regulation of these targeted genes and their influence on maturation of the fetal/ neonatal respiratory centers and peripheral chemoreceptors.

The neuro-pharmacologic effect of cocaine is due to its effect on three neurotransmitters: norepinephrine, dopamine, and serotonin. Cocaine inhibits the reuptake of norepinephrine and dopamine, which accumulate at the synaptic cleft, leading to prolonged stimulation of their corresponding receptors. Therefore, the effects of norepinephrine stimulation (e.g., tachycardia, hypertension, arrhythmia, diaphoresis, tremors) and dopamine stimulation (e.g., increased alertness, euphoria or enhanced feeling of well-being, sexual excitement, heightened energy) are experienced (88). Cocaine also decreases the uptake of tryptophan, which affects serotonin biosynthesis (89). A diminished serotonin level is associated with diminished need for sleep, because serotonin regulates the sleep– wake cycle. The mechanism of cocaine addiction is likely mediated by its effects on the dopaminergic system (90). The immediate response to cocaine is an increased extracellular concentration of dopamine, and in the brain, the nucleus accumbens appears to be involved in the initial rewarding effects of

Cocaine also decreases the uptake of tryptophan, which affects serotonin biosynthesis (89). A diminished serotonin level is associated with diminished need for sleep, because serotonin regulates the sleep– wake cycle. The mechanism of cocaine addiction is likely mediated by its effects on the dopaminergic system (90). The immediate response to cocaine is an increased extracellular concentration of dopamine, and in the brain, the nucleus accumbens appears to be involved in the initial rewarding effects of cocaine.

What is serotonin? http://www.healthline.com/health/mental-health/serotonin#mental-health3

- Serotonin is a chemical nerve cells produce. It sends signals between your nerve cells. Serotonin is found mostly in the digestive system, although it's also in blood platelets and throughout the central nervous system.

- Serotonin is made from the essential amino acid tryptophan. This amino acid must enter your body through your diet and is commonly found in foods such as nuts, cheese, and red meat. Tryptophan deficiency can lead to lower serotonin levels. This can result in mood disorders, such as anxiety or depression.
- Functions: Serotonin impacts every part of your body, from your emotions to your motor skills. Serotonin is considered a natural mood stabilizer. It's the chemical that helps with sleeping, eating, and digesting. Serotonin also helps: 1) reduce depression, 2) regulate anxiety, 3) heal wounds, 4) stimulate nausea: Production of serotonin rises to push out noxious or upsetting food more quickly in diarrhea. The chemical also increases in the blood, which stimulates the part of the brain that controls nausea.5) maintain bone health and 6) also other functions as; control your bowel movements and function, 7) Mood: Serotonin in the brain is thought to regulate anxiety, happiness, and mood. Low levels of the chemical have been associated with depression, and increased serotonin levels brought on by medication are thought to decrease arousal. 8) Sleep: This chemical is responsible for stimulating the parts of the brain that control sleep and waking. Whether you sleep or wake depends on what area is stimulated and which serotonin receptor is used. 9) Blood clotting: Blood platelets release serotonin to help heal wounds. The serotonin causes tiny arteries to narrow, helping form blood clots. 10) Bone health: Serotonin plays a role in bone health. Significantly high levels of serotonin in the bones can lead to osteoporosis, which makes the bones weaker. 11) Sexual function: Low levels of serotonin are associated with increased libido, while increased serotonin levels are associated with reduced libido.
- Serotonin affects every part of your body. It's responsible for many of the important functions that get us through the day. If your levels aren't in balance, it can affect your mental, physical, and emotional well-being. Sometimes, a serotonin imbalance can mean something more serious. It's important to pay attention to your body and talk with your doctor about any concerns.
    - Serotonin and mental health: Serotonin helps regulate your mood naturally. When your serotonin levels are normal, you feel: happier, calmer, more focused, less anxious, more emotionally stable. … Serotonin deficiency has also been linked to anxiety and insomnia. … High levels of serotonin may be a sign of carcinoid syndrome (… The symptoms of serotonin syndrome include: shivering, diarrhea, headache, confusion, dilated pupils, goose bumps, twitching muscles, a loss of muscle agility, muscle stiffness, high fever, rapid heart rate, high blood pressure, irregular heartbeat, seizures).
    - Low levels of serotonin in the brain may cause depression, anxiety, and sleep trouble. Many doctors will prescribe a selective serotonin reuptake inhibitor (SSRI) to treat depression. SSRIs include Prozac and Zoloft, among others. They're the most commonly prescribed type of antidepressant.
    - … According to a paper published in the Journal of Psychiatry and Neuroscience: Exposure to bright light: Sunshine or light therapy are commonly recommended remedies for treating seasonal depression. Exercise: Regular exercise can have mood-boosting effects. A healthy diet: Foods that can increase serotonin levels include eggs, cheese, turkey, nuts, salmon, tofu, and pineapple. Meditation: Meditating can help relieve stress and promote a positive outlook on life, which can greatly boost serotonin levels.

Fast facts on serotonin

- Serotonin is an important chemical neurotransmitter in the human body.
- It is commonly regarded as a chemical that is responsible for maintaining mood balance.
- Serotonin is created by a biochemical conversion process.
- Serotonin is manufactured in the brain and the intestines. The majority of the body's serotonin, between 80-90%, can be found in the gastrointestinal tract.
- Serotonin that is used inside the brain must be produced within it.
- It is thought that serotonin can affect mood and social behavior, appetite and digestion, sleep, memory and sexual desire and function.
- An association has been made between depression and serotonin. Scientists remain unsure whether decreased levels of serotonin contribute to depression or depression causes a decrease in serotonin levels.
- Drugs that alter serotonin levels have important clinical uses such as in the treatment of depression, nausea and migraine.
- Medical research continues to evaluate the role of serotonin in obesity and Parkinson's disease.
- Other ways to increase body serotonin levels include mood induction, light, exercise and diet.

Functions of serotonin. http://www.medicalnewstoday.com/kc/serotonin-facts-232248What is serotonin?2

MNT - Hourly Medical News

- Serotonin is created by a biochemical conversion process which combines tryptophan, a component of proteins, with tryptophan hydroxylase, a chemical reactor. Together, they form 5-hydroxyltryptamine (5-HT), also referred to as serotonin.
- Serotonin is most commonly believed to be a neurotransmitter, although some consider the chemical to be a hormone.
- Serotonin is manufactured in the brain and the intestines. The majority of the body's serotonin, between 80-90%, can be found in the gastrointestinal (GI) tract. It can also be found in the blood platelets and the central nervous system (CNS).

- As serotonin can be found widely across the body, it is believed that the chemical plays a role in influencing a variety of body and psychological functions.
- Serotonin cannot cross the blood-brain barrier, therefore, serotonin that is used inside the brain must be produced within it.
- As a neurotransmitter, serotonin relays signals between nerve cells (neurons), regulating their intensity.
    - Serotonin is widely believed to play a key role in the central nervous system, as well as in the general functioning of the body and in particular the GI tract. Studies have found links between serotonin and bone metabolism, breast milk production, liver regeneration and cell division.
    - As a neurotransmitter, serotonin influences both directly and indirectly the majority of brain cells. The following is a list of things that it is thought that serotonin could affect:
- Bowel function. Most of the body's serotonin is found in the gastrointestinal tract where it regulates bowel function and movements. It also plays a part in reducing the appetite while consuming a meal.
- Mood. It is most well-known for its role in the brain where it plays a major part in mood, anxiety and happiness. Illicit mood-altering drugs such as Ecstasy and LSD cause a massive rise in serotonin levels.
- Clotting. Its third major role is in the formation of blood clots. Serotonin is released by platelets when there is a wound, and the resulting vasoconstriction (narrowing of the tiny arteries - arterioles) reduces blood flow and aids the formation of blood clots.
- Nausea. If you eat something that is toxic or irritating, more serotonin is produced in the gut to increase transit time and expel the irritant in diarrhea. This increase in blood serotonin levels also causes nausea by stimulating the nausea area in the brain.
- Bone density. Studies have shown that a persistent high level of serotonin in the bones can lead to an increase in osteoporosis.2
- Sexual function. Low serotonin levels in the intoxicated state are thought to contribute to the associated increase in libido, while those taking medication that increase serotonin levels are seen to have a reduction in libido and sexual function.3

Depression, Serotonin: Depression and SSRIs.

Written by James McIntosh Reviewed by Dr. Helen Webberley
Neuroscience Mental

An association has been made between depression and serotonin, although scientists are unsure whether decreased levels of serotonin contribute to depression or depression causes a decrease in serotonin levels. … it is currently not possible to measure serotonin levels within the brain. Researchers do not know whether serotonin levels in the bloodstream reflect the serotonin levels in the brain.
It is believed that medication such as selective serotonin reuptake inhibitors (SSRIs) that can affect the levels of serotonin in the body work as antidepressants and are able to relieve the symptoms of depression. It is unknown precisely how they work, however.
The BMJ in April 2015, low serotonin is a mythical cause of depression, thus, mice deficient in serotonin were more vulnerable to social stressors than a group of healthy control mice (Duke University in Durham, NC, February 2015). SSRIs are approved by the Food and Drug Administration (FDA) to treat depression and are the most commonly prescribed antidepressants. Common examples of SSRIs are fluoxetine (Prozac), citalopram (Celexa) and sertraline (Zoloft). The less commonly used MAOI (monoamine oxidase inhibitors) such isocarboxazid (Marplan) prevent serotonin breakdown. … anti-depressants with selective serotonin (SSRIs) and norepinephrine (SNRIs) reuptake inhibitors.
Serotonin gives insight into sudden infant death syndrome: Researchers from the Geisel School of Medicine at Dartmouth, NH, recently investigated the role of serotonin on breathing responses in sleeping infants. The findings, published in Experimental Physiology, offer a new avenue of research into sudden infant death syndrome.

Comment

The newborn infants are so close and dependent to mother, physiological health and mainly as the motherhood attitudes and behavioral acts. The hormones effect to mother, directly concerns the newborn infant. Seratonin indicates as "Serotonin is widely believed to play a key role in the central nervous system, as well as in the general functioning of the body and in particular the GI tract. Studies have found links between serotonin and bone metabolism, breast milk production, liver regeneration and cell division" means the newborn status. Distention, feeding and digestion is the primary problems of babies, especially for the preterm infants. Thus, we should concern the serotonin also at the Neonatology Period.

Pain confirmed Hormones

The mostly mentioned hormones, secreted in the case of pain are;

- Sex hormones like estrogen, and

- Genes appear to play a big part in how individuals' bodies, and
- Emotions,
- Reactions to pain.

- **Pain**

MacDonald, Mhairi G.; Seshia, Mary M. Avery's Neonatology: Pathophysiology and Management of the Newborn (Avery's Neonatology Pathophysiology and Management of the Newborn)

… The birth of a newborn who requires intensive care is immediately followed by physical separation from the mother and her cohesive protective role, impacting the mother, the infant, and their relationship. The NICU experience includes frequent aversive procedures, excess handling, disturbance of rest, noxious oral stimulation, noise, and bright light. These events and conditions are all sources of stress and physiologic instability. Noxious stimuli disrupt sleep, which can also have biologic consequences for the neonate. Even some medical complications commonly associated with prematurity per se, such as bronchopulmonary

… Touch and Handling in the NICU: The type and frequency of tactile stimulation imposed on a sick newborn in the NICU would be overwhelming even for a healthy adult. They may be handled by more than 10 different nurses in the course of a month, in addition to physicians, occupational or physical therapists, laboratory and x-ray technicians, and the parents. Handling occurs more often among the sickest infants, typically is related to procedures, generally is disturbing, and often is painful. Sleep has important biologic and immunologic consequences (18,19) and may be disrupted by frequent intrusions. In addition, excess handling may have other negative physiologic consequences, such as effects on blood pressure, cerebral blood flow, and oxygen saturation. More benign manipulations, such as those that occur during neurodevelopmental assessment, are associated with elevated cortisol levels (20,21). It is not clear whether this is a response to the assessment itself or to stress associated with crying, but handling per se appears stressful even for a stable preterm infant.

… Nonnutritive Sucking Nonnutritive sucking (NNS) is an important oral– tactile intervention that supports both feeding and behavioral regulation. It represents an early endogenous rhythm and manifestation of sensorimotor integration (26), is reported to occur in the fetus (27), and is observed in the preterm newborn prior to 28 weeks of gestation. The number of sucks per burst increases with maturation, whereas the duration of burst remains fairly stable. NNS experience may facilitate important physiologic and behavioral mechanisms that potentially reduce cost of care (28,29). It has a positive effect during gavage feeding by improving gastrointestinal transit time, improving suck pressure and number of sucks per burst, and decreasing sporadic sucks. NNS is associated with earlier onset of bottle feeding, better weight gain, and shorter hospital stays. However, having a pacifier continuously available may not be beneficial and may encourage inappropriate sucking patterns, particularly in the chronically ill neonate. NNS also serves as a behavioral organizer by increasing quiet/ alert state and decreasing motor activity, which in turn facilitates social interaction. In addition, NNS dampens an infant's behavioral response, but not the cortisol response, after a painful procedure (i.e., heel stick, circumcision) (20,30,31). It is noteworthy, however, that sucking on a pacifier before and during repeated painful procedures may be inappropriate, because aversive conditioning to the pacifier could result. This cautionary note is also included in recent studies showing a similar decreased behavioral response to heel stick during nursing.

… GOALS OF NEONATAL– PERINATAL MEDICINE In the first part of this chapter, broad goals and moral priorities of neonatal– perinatal medicine (NPM) are discussed in relation to patients and society in developed and developing nations. In the second part, some specific ethical issues that frequently arise in clinical decision making in the neonatal period are reviewed. Medicine is a goal-oriented profession. One approach might argue that healing is the sole and overriding goal of medicine. This view is unconvincing, because some valid goals of medicine (e.g., prevention) cannot be collapsed into healing. The practice of NPM illustrates that;

- To save life and cure disease
- To relieve pain, suffering, and disability
- To rehabilitate and restore function
- To prevent disease
- To improve the quality of living and dying
- To seek new knowledge

… Standards for Decision Making: The usual broad standard for decision making for this population is to decide what is in the child's best interests. However, defining "best interests" can be difficult and reflects a basic problem with the use of terms that may carry very different meanings for different individuals.

… The severity of the patient's medical condition The achievability of curative or corrective treatment The important medical goals in the case (such as prolongation of life, relief of pain, or amelioration of disabling conditions) The presence of serious neurologic impairments The extent of the infant's suffering The multiplicity of other serious medical problems The life expectancy of the infant The proportionality of treatment-related benefits and burdens anencephaly, treatment is not required. Coulter and associates (43) define interests that would constitute a "minimal quality of life" as: Freedom from intractable pain and suffering. Mental retardation, paralysis, or cerebral palsy would not be considered physical

suffering; dyspnea or intractable physical pain would. Capacity to experience and enjoy life— the ability to enjoy food, warmth, or the caring touch of another; the ability to give or receive love. Expectation of continued life— heroic treatment, when death will likely occur in a few weeks or months, may be cruel.

… Palliative/ Comfort Care and Pain Control: When aggressive care or life-sustaining technology is withheld, or withdrawn, care does not stop. The clinician has a strong ethical obligation to the patient and the parents to provide comfort care, relief of symptoms, adequate pain control, warmth, feedings, if desired, and emotional support (83). Catlin and Carter (84) have developed a protocol for neonatal end-of-life palliative care. Palliative care should be available for an infant with a life-threatening condition, for example, trisomy 13, or with a refractory or chronic debilitating condition for which there is little hope of long-term survival. Palliative care functions on a multidisciplinary model that includes the parents and family. When possible, the approach may continue at home, progressing into a community-based hospice program. The availability of palliative and hospice care should be discussed with parents antenatally when a fetus is diagnosed with a condition likely to be incompatible with postnatal prolonged survival (85,86).

PAIN MANAGEMENT: For most women, childbirth is one of the most painful events in their lifetime. There are both physiologic and psychological aspects to pain and its management (28). Labor pain evokes a generalized neuroendocrine stress response that has widespread physiologic effects on the parturient and fetus (29). The neuroendocrine model, presented in Figure 15.2, examines the potential detrimental consequences of untreated pain. The sequelae of hyperventilation, secretion of stress-related hormones, and increased oxygen consumption can be prevented, obtunded, or abolished by central neuraxial blockade (epidural or spinal anesthesia) (30).
Labor Pain: Implications for the Fetus Neural pathways and neurochemical systems involved in pain perception are functional from mid-gestation and are well developed by the third trimester. Gitau et al. (34) conducted a parallel study of the fetal and maternal hormonal responses to fetal blood transfusion. They confirmed that the fetus mounts a hypothalamic– pituitary– adrenal response to transfusion via the intrahepatic vein, which involves piercing the fetal trunk, but not to transfusion in the umbilical vein at the placental cord insertion, which has no sensory innervation. The rise in fetal cortisol and endorphin occurred independently of the maternal reaction. Pretreatment of the fetus with fentanyl for this same procedure attenuated the rise in β-endorphin (35). Hormonal stress responses do not provide a direct index of pain. While it is true that a rise in cortisol and endorphin is seen as a consequence of painful stimuli in children, other nonpainful situations (e.g., exercise) are also associated with an increase in the levels of these hormones. Nonetheless, the editorial review of Fisk's fentanyl pretreatment study suggests that fetal analgesia should be given during invasive in utero procedures (36). At present, there is no literature on fetal "pain" during labor or delivery.

… Whether the fetus feels pain, and from what gestational age, has been the subject of vigorous debate (112,113). Prior to 22 weeks, the fetus does not have the neuroanatomic pathways in place to feel pain; between 22 and 26 weeks, thalamocortical fibers, considered to be crucial for nociception, are forming; and after 26 weeks, the fetus has the necessary neurologic development to feel pain; however, electroencephalography suggests the capacity to perceive pain probably does not exist before 29 weeks post– conceptual age (114). Investigators have used surrogate end points, including fetal "reflex" movement away from and biochemical stress response to noxious stimuli in an attempt to define markers of pain. Hormonal and circulatory stress responses to invasive procedures are observed by 20 weeks (34– 36). Further definition of the neuroanatomic and neurophysiologic maturation of sensory pathways involved in pain transmission in the human fetus may provide more direct information about the fetal pain experience.

Comment

The newborn infants, even the preterm babies noticed and feel the pain, therefore we must have considered painkilling status. To overcome pain is also an ethical consideration, even the infant is prone or near to death.

- **Pain and the brain: Sex, hormones & genetics affect brain's pain control system**
  https://www.eurekalert.org/pub_releases/2003-02/uomh-pat020703.php
  University of Michigan Health System. … annual meeting of the American Association for the Advancement of Science (AAAS)

  Researchers at the University of Michigan believe many answers to these questions lie in the brain -- specifically, how the brain controls our responses to pain. … At AAAS, the team will report that gender, sex hormones like estrogen, and genes appear to play a big part in how individuals' bodies, and emotions, react to pain.
  When estrogen levels are high, the brain's natural painkiller system responds more potently when a painful experience occurs, releasing chemicals called endorphins or enkephalins that dampen the pain signals received by the brain. But when estrogen is low, the same system doesn't typically control pain nearly as effectively.
  … gender-based and genetic differences in pain response. And they hope their effort to understand pain may aid studies about the brain's response to many other kinds of stressors. … gender, hormones, genetics and brain neurochemistry appears to induce our individual response to it. … When pain or other sources of stress become, significant and threatening, groups of cells in the brain release chemicals called endogenous opioid chemicals, commonly known as endorphins or enkephalins. … The effect is called antinociception, because the neurotransmitters typically suppress the pain response, as opposed to nociception, which is the actual perception of pain.

Comment

The newborn infants cannot be considered as gender, thus, prone to pain.

- **The Pain Experience**

  http://www.saragottfriedmd.com/hormones-and-their-interaction-with-the-pain-experience-by-dr-joe-tatta-dpt/ and *http://www.drjoetatta.com*
  Joe Tatta,
  Sara Gottfried. Harvard Medical School, MIT, residency at the University of California at San Francisco. Gynecologist, who teaches natural hormone balancing.

  If pain has been present for more than three months, central sensitization has probably occurred, which means tissue damage and inflammation are no longer the only causes of pain. At this point, processes deep within the brain, as well as thoughts, emotions, or negative cognitions may be contributors to producing pain.

  - **Estrogen:** For females, estrogen is important for its ability to reduce the sensation of harmful stimuli and pain signaling. If estrogen levels decline (and they do with age), the pain management benefit of estrogen declines as well. With restoration of appropriate estrogen levels, pain modulation benefits return.[2]
  - **Thyroid hormones:** An overactive thyroid is associated with increased excitability in the brain and spinal cord, which contributes to a lower threshold in central sensitization. Increased thyroid concentrations in the brain reduce binding sites for GABA, a naturally occurring neurotransmitter that calms the brain. Conversely, with hypothyroidism, regional hypoxia (tissues not getting enough oxygen) may develop, which may lead to muscle spasms, cramps, and pain.[3]
  - **Cortisol:** This hormone is key for healing, but when levels are high from living in a "hypervigilant" or continually stressed state the threshold for pain is lowered. A benefit of cortisol is that its presence helps protect our brain from forming traumatic memories, but researchers have shown a significantly higher memory recall of trauma when cortisol is low.[4]

  As this decline progresses the anti-inflammatory benefits are lost. A 2014 study showed that hypo-cortisolism was also associated with higher levels of pain.
  HPA Axis: The HPA axis is composed of the hypothalamus, the filter that provides information to the pituitary gland, which in turn releases several hormones, which result in a specific response of the target tissue. The "A" refers to one of the areas receiving those signals, the adrenal glands, but the others include; thyroid, gonads (ovaries or testes), liver, mammary glands, and adipose tissue. Chronic stress is one of the biggest enemies of HPA axis health. Five key steps can help balance hormones and reduce persistent or chronic pain.

- **Modulate stress and improve sleep.** The perception of stress is more important than the stress itself, but changing perception takes time and examination of your responses. Try to continually look at your responses as an impartial bystander. If you were to see someone respond how you just did, would you think it appropriate? … Poor sleep is associated with increased sensitivity to pain.
- **Start moving again.** Movement is abundantly important for the body. With chronic pain, the body is usually imbalanced so healthy functional movement must be restored before engaging in an exercise program. At this stage, enlist an expert to guide your body back to a higher functional capacity. Excellent options include physical therapy, …
- **Heal with food.** Food sends powerful signals to every tissue in your body. What type of signals do you want to send? Eating real, whole foods provides nutrients, such as antioxidants and trace minerals, which support appropriate signaling to the brain in the pain pathway.
- **Get your mind right.** Since pain is both a sensory and emotional experience, addressing the emotional component carries tremendous importance. Confronting both present and past trauma will help quiet a sensitive nervous system. Multiple options exist to address the emotional component of the trauma including: cognitive behavioral therapy, acceptance and commitment therapy, progressive relaxation, and spiritual practices. Look for qualified clinicians in your area.
- **Targeted nutrition.** Every single nutrient that goes into the body sends a signal to your cells, organs, and nervous system. At times the signal volume needs to be turned up with dietary supplements targeted to a specific need.

Comment

Touch, skin to skin contact, breast feeding and mother's milk, not only sugar given, just holding as kangaroo method is more important for pain relief or even lessening of pain at the newborn infants, even at the preterm infant, even by holding his/her hand.

- **Hormones and their Interaction with the Pain Experience**
  Katy Vincent and Irene Tracey

  https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4589942/

Rev Pain. 2008 Dec; 2(2): 20–24.

Abstract

- Sex differences in the prevalence of painful conditions appear after puberty
- Variation in symptom severity across the menstrual cycle occurs in a number of clinical pain conditions
- Sex steroid hormones act at a number of sites in both the peripheral and central nervous systems and in both reproductive and non-reproductive tissues
- Sex steroid hormones have traditionally been thought to alter transcription; however, there is evidence that there are also non-genomic effects
- Sex steroid hormones can have organizational effects from as early as in utero
- The relationship between sex hormones and pain is complex

Introduction

One of the most striking physiological differences between men and women is in sex steroid hormones, both the absolute levels and the occurrence of cyclical fluctuations in women (Fig.1). These hormones are known to be responsible for the embryological development of a male or female phenotype and for successful reproductive function after puberty. More recently, observations such as the marked differences in pain symptoms between males and females in the period between puberty and the menopause, and the cyclical variations in many clinical pain symptoms in women have suggested that they may also have a role in altering the pain experience. The aim of this review is to examine the available evidence that sex steroid hormones have a role in pain and to identify possible mechanisms of action for these effects.

Possible sites and mechanisms of action

… It is now known that the actions of sex steroid hormones on the brain can be both organizational (during in utero development and early neonatal life) and activation. Exposure to steroid hormones during brain development has been shown to effect a variety of sexually dimorphic behaviors in a number of species, including play patterns, sexual behavior, spatial learning, maternal behavior and bird song[20]. These hormones can originate from the maternal circulation (either endogenous or exogenous), the fetus itself or a twin/litter sibling. Animal studies suggest that neonatal exposure to testosterone is necessary to see a male response to pain[7] and to morphine analgesia[21] whilst early exposure to estrogens alters both the anatomy and physiology of the hippocampus[9]. In the developed nervous system, steroid hormones can modulate neurotransmission in the brain, spinal cord and peripheral nerves, alter the excitability of specific brain areas and influence the availability of receptors for themselves and other ligands including opiates and serotonin[7,9,22]. Furthermore, progesterone is well known to have GABAergic actions and thus is likely to influence pain[7]. We believe that these effects on the CNS could have a substantial influence on pain perception.

Peripheral structures outside of the reproductive and nervous system can also be affected by steroid hormones, including the immune system, bone, joint surfaces, ligaments and blood vessels[7]. Thus, alterations in the structure or function of these “end-organs” secondary to variations in sex steroid hormone levels could also increase or decrease the sensation of pain and/or could be involved in the disease process itself. It is likely, therefore, that hormones exert their effect on pain at a number of sites

Conclusions

Thus it can be seen that there is copious evidence that sex steroid hormones affect pain and that this may be, at least in part, responsible for the differences in pain experience between men and women. However, it is also clear that the relationship is not a simple one. It is likely to involve dose-dependent organizational and activation effects and actions at a number of sites outside the reproductive system, including a wide variety in the nervous system, as well as effects on disease processes themselves. Furthermore, there may be interactions between the different hormones which also need to be taken into account. More research is necessary to improve both our understanding of this complex area and our management of painful conditions. It is therefore important in future pain studies that both the sex and hormonal status of the subjects are taken into account.

Comment

Cortisone and such might be considered for reduction of pain at the newborn infants.

Conclusion

Physicians and all the medical staffs are on the love and happiness, grounding on Humanity and Civil Liberties/Rights, contrary against the pain/cruelty, and their duty must be leading peace, goodness and esteem, simply they are pain-killers.

Prof. Dr. Aksit /From Prof. MD. M. A. Aksit's collection