Natural versus Artificial Hormonal Cyclicity and Estrogen-Induced Hippocampal Cognitive Strategies in Coping with Stress and Pain

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Abstract:

The aim of this paper is to shed some light on the influence of natural hormonal cyclicity (as opposed to artificial or manipulated hormonal cyclicities) on cognitive coping strategies. The paper approaches three contemporary interdependent issues or fields of enquiry : contraception, emotional intelligence & hippocampal cognitive strategies. The conclusions and findings, arrived at, point to the fact that cognitive strategies in coping with stress and pain, in women, depend essentially on a lunar-menstrual phase-locking and a natural cyclic activation of estrogen receptors in the hippocampus.

الملخص:

يهدف المقال إلى الكشف عن علاقة كل من هرمون الاستروجين و الدورة الشهرية الطبيعية لدى المرأة بتفعيل بعض الستراتيجيات المعرفية للتعامل مع الضغط و الألم، حيث تم التطرق إلى مخاطر حبوب منع الحمل، من جهة، و إضطرابات الدورة الهرمونية الطبيعية، من جهة أخري، على الصحة النفسية و عمليات التعلم على مستوى الدماغ العاطفي.

الخلاصة التى تم التوصل إليها تتمثل في أن إستراتيجيات التعامل مع الظغوط و الألم عند الرأة تعتمد أساسا على علاقة ثلاثية بين دورة هرمون الأستروجين، الدورة القمرية (الشهر القمري) و تنشيط مستقبلات الأستروجين على مستوى خلايا الحصين (حصان البحر) بالدماغ العاطفي.

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Introduction:

During the last decade of research on the neuropsychology of emotional processing, and on the adaptive role of cognitively learned emotions, scientists showed increasing interest in the role of the limbic-prefrontal system in general, and the hippocampus in particular, in what has been termed "somatic markers" by Damasio (1994) and "emotional intelligence" by Mayer and Salovey (1995)..

Therefore, without going back to the past theoretical and empirical work, from James & Lange in 1884 to Scachter in 1962, on whether emotions are maladaptive or adaptive responses, we can say that the neuropsychological and behavioural studies, between 1969 and 2001, on the motivational nature of emotions, proved very valuable for our understanding of some aspects of the very complex mammalian chronobiology and the neurobiological nature of the female response to stress, and showed that regulated and evaluated emotions can have a rather organizing and adaptive role through learned hippocampal enteroception and limbic-prefrontal cognitive cyclicity hormonal readjustment of and biological clocks (Leeper, 1969; Pribram, 1969; Lazarus, 1971; Gray, 1982 & 1987; Damasio, 1994; Lathe, 2001; Shors et al, 2001).

1. Natural Versus Artificial Hormonal Cyclicity :

A chronobiological approach to the human menstrual cycle :

Evidence as to a possible relationship between solar-lunar influence and menstrual cycle in humans has often been consciously

or unconsciously overlooked and overshadowed by empirical technologico-commercial & industrial work on culturally based and artificially estimated hormonal periodicity and on chemically (not chronobiologically) programmed inhibition of ovulation.

Despite the insistence of western pharmacological industries in continuing to produce and experiment all sorts of sequential contraceptive pills*1, there is an exponentially increasing hostility to these artificial hormonal blockers of ovulation, owing to the relative importance of their long-term side-effects. To name but few of these effects, there is, on the one hand, the legitimate and well founded fear of breast &/or cervix cancer(Wilkinson, J. 1973), as far as the used contraceptive pill is a "predominantly" estrogenic pill, or the risk of osteoporosis &/or premature menopause, as far as the used contraceptive pill is a "predominantly" progestative pill, and, on the other hand, the risk of unwanted or unpredicted pregnancy (as could happen following modification of cycle after interruption or cessation of pill intake).

The contraceptive pill is also known to deplete the body of key nutrients, including thyroid hormones and zinc. Therefore, these well established side-effects can only be interpreted in terms of a profound disruption of the natural biological oscillator clocks, <u>knowing that this disruption is of a phasic nature rather tonic-dependent</u>. Indeed, this causes natural hormonal cyclicity in general, and natural menstrual periodicity (which in fact lasts 29.53 days on average and not 28 days

as commonly believed in western civilization) in particular, to be upset by exogenous disrupting and phasically desynchronizing chemical compounds.

Moreover, the continuous or "phasic" intake of these compounds (21 daily pills followed by 7 days rest, or 28 daily pills*2, instead, for exemple, of 22&/or 23 daily pills followed by 7 or 6 days rest*3) does neither match the continuous and periodic flow of natural neuro-secretions, nor coincides with the natural circadian, monthly and seasonal rhythms of hormones, enzymo-metabolic changes, and cellular or tissue regenerations.

In summary, it is suggested here, that because there is, on the one hand, strong Archetypal Symbols*4 and strong mounting cultural and anthropological evidence, based on universal ancient history and culture (see Knight,C.1991 & Grahn,J.1993) and eastern traditional popular belief [deeply rooted in the human Collective Inconscious (Jung,C.G.1936/1937)], of an ancestral relationship between menstrual cycle and lunar cycle*5, and, on the other hand, several concordant and conclusive reports concerning this functional chronobiological relationship (Gauquelin,M.1970; Menaker,W.& Menaker,A.1973; Cutler,W.B.et al.1987...etc.) any future research on hormonal cyclicity-dependent behaviour and on the psychoneuroendocrinology of obstetrico-gynecologic problems, should be conducted bearing in mind this particular and intriguing relationship. For our part, we can state this cosmic-chronobiological relationship between lunar cycle

and menstrual cycle as follows: <u>astronomical synodic moon</u> <u>periodicity is closely and functionally linked to ovulatory phase</u> <u>periodicity in normally cycled fertile woman</u>. This means that fertile menstrual cycles must, and often do, coincide with the synodic lunar cycle, which oscillates between 29 days & 6 hours and 29 days & 20 hours, to last 29.530588 days on average (or 29 days 12 hours 44minutes2.8seconds)(Couderc,P.1981).

<u>Consequently, a fertile ovulatory cycle is also a cycle which</u> <u>must include the six(06) natural phases of proestrus 1&2 (with estrone</u> <u>& estradiol), estrus(FSH & LH peaks), diestrus1&2 (with 17-</u> <u>hydroxy--progesterone & progesterone) & menses (or</u> <u>menstruation)*6, each phase lasting five (05) days on average</u>.

However, what remains unclear, from a number of studies, strongly confirming the existence of a lunar & menstrual phaselocking, is whether ovulation coincides with the full moon or with the new moon. Some authors found that, when lunar cycle and menstrual cycle coincide, ovulation coincides with the new moon (Cutler,W.B.et al 1987), while others found ovulatory peak to often coincide with the full moon (Menaker,W.& Menaker,A.1973; Criss,T.B.& Marcum,J.P.1981; Knight,C.1991),and some still, go so far as to speak of women menstruating twice during a lunar month, suggesting influence of artificial light & artificial hormones on women's menstrual cycle and the pineal gland*7.

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For our part, and relying on personal unreported observations and empirical studies, covering a period of more than twenty years*8, we think, that, in normal fertile cycles, ovulation must always coincide with the full moon, and menstruation must always coincide with the new moon. Thus, we share the same views as a large number of scientists, who, in several recent reports, confirm the existence of a strong link between ovulatory cycle and full moon cycle. We agree, with the Menakers, that « biological and medical scientists...would take a step forward in scientific thinking and teaching if they abandoned the use of the fictitious 28 day "lunar" month and if they adopted the view that human gestation is 9.00 + 0.01 synodic lunar months from conception(or ovulation)...and that the ovulatory or menstrual cycle is 1.00 + 0.01 such month in length »(Menaker, W.& Menaker, A. 1973). We also agree, with C.J.Calleman, that, despite the fact, that « medical and biological textbooks will mostly state that the female cycles typically have durations of 28 days, with a range of variation between 21 and 35 days » it turns out, upon closer study « that 28 days is not the true average of the natural female cycle », that « in the modern world the female cycle is disturbed above all by the existence of artificial lights and the use of artificial hormones on a scale that has left no woman unaffected », as « the many moonmimicking light sources, probably including TV and computer screens, has perturbed the female cycle and generally shortened it », and that, « it is however obvious from these disturbances that it is the

light of the moon, in other words the full moon cycle of 29.5 days, that the female body is responding to.»(Calleman,C.J., 2004).

2.Natural Hormonal Cyclicity & Cognitive Emotional Processing : Behaviourally and cognitively dependent readjustments of hormonal cycles and EEG rhythms, and their effects on adaptive

behaviour :

2.1- Cognitively (& operantly) learned emotional responses versus primary (& classically learned) emotional responses : It is a well established fact that primary & classically learned consummatory non-cognitive emotional responses depend on the autonomic nervous system and the hypothalamo- pituitary-adraenal axis (HPA axis), while cognitively evaluated and operantly learned emotions depend on the limbic system and prefrontal cortex (Gray,

1982, 1987; Damasio, 1994; Lathe, 2001).

Furthermore, we have pointed out, in a previous reported research (see Belloum, M.1979, p:156 & 2004b, p:19), to an experimental finding that operantly conditioned neuronal unit responses, recorded from areas of the auditory system of an animal, responded electively to the negative stimulus (signaling no reinforcement or no food) rather than to the positive stimulus (signaling reinforcement or food availability), in a delayed reinforcement discrimination learning schedule, as opposed to classically conditioned neuronal unit responses, during an appetitive conditioning task, which typically responded to the positive stimulus. This is a suggestion that, operantly conditioned discriminative emotional responses are expectancy-dependent and cognitivelyorientated, whereas classically conditioned appetitive (consummatory) responses remain reflex-dependent and drive-orientated. In addition to that, it is a well known fact, that, in normal active learning strategies (i.e strategies involving long-term changes), motivation and emotion go hand-in-hand, in that emotions express the relationship between perception and action. Thus, motivation and emotion occur together when the organism attempts to extend his control to the limits of what he perceives. And, if the attempt is appraised as feasible, at any moment, the organism becomes motivated, or, if the attempt is appraised unfeasible, at any moment, the organism becomes, by internal necessity, "primary emotional", that is, relies more on homeostatic self-regulatory mechanisms (Pribram, K.H., 1969.).

As to the emotional responses that depend on monthly hormonal cyclicity, they are more likely dependent on cognitive processing, and on motivation-oriented sensory discrimination processes and search behaviours; and as such, they come to qualitatively differ from the daily endogenous homeostatic and autonomic emotional responses, which rely more on the circadian rhythm of glucocorticoids, the HPA axis, and the no-search-type of behaviour.

2.2- Behaviorally and cognitively dependent readjustments of natural hormonal cyclicity & Theta rhythm, and their effects on emotional appraisal and adaptive behaviour :

There are well documented instances of possible exogenous manipulations and modifications of endogenous hormonal cycles in general and menstrual cycle in particular, through either conditioning procedures or appropriate hormonal replacement therapies (Cutler et al, 1987; Dewan et al, 1967 & 1978, Krug et al, 2003 ; Lacey, 1975).

There is also mounting evidence, supported by recent behavioural and neurobiological laboratory findings, pointing to a new conception for the neuropsychological basis of cognitive emotional processing. This new conception states that overall chronobiological readjustments, as well as long-term neurohormonal modulations, leading to emotional appraisal, coping strategies, and adaptive behaviour, often depend on the integrity of the limbic system in general and the septo-hippocampal system in particular (Rotenberg & Boucsein, 1993; Figueiredo et al, 2002; Lathe, 2001; Sapolsky, 2003; Pavlides et al, 2002). Moreover, after several decades of research on the enigmatic limbic system, it is a well established fact now that the hippocampus functions as a peripheral (or rather interface-like) endogenous synchronizer, essential in a number of fundamental behavioural & cognitive processes (such as behavioural inhibition, passive avoidance learning, cognitive mapping & spatial memory, associative & working memory), and is well suited for cognitive

hormonal enteroception, for control over the immunosuppressive glucocorticoids of the HPA axis, for frequency-modulated Thetadependent pacemaker activity, and for learned chronobiological readjustements.

Now, concerning learned and/or manipulated regulation of biological rhythms, hormonal cyclicity and EEG rhythms, in view of a better life or improved health, the cognitive, behavioural and experimental therapies and strategies (old and new), range from biofeedback & self-regulation techniques, to hormone replacement therapies, and from meditation exercices & practicing certain sports to alternative medicine & natural therapies. Nevertheless, the use of natural, as well as artificial, exogenous cues or factors, modifying and regulating endogenous hormonal cyclicity, menstrual cycle and EEG rhythms, and their direct effect*9 on fertility, menopause & aging, emotional processing, memory tasks, cognitive coping strategies and adaptive behaviour, is well known, and has been abundantly publicized. However several scientific reports, findings, and biomedical or prophylactic advices, in this respect, have been disclosed or put forward by a number of authors or organisms and deserve to be briefly summarized here; namely that:

* the use of sequential contraceptive pills, such as Ovanon & Physiostat (which contain $50\mu g$ of Ethinylestradiol per pill) minimizes the side-effects caused by biphasic "minidosed" pills such

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as Adepal or Miniphase (which contain only 30µg to 40µg of Ethinylestradiol per pill)(Organon Laboratories, France).

* a three days estrogen replacement treatment in postmenopausal women induces a shift from a divergent towards a more convergent mode of thinking, and enhances encoding of stimuli in working memory (Krug et al, 2003).

* stress activation of cortex and hippocampus is modulated by sex and stage of estrus[and estrogen has been found to facilitate successful coping with stress through functional inhibition of hippocampal CA1 pyramidal neurons in adult female animals during proestrus (estrogenic phase) (Shors et al, 2001; Figueiredo et al, 2002)].

* regular weekly heterosexual intercourse tend to readjust female menstrual cycle within its natural limits of 29.53 days (Cutler et al, 1987).

* women's menstrual cycle becomes regular by sleeping in complete darkness during days 1 to 13 of the cycle, sleeping with a 100-watt bulb burning all night (under a lamp shade) during days 14 to 17, and then returning to sleeping in complete darkness from day 18 to end of cycle (Dewan et al, 1978).

* practicing Lunaception technique (a variant of the Dewan technique, with temperature charts), a number of women developped regular and healthy menstrual cycles, and avoided pregnancy effectively by avoiding intercourse on the days they slept with light on (Lacey, 1975). * chronic stress, but not acute stress, caused atrophy of apical dendrites of hippocampal CA3 neurons and suppression of long term potentiation (LTP) (Pavlides et al, 2002), suggesting that acute stress, but not chronic stress, can have enhancing effects on hippocampal CA1 pyramidal dendritic spine density, and thus stimulating effects on hippocampal plasticity, on memory coding & retrieval, and

emotional intelligence (Shors et al, 2001).

* the use of behaviourally and cognitively reinforced normal Theta rhythm (chosen between 5 & 6 Hertz*10), associated to normal Beta1 & Beta2 rhythms (chosen at 25 Hertz & 50 Hertz respectively), through a positive biofeedback technique, may be proposed as a behavioural indicator of memory retrieval, during wakefulness, in patients, undergoing treatment for temporo-hippocampal amnesia,

and relying on cognitive strategies (Belloum, M. 2004a).

* high frequency stimulation (HFS) of hippocampal CA1 region in behaving rats, using "tetanic"pulse bursts at 200Hz or 400Hz, induces Long-Term-Potentiation (LTP) when delivered to the peak of Theta and Long-Term-Depression (LTD) when delivered to the trough (Hyman et al, 2003).

* high frequency (7 to12Hz) serotonergic Theta is associated with Type1 behaviour (that is with behavioural activation and voluntary vigorous movements), while low frequency (4 to 6 Hz) cholinergic Theta is associated with Type 2 behaviour (that is with behavioural inhibition, immobility during stressful events, sensory processing and

exploratory behaviour); and both Type1 Theta and Type 2 Theta can be conditioned or modified by anxiolytic drugs or high frequency stimulation of Medial Septum (Gray & Ball, 1970; Vanderwolf, 1988; Wyble et al, 2004).

* acute exposure to exogenous estrogen enhances associative memory formation in ovarectomized female rats trained on the hippocampaldependent learning task of trace eyeblink conditioning (Leuner et al, 2003).

In the end, we can say, that the rightly programmed regulation of hormonally dependant changes in hippocampal synaptic plasticity, combined to an appropriate training of the septo-hippocampal Theta rhythm*11, may have very important behavioural, cognitive and therapeutic implications for mammalian species, animal and human alike. However, the neuropsychobiological mechanisms underlying cognitive emotional processing, behavioural responses to stress and hormonally dependent adaptive behaviour, remain very complex, need more interdisciplinary investigation, and require a fundamentally new vision of things. This new vision, is asking, more and more, for the necessity of an alternative, non-linear, and non-macroscopic mechanism explaining emotionally intelligent behaviour. This non linear mechanism is thought to be imbedded in a fluctuating pacemaker-like chronobiological device, located in the septohippocampal system*12, and functioning as a synchronizing interface between the autonomous nervous system and the somatic nervous system. This synchronizing interface, with its Theta rhythm phase precession*13, and peculiar sensitivity to stages of estrus (or phases of menstrual cycle), seems to be well suited, to respond, in a conditioning and cognitively oriented manner, to internal and external factors or cues, properly programmed in time*14, in order to, readjust fecundity cycles within natural limits, appropriately adapt hormonal cyclicity to coping strategies in face of stress exigencies, and reinforce emotional maturity and adaptive behaviour.

3. Estrogen-Induced Hippocampal Plasticity and Female Cyclic Cognitive Responses to Stress & Pain :

Concerning more recent studies linking female responses to stress, to cyclic hormonal secretions, hippocampal neuronal activity, and lunar phases, it has been reported that:

- responses to stress are best expressed in hippocampal neurons, as stress alter dendritic spine density in area CA1 of the hippocampus but not in the somatosensory cortex (Shors et al, 2001).

 - exposure to estrogen and estradiol (rather than to male androgens or female progesterone), endogenously or exogenously during proestrus, enhances hippocampal dendritic spine density (Shors et al, 2001; Figuieredo et al, 2002).

- female rats in proestrus outperfom males and females in other stages of estrus (Shors et al, 1998).

- estrogen and estradiol effects on hippocampal dendritic spine density
are reversed by progesterone and its metabolites (Murphy & Segal, 2000).

- responses to stress during lunar month, as reflected by a number of conclusive observations in a crisis-call center, confirm that « distress-calls by women were more strongly linked to the lunar month » (Kollerstrom & Steffert, 2003), and that stress telephone calls by females tended to increase during the new moon period and decrease during the full moon (Kollerstrom & Steffert, 2003).

- a significant peak in frequency of self poisoning by women occurred on days that followed the new moon (Buckley et al, 1993).

- many conclusive statistical results showed that women with a 29.5 days menstrual cycle (i.e a cycle coinciding with the lunar cycle) showed increased number of most fertile cycles as compared with women with cycles not coinciding with the lunar cycle (Menaker, W & Menaker, A, 1973; Cutler, B et al, 1987; Knight, C, 1991).

- the basis of lunar control of the menstrual cycle is due to lunar light effects on melatonin secretion by the pineal gland (Cohen, S, 2005).

Other reported experimental studies and statistical results, in support of our argument of a close relationship between natural estrogen cyclicity (versus estroprogestative pills),emotional intelligence (versus emotional maladjustment), cholinergic hippocampal plasticity (versus impaired hippocampal &/or rhinencephalic function), and lunar light cycle (versus artificial light cycles) can be summed up as follows:

- stress activation of hippocampal neurons is modulated by stage of estrus, and <u>estrogen has been found to facilitate successful coping</u> with stress through functional inhibition of hippocampal CA1 pyramidal neurons in adult female animals during proestrus (Shors et al, 2001; Figueiredo et al, 2002).

- olfactory sensitivity vary during the menstrual cycle, with the highest sensitivity to odours coinciding with ovulation (Caruso et al, 2001).

- oral contraceptive use was found to cause Kallman syndrome, a disorder characterized by hypogonadotrophic hypogonadism and anosmia (Goldzieher, J.W. and Zamah, N.M, 1995).

- estrogen replacement therapy in postmenopausal women was found to protect againt intellectual decline (Kimura, D, 1995).

- estrogen replacement therapy enhances convergent thinking at the expense of divergent thinking in postmenopausal women (Krug et al, 2003).

- estrogen replacement therapy has significant beneficial effects on cognition, and helps maintain cognition in healthy postmenopausal women that normally deteriorate somewhat with aging (Sherwin, B.B, 2003).

- ongoing E.E.G. activity, recorded during cognitive tasks performed across different phases of the human menstrual cycle, showed that estrogen tended to enhance Theta activity, convergent thinking and analytical & logical thinking (Krug et al, 1999 & 2003).

- the neurotransmitter that estrogen up-regulates most profoundly is acetylcholine (Luine, V.N, 1985).

- <u>the hippocampus regulates reproductive hormones FSH &LH</u> (McGowan-Sass, B.K and Timiras, P.S, 1975).

- the hippocampus mediates a particular cognitive enteroception of internal metabolites and hormones, while the hypothalamus mediates internal non-cognitive homeostatic sensing (Lathe, R, 2001).

- <u>melatonin secretion by the pineal gland is highest during the new</u> <u>moon</u> (and the first days of the menstrual cycle, as well as during a night without light) <u>and</u> <u>lowest during the full moon</u> (and the ovulatory phase of the menstrual cycle, as well as during daylight) (Cohen, S, 2005).

- oral contraceptives and artificial lights have been proven to alter the circadian rhythm of melatonin and disrupt its oncostatic activity, therefore leading to breast cancer (Cohen, S, 2005).

In further studies, reported by Sniezek(2005), this time on hormone-dependent female responses to pain, it was also shown that:

- women are more prone to feeling pain than men, but are able to regulate their pain with hormones.

- women with high levels of estrogen dealt with pain much better than women with low levels of estrogen.

- high levels of estrogen seemed to activate recently discovered muopioid receptors in the brain for the release of endorphins, the natural pain-killers.

Taken together, all the above cited reports and well documented experimental studies, suggest that females of mammalian species respond in a cyclic manner to stressful events; and while high levels of endogenous estrogen, during proestrus, and a particular type of Theta activity (most likely Type 2 Theta activity) tend to enable females, to cope with acute stress and improve their performances in hippocampally dependent learning tasks, other neurohormonal and chronobiological factors*15 may be needed to appropriately orient behavioural responses, in face of chronic stress (rather than acute stress) or skilled learning task exigencies.

The reported experimental results also suggest that the female limbic system tends to be more cholinergic (and naturally more oriented towards Type 2 behaviour), while male limbic system tends to be more serotonergic (and naturally more oriented towards activation & Type1 behaviour). As to cognitively learned responses to stress, and their possible dependence on lunar cycle, only Kollerstrom and Steffert (2003) unequivocally reported, that women with menstrual cycle coinciding with lunar cycle (therefore with menstruation coinciding with new moon*16), are more prone to

anxiety and depression, during new moon days, and are less depressed during full moon days.

So far, we have stressed the role of the hormone estrogen as the most salient and most powerful factor responsible for emotional intelligence, cognitive coping with acute stress and neurohormonallyinduced hippocampal plasticity. This is as far as cholinergic and glutamatergic neuromodulations are concerned. Nevertheless, it remains to be said that other non-estrogen-induced neuromodulations are at play in the septo-hippocampal system, involve GABAergic influenced), receptors (progesterone noradrenergic receptors (glucocorticoid influenced?), serotonergic receptors and dopaminergic receptors, and may probably be activated in face of persistent &/or chronic stress situations or during active approach or active avoidance behaviour.

CONCLUSION:

In this theoretical and empirio-critical study, we propose alternative views on natural hormonal cyclicity, and provide new interpretations of the chronobiological and neuropsychological bases of emotional intelligence and hippocampal cognitive strategies. These new interpretations, based on new evidence from recent studies and theories, and supported by personal unreported empirical studies, over a period of more than twenty years, favour the hypothesis of a lunarmenstrual phase-locking as the fundamental synchronizing mechanism for female natural hormonal cyclicity and natural fertility. As for the chronobiology and neuropsychology of cognitive coping strategies, we suggest that emotional intelligence in women, must be cyclic, selectively depend on this lunar-menstrual phase-locking, and must remain governed by a tight interdependency between cyclic estrogen and melatonin secretions, hippocampal plasticity, septohippocampal Type 2 Theta activity, convergent mode of thinking, and endorphin-induced analgesia. We also think that this tight psychoneuroendocrinological interdependency may be dependent upon an appropriate and adaptive Theta-induced neuronal pace-maker activity, which in turn synchronizes a number of other biological rhythms, including heart rhythm, circadian & circaseptan rhythms, and circalunar (or circatrigintan) rhythm (or ovulatory or menstrual rhythm), and which needs further scientific investigation in the future.

Notes:

*1: monophasic, biphasic, triphasic and even sequential, as well as entirely progestative pills

*2: such as, "predominantly" estrogenic pills like Stediril, Miniphase, Minidril &Adepal (mostly responsible for congestive dysmenorrhea in the short-term or breast & cervix cancers in the long term), or "predominantly" or entirely progestative pills like Milligynon or Exluton (mostly responsible for amenorrhea in the short-term or premature menopause & osteoporosis in the long-term).

*3: as in the case of the so-called chinese pill (cf E. Snow, 1974,p:45) or Ovanon &Physiostat pills.

*4: see Jung, C.G.(1964), p:186-227.

*5: as a reminder here, foetal growth and pregnancy duration are officially counted in lunar months.

*6: and we may color-code theses phases successively in purple, blue, green, yellow, orange & red.

*7: the pineal gland, secreting the hormone melatonin at night, controls the onset of puberty and the menstrual cycle, and is inhibited by improper exposure to night light, especially artificial light.

*8: between 1982 & 2006: Some of these observations can be summed up as follows:

- well cycled women (those women with an average 29.5 days cycle) often start fasting few days after the beginning of the month of Ramadhan (say the 3d day) and break their fast often few days before the end of this month (say the 27th or 28th)

- <u>conjugal intercourse programmed when ovulatory phase coincided with full</u> <u>moon phase often resulted in fecundation (and one or two intercourses during the</u> <u>week were sufficient), whereas it never caused fecundation if programmed when</u> <u>ovulatory phase coincided with new moon days (no matter how frequent the number</u> <u>of intercourses during the week).</u>

- short menstrual cycles (of 25 days for example) were found to be predominantly progesteronic cycles that lack one of the two phases of proestrus (most likely the estradiol phase); as women with these kinds of short cycles often find difficulty giving birth naturally.

Logynon pill intake increased the menstrual cycle duration of a woman from a fixed 25 days natural cycle to a fixed 28 days artificial cycle, with cycles returning to natural limits some time after stopping pill intake, <u>but with a cycle reduced to 20</u> <u>days immediately after stopping the pill</u>.
*9: through behavioural and neurobiological counterparts of septo-hippocampal modulation

*10: as standard optimum Type2 Theta (n.b:Type2 Theta is mainly observed in humans & rarely in rats).

*11: via conditioning task procedures, high frequency stimulation or learned chronobiological synchronizations.

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*12: with a relay for sensory-motor integration & goal directed behaviour in the prefrontal cortex.

*13: of hippocampal place cells firing during process of recall of a well known track.

*14: to reflect or mimic either natural external synchronizers and natural cosmic cycles (such as the alternation of light and darkness, heat and cold, moon phases, seasons, etc...) or natural biological oscillators.

*15: such as factors switching behaviour from Type2 behaviour to Type1 behaviour for example.

*16: and thus with estrogen at its lowest level.

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