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The Menstrual Cycle and Vision: The Eye is a Gender Specific and Hormonally Sensitive Target Organ[1]

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The menstrual cycle is an integral component of life for most women, and it exerts its influence for a major portion of their lives. Much research has been directed to the hormonal changes across the cycle, and their potential to alter a female's physical, physiological and psychological wellbeing. The physiology of the menstrual cycle and paramenstrual symptomatology is well documented. Entities such as premenstrual syndrome are now well accepted. It is less well known that visual and ocular changes also result from menstrual periodicity and alterations in endogenous hormones. This paper reviews the literature pertaining to vision and the menstrual cycle and postulates that the eye is a gender-specific and hormonally sensitive target organ.

Keywords: Vision, Menstrual Cycle, Estrogen

Introduction

The visual system and the female reproductive cycle are not traditionally discussed in the same forum. A *cursory* assessment of the two systems might suggest that they are independent physiological facets of human existence with little or no interplay. As the wealth of knowledge about the intricacies of human biology and physiology expands, it is becoming more apparent that this is not the case. The eye is an extension of the human brain, and there is a growing body of evidence that the functioning of the brain and menstrual cycle are intricately related. This interdependence is perfectly plausible and reasonable given the intimate relationship between the endocrine and nervous systems (by virtue of delicate feedback loops and neural pathways between the brain, hypothalamus, and pituitary). Evidence that the central nervous system and the menstrual cycle impart influences upon each other will be presented in a separate paper. This paper is dedicated to how the female reproductive cycle may specifically influence visual performances and parameters.

There has been much research devoted to the menstrual cycle and how it influences female health and function. It is now well accepted that the reproductive cycle, especially the premenstrual/menstrual phase, can modify performance and wellbeing. It is also accepted that many of the changes and effects noted perimenstrually (however minor or otherwise) tend to be of a negative character. These effects may be mediated via physiological, physical, and psychological means. Despite the general acceptance of changes/symptoms being precipitated by menstrual periodicity, potential disparities in ocular function are almost invariably "overlooked". Relatively small discrepancies in performances and parameters, coupled with other more dramatic premenstrual symptomatology, probably account for the infrequent consideration of any eye effects. Additionally, the eye is not normally considered to be a gender-sensitive or sex hormone-dependent structure in day to day medicine.

Historical Research

Despite the apparent anatomical and functional disparity of the two systems, a substantial body of evidence is being compiled on their affiliations. Visio-menstrual research and findings date well back into the 19th century. In 1887, a physician by the name of Finkelstein[1] made some interesting observations. He reported a concentric narrowing in the visual fields of healthy women during the premenstrual/menstrual phases. The constriction of field began one to three days prior to menstruation and peaked at about the third day of bleeding. The degree of field loss mirrored the severity of any classical premenstrual symptoms that were experienced. Colour fields also

demonstrated this constriction, and there was some perversion of colour perception (especially green), although refraction appeared unchanged [1]. Lorenzetti in 1926[2] confirmed Finkelstein's findings namely a slight but significant constriction in red and green colour fields, and some perversion in colour perception. Although the changes described by these two authors were slight and subtle, it was sufficient to suggest that ocular and visual variables were influenced by menstrual periodicity, and their work continues to spawn inquiry. A 1974 study [3] specifically designed to assess visual field size for green supported the early findings. Although the numbers of subjects were small, there was a 3 to 6 percent reduction in field size in the pre/Para menstruum for those women not using regulatory medication. By comparison, women taking the oral contraceptive pill did not exhibit a diminution in field size.

Visual Acuity

Visual acuity refers to the spatial limit of visual discrimination. It is the single most significant measure of the functional integrity of the visual system. Visual acuity is analogous to refractive error. On the basis of these measurements alone, decisions are made ranging from the need for spectacle wear/prescriptions up to occupational and industry standards for employment. Knowledge of any fluctuations of these variables associated with the menstrual cycle would be exceedingly valuable. Unfortunately, data pertaining to refractive error and visual acuity relative to menstrual periodicity is scant. In one of the pioneering studies quoted above, no refractive changes were noted with the menses. Another study in 1952 suggested that a shift of somewhat less than 0.250 in the myopic direction occurred at menstruation[4]. A more recent study found that visual acuity was significantly better (l;>y about 10 per cent) just after ovulation. This same study reported an outward shift (i.e. opposite to myopic shift) in dark-focus of about 0.25D at ovulation (dark-focus is the accommodative state of the eyes in complete darkness). In another study of "acuity", per cent correct forced-choice identification of a briefly flashed letter under dark adaptation was administered to healthy females[6]. Paradoxically, the study showed reduced acuity at the time of ovulation, but the authors explained the finding in terms of visual sensitivity versus retinal saturation. That is an increase in sensitivity at ovulation would mean greater potential for saturation of the retina in response to a bright stimulus, leading to a reduction in the contrast (and acuity) of a target/letter[6]. Although not homogeneous, the evidence infers a small decline at menses and/or a small improvement at ovulation in visual acuity and refractive indices. This has been the authors' experience anecdotally, especially with mildly myopic females. Such women are more likely to wear their spectacles during the menses (These and other parameters of visual performance are currently being formally investigated by the authors).

Visual Detection and Discrimination

Like visual acuity, visual detection and discrimination are vital for optimal interpretation of the surrounding environment. This function is required to be operational irrespective of good or poor ambient lighting. Visual sensitivity, as measured by the ability to detect a flash of light under dark adaptation, has been shown to increase in the midcycle/ovulatory phase[7.8], and to decrease in the premenstrual phase[9]. These rises and falls in sensitivity directly correspond to the monthly estrogen cadence. In contrast to subjects tested under dark-adapted conditions. the visual sensitivity of light-adapted subjects did not change across the cycles. One of the cited studies also tested subjects with a visual pattern discrimination task[9]. The authors found an improved performance for this task at the premenstrual phase. This finding is consistent with other research on how the menstrual cycle influences this entity of cerebra-visual function, as it has been shown that perceptual / spatial / restructuring tasks improve paramenstrually [10.11]. In another study, a visual search performance task was administered over phases of the menstrual cycle [12]. Although the researchers failed to demonstrate any cyclical fluctuations. They noted that women who reported more severe premenstrual symptoms exhibited a substantial and significant increase in response latency. Visual contrast sensitivity has also been studied relative to the female reproductive cycle[13], and it appears that this parameter is also influenced by menstrual periodicity probably reaching peak sensitivity in the immediate post ovulatory phase.

Temporally spaced paired flashing of lights has frequently served as a means of assessing Cerebro-visual function. Two flash fusion threshold (TFIT) is the point at which a subject perceives two successive flashes of light as one. A lower TFIT indicates an increased sensitivity, as the time between the two flashes (the inter flash interval) is less.

Conversely, as the inter flash interval increases, so does the TFIT, and sensitivity is thus decreased. Two flash fusion has been demonstrated to be a measure of cortical arousal and alertness [14]. By definition, it must also be a measure of visual sensitivity, as visual pathways are responsible for the carriage of the signal to the cortex. Cortical arousal and TFIT have been shown to fluctuate with menstrual periodicity [14]. In the pre and perimenstrual phases, TFIT has been found to increase, signifying a fall in sensitivity [15.16]. A corresponding increase in sensitivity (shorter TFIT) has been identified in the late follicular and ovulatory phases of the cycle [16.17]. The estrogen peak at midcycle parallels the increase in two flash fusion sensitivity and reinforces the argument for estrogen being a facilitator of visual sensitivity. A notable subsidiary finding was that changes in two flash fusion were not demonstrable in women stabilised on exogenous estrogen and progesterone preparations (the oral contraceptive pill). indicating that cyclical endogenous hormone levels were responsible for the observations [16,17].

Cornea

The cornea is the first and most powerful refracting surface of the optical system of the eye, and production of a sharp image on the retina requires a cornea of appropriate clarity, thickness, and contour. As such, the cornea is a very important ocular variable, and potential changes in corneal parameters across the menstrual cycle have attracted more research interest than straightforward acuity measurements. The cornea accounts for 70 per cent of the eye's refractive power, so hormonal or menstrual influences upon it may have a substantial bearing on visual function.

Corneal thickness and corneal curvature are proportional to corneal hydration, and it is thought that the menstrual cycle may influence the degree of corneal water retention. It is worth noting that the findings of studies evaluating corneal thickness are not uniform. [18] One sector of research groups could not demonstrate any appreciable change in these parameters. These groups found no temporal correlation between the menstrual cycle and variations in corneal thickness and/or curvature [19.20]. Conversely, other research demonstrates measurable changes in these parameters and implicates fluctuating estrogen levels as the basis of such variation. [21.23]

Another notable finding is that women established on the oral contraceptive pill (OCP) do not exhibit any changes in corneal thickness or curvature relative to menstrual periodicity [23]. Such a finding may have practical relevance for wearers of contact lenses. Many women report changes in contact lens comfort during different phases of the menstrual cycle. Dryness, tearing, decreased visual acuity, swollen lids, foreign body sensations, and visual coordination problems are examples of what may occur [24]. Any variation in corneal thickness or curvature during the menstrual cycle may contribute to symptoms and could complicate contact lens fitting [15.24]. A corollary of this is that women established on the OCP have a stabilised corneal thickness and should experience fewer complications of contact lens fitting [24]. Further to this issue, it has been demonstrated that pregnancy causes an increase in corneal curvature during the second and third trimesters [25]. This results in previously successful contact lens wearers becoming contact lens intolerant whilst pregnant and dictates that contact lens fitting is inadvisable during pregnancy.

As stated above, corneal thickness and curvature is directly related to corneal hydration. Likewise, if the hydration level of the cornea is increased, then corneal sensitivity will be reduced. Corneal sensitivity is also reduced in the presence of raised intraocular pressure. Sensitivity of the cornea may also be modified by fluctuating hormone levels and the menstrual cycle. An increase in corneal touch threshold (i.e. a decrease in corneal sensitivity) has been demonstrated in the paramenstrual period [26]. Another study has established that corneal sensitivity is decreased in the immediate pre ovulatory period [27], and implicated estrogen as being at least partly responsible. Corneal sensitivity has also been shown to decrease in pregnancy [28]. It would seem that there is a complex (and as yet not fully understood) relationship between fluctuations in sex steroid hormones

and the corneal parameters of hydration, thickness, curvature, and sensitivity. Although yet to be fully determined, these effects may influence visual performance across the menstrual cycle.

Conjunctiva

Dryness of the eyes is a frequently reported ocular climacteric symptom [29]. There is also a greater incidence of dry eye condition in postmenopausal women. These observations suggest that withdrawal of female sex hormones may play a role in the aetiology of these complaints. Cytohormonal evaluations are frequently and accurately used for the assessment of the estrogenic effects on vaginal, cervical, and buccal mucosal cells. In a study using Papanicolau preparation techniques, conjunctival smears were assessed for estrogenic effect and assigned a maturation index [30]. The smears were taken from healthy cycling females, postmenopausal females, and males. The maturation index of the epithelial cells peaked around ovulation, paralleling the rise in estrogen levels. No cyclical change was shown in the smears taken from men or postmenopausal women. This established that another part of the ocular system, that being the conjunctival epithelium, was also estrogen-sensitive [30].

Saccadic System

Another ocular entity that has been shown to have direct links to hormonal and menstrual function is the saccadic system. A saccade is a rapid, jerky, skip-like movement of the eye from one fixation point to another. The purpose of these rapid eye movements is usually to search a large visual field in order to locate and then fixate on a visual target. A simple example would be searching for an aircraft in the sky. Once a saccade has started, it is considered to be an involuntary action outside of conscious control. Menstrual periodicity may affect saccadic eye velocity (SEV). The symptoms of premenstrual syndrome (PMS) appear when progesterone levels are raised, and pregnanolone is an endogenous progesterone metabolite[31]. Pregnanolone is a neuroactive steroid and exerts an influence on the brain via interaction with gamma-amino butyric-acid (GABA) receptors.[31] It has been shown that patients suffering from PMS have decreased saccadic eye velocities[32]. When the neuroactive steroid pregnenolone is administered intravenously to normal/non-PMS affected females, a dose-related reduction in SEV is noted[31]. It so happens that saccadic eye velocity has proven to be a reliable and highly quantifiable parameter in assessing benzodiazepine/GABA receptor sensitivity in humans, thus it has been mooted that pregnanolone may be involved in the pathogenesis of PMS3J, and one of the effects is expressed cerebra-visually.

Intraocar Pressure

The importance of raised intraocular pressure cannot be underestimated, as glaucoma is responsible for substantial ophthalmological morbidity, namely loss of vision. Considerable effort has been invested in probing the association between intraocular pressure (1OP) and sex hormones and the menstrual cycle. Earlier work suggested that the menses may cause a rise in 1OP, but the study examined subjects who were already suffering from glaucoma[33]. It was demonstrated that in women already diagnosed with glaucoma that there was a simultaneous rise in intraocular pressure, blood pressure, and body weight during the paramenstrual period [33]. Subsequent studies have failed to demonstrate a correlation between 1OP and aqueous humour flow rate relative to the menstrual cycle and endogenous sex hormones [34.35]. The women in these studies were free from eye disease. The most recent research corroborates and fortifies the notion that endogenous sex hormones and the menstrual cycle do not influence 1OP to any degree in those women free of any eye disorder [36].

In addition, it was noted that 1OP fell simultaneously with blood pressure in healthy pregnant females and that the 1OP of postmenopausal women was higher than in those of the same age that were still menstruating [36]. This again infers that a positive or beneficial influence may be provided by estrogen supplementation in the postmenopausal era.

Ageing

Ageing is known to affect virtually every organ and its biological and physiological functions. The eye is no exception, and longitudinal studies report age correlated deteriorations in visual parameters. Many aspects of visual function decrease linearly with age, not just visual acuity. Contrast sensitivity, glare, visual field, and

stereoacuity assessments are all affected [37]. Although men and women show no gender differences after age-adjustment for visual impairments, women are more likely to report disability and functional impairment. The menopause is a time of significant change, and climacteric symptoms may be broad-ranging. Just as menstrual periodicity may influence the eye, so to may the menopause. One study 29 found that fully one-third of women (430 out of 1,287) presenting for peri-menopausal assessment and treatment reported ophthalmic complaints. Dryness, tearing, red and swollen lids, decreased visual acuity, foreign body sensations, and visual coordination problems were documented[29]. These are the same symptoms that may be reported with menstrual periodicity. As has been detailed previously, estrogen imparts a positive influence to female function, both pre and post-menopause. According to the authors of the above study, all women with ophthalmic complaints reported improvement with estrogen replacement therapy, even when the estrogen was applied locally to the eye [29]. An intriguing area of age versus visual function where estrogen replacement may not be beneficial is with excimer laser photorefractive keratectomy (PRK). A study examining uncorrected vision following PRK showed less favourable outcomes in postmenopausal women taking estrogen supplementation [38]. Because hormonal levels influence corneal hydration/thickness, it follows that estrogen replacement therapy and menopausal status may affect the outcome of PRK, (possibly via under correction in a thicker cornea). Pregnant females are also subject to increases in corneal thickness 25 and would probably be well advised to delay PRK until after delivery.

Other Eye Conditions

Further evidence that the eye may be influenced by the menstrual cycle is the sporadic case reports detailing the interaction between the two systems. Various forms of iritis, conjunctival inflammation, and conjunctival haemorrhages have been reported that bear a direct and reproducible correlation to the premenstrual/menstrual phase [39-41]. The dramatic falls in estrogen levels at this phase of the cycle were mooted to be responsible. Cyclic presentation of macula oedema with visual disturbance has also been reported [42]. The symptoms would start with onset of menstruation and cease therewith, and it was proposed that an association between cyclic hormonal and immunological changes may have been responsible. Cases of drug-induced myopia with treatment for gynaecological problems have also been reported, including for premenstrual oedema [43]. As detailed in an earlier section, any influence imparted to general medical entities by the menstrual phase of the cycle is almost invariably negative. Likewise, estrogen almost invariably has a positive influence on female health and function. It would appear that diseases of the eye also follow this trend.

Conclusion

The body of evidence suggesting that the eye is influenced by the menstrual cycle and fluctuating hormone levels is substantial. For most measures of function, optimum performance is at the midcycle phase, and the least efficiency is concurrent with the paramenstruum. This holds true not only for vision. The other sensory modalities of olfaction, audition, taste, and touch generally show increased sensitivity and enhanced performance at midcycle, with the opposite being evident in the premenstrual/menstrual phase.[44] It is well known that estrogen levels peak at midcycle, and this hormone is strongly implicated in many performance changes. But, vitamin A also peaks at midcycle and is at its lowest level during menstruation. [45] It has long been known that vitamin A deficiency, especially in dark conditions, results in a significant decline in vision, so it has been suggested that lower vitamin A levels at menstrual time may play a contributory role in falls in visual sensitivity, especially in the dark [7].

Nevertheless, estrogen remains the principal substance implicated in performance changes. either across the cycle or after the menopause. It has been shown that estrogen facilitates neural transmission of visual pathways [46], and it is without question the critical hormone in cerebral performance changes throughout the menstrual cycle [11]. The eye and brain are most definitely gender and sex hormone-sensitive target organs. Although the depth of interaction between the Cerebro-visual and reproductive systems is yet to be fully explored and documented, an appreciation of its great significance has been established. This should serve to optimise the care and management of females in both their reproductive years and beyond.

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