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Research Article

Eroticism as a hormetic stimulus in health and ageing

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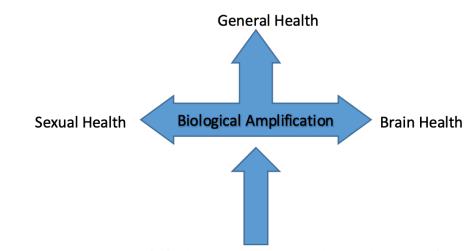
Eroticism in later life is, on the whole, a taboo subject, and the stigma attached to expressions of sexual intent by older people is widespread in most cultures. However, sexuality and eroticism have an important role to play in maintaining healthy ageing. Sexuality is an essential aspect of our biology and its effects have repercussions in systems and organs other than the sexual. In this paper I review the importance of developing a sexualerotic element in later life, an element that is intimately coupled with the phenomenon of hormesis. In hormesis, there is biological benefit following exposure to a mild stimulus or challenge, whereas exposure to a higher dose of the same stimulus becomes detrimental. Innovative sexual stimulation can be seen as a hormetic opportunity to initiate beneficial effects on the entire ageing human organism. The intention is to show that, health benefits may be obtained not only through physical (exercise), nutritional, mental or pharmacological challenges, but also through sexual stimulation of the appropriate magnitude and quality. By enhancing erotic stimulation it may be possible to experience many other benefits spanning several domains such as the endocrine, immune, circulatory and neurological. In addition, within an increasingly information-rich world, sexuality may play a part in improving adaptation to various cognitive external stimuli originating from our technological ecosystem.

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Kyriazis, **Graphical Abstract**



Hormesis (a dose-response, novel sexual stimulus)

Highlights

- Hormesis operates within the sexual realm
- Innovative sexual stimulation leads to health improvements in later life
- Hormetic effects can be invoked via 'sex hormetins'
- Inventive erotic activities may result in cognitive benefits

1. Introduction

Hormesis is a concept which is gaining increased importance in the biomedical and biological fields (Kyiazis, 2016). The concept was originally born in the field of toxicology but it gained acceptance in many other disciplines. Clinically, the concept of hormesis is grounded on a basic principle, the 'dose –response relationship': exposure to low doses of a stimulus may result in beneficial health effects, whereas exposure to a higher dose of the same stimulus may result in detrimental effects. The stimulus can be physical, chemical, environmental, cognitive, etc. Here I will review the evidence regarding an additional potential stimulus which may be capable of achieving a hormetic effect: that of sexuality (Kyriazis, 2010).

It is necessary to highlight that, in this paper, the terms 'sexuality' and 'eroticism' are used without making a distinction. Strictly, 'sexuality' is the primary urge to procreate, whereas 'eroticism' is also a reflection of other instincts or qualities such as lust, desire, emotion and creativity. For the purposes of

this discussion it is the stimulation quality that matters, and not merely the emotional element attached to such a stimulation.

Although it is generally believed that ageing restricts sexual expression (Hernández Carrasco et al., 2018), it is nevertheless possible to experience some positive effects. For instance, after a long-term partner dies, the surviving partner may have an opportunity to explore other aspects of sexuality, even same sex relationships (Wylie et al., 2013). Impediments to a healthy sexual function in older life may include physical restrictions or pain due to arthritis etc., lack of autonomy, and multiple side effects of drugs. In addition, lack of confidence and social exclusion play a role (Cybulski et al., 2018) as well as concerns as to how expressions of sexuality may be perceived by society (Roney and Kazer, 2015). Nonetheless, it is possible to examine the subject of sexuality in later life with the intention of encouraging not only social expression but also actual physical contact, in order to promote both sexual and general health (Morton, 2017, Lindau et al., 2018)

2. Discussion

2.1. Sexuality and biological amplification

We know that sexual function has a variety of effects in several parts of the body, albeit many of these effects were shown specifically with penile-vaginal intercourse and less so with other forms of eroticism (Brody, 2010). Therefore, enhancing sexual activity and physical stimulation may result in various effects which do not always have an impact exclusively upon the sexual system (Emerenziani et al., 2018). These effects may be amplified and felt in other organs or through process biological systems. а of amplification. Biological amplification is а phenomenon whereby the effects of a biological event which affects one organ, may be sensed by and influence other organs or tissues distant to where the original event has taken place. It can also mean that the scale of the original stimulation has been magnified and the result is enhanced compared to what would have been expected by considering only the magnitude of the original stimulation. For example, a reduction of sexual hormones (estrogens and testosterone) seen in ageing may be associated with increased risk of Alzheimer's disease (Barron and Pike, 2012). Engagement in sexual activities in later life can increase the levels of these hormones and thus reduce the risk (Taziaux et al., 2007, Seredynski et al., 2013). It may be that sexual activities stimulate other aspects of our biology which, in turn, may reduce the risk of AD, however this still needs further study

2.2. Evidence of hormesis in sexuality

Research suggests that hormesis is involved in sexuality, at least in some animal models. For example, sublethal (hormetic) doses of the poison deltamethrin increases sexual behavior and responses to sex pheromones in insects (Lalouette et al., 2016) which is an adaptation effect of the insect to agricultural pesticides. In addition, mild oxidative stress improves sexual performance in the fruit fly (López-Martínez and Hahn, 2012) and results in a healthier lipid profile and mitochondrial function. Another study (Hirsh et al., 2003), showed an improvement in fecundity following exposure to low doses of lead, and a reduction in fecundity following exposure to higher levels of lead, a typical U shaped non-linear (biphasic) dose-response relationship. Moreover, low doses of the mycotoxin Zearalenone in pre-pubertal dogs improve ovarian and uterine function, and normalize metabolic processes (Gajecka et al., 2015), whereas higher doses are toxic (Schoevers et al., 2012).

Autophagy, one of the hallmarks of hormesis, is involved in improving erectile dysfunction (Lin et al., 2018, Zhu et al., 2018) and it improves synthesis of testosterone and sexual behaviour (Gao et al., 2018). These studies suggest that the general phenomenon of hormesis is present within the sexual realm, and plays a role in defining sexual function (Kyriazis, 2010). Therefore, a stimulus that is novel (not routine and not predictable) and able to elicit an appropriate adaptive response, without causing damage, is defined as 'hormetic'.

Hormesis may be found in many aspects of eroticism. For instance Abler et al. have described how exposure to mild ('low-dose') visual-erotic stimuli may produce significant hormonal effects on the brain, whereas a more direct and explicit exposure ('highdose') does not result in significant effects on hormonal secretion or on brain activation patterns (Abler et al., 2013). This is typical of hormesis where the dose in order to produce a positive effect is constrained within certain boundaries, and bears a 'U-shape' characteristic - neither too low nor too high. On the other hand, modest monotherapies (i.e. very 'low-dose' interventions) may not have significant effects either. In a study of vaginal electrical stimulation as a single, isolated (detached from environmental influences) intervention did not produce significant differences between the treatment group and the placebo group (Aydin et al. 2016). In this instance it is shown that an insufficient level of stimulation (i.e. well below the critical level of a Ushaped relationship) does not produce any beneficial effects.

2.3. Magnitude and quality of stimulation

Sexual stimulation is subjected to principles common to any type of external stimulation. In this sense, stimulation is interpreted as a 'challenge' i.e. a biological change in response to a perturbation. A 'challenge' is a situation which has value for an organism, so that the organism is inclined to act and adapt following exposure to any given external or even internal stimulus. In this sense, a challenge provokes appropriate action from the organism. One type of stimulation is breast (nipple) stimulation. This may be associated not only with sexual pleasure but also with a reduction in the risk of uterine, breast, endometrial, and ovarian cancers, and also with a reduction in the risk of depression and an increase in positive emotions (Robinson, 2015).

In devising practical interventions whereby clinicians may advise patients about sexual erotic (hormetic) stimulation, gender differences must be taken into account. For instance, it was shown that men have a preference for direct, crude exposure of sexuality, genitals and intercourse, whereas women have a preference for emotional, structured and softer erotic videos (Chung et al. 2013). It is important to also highlight that sexual behaviour is intricately connected to other pleasures, social interactions and reward cycles. Therefore, achieving a hormetic level erotic state could also have repercussions on other aspects of behaviour and thus on brain function. This shows how important it is to consider integration of hormetic stimulation, i.e. not to rely on linear increments of activity but to follow the U-shaped principle (Georgiadis and Kringelbach, 2012).

Examples where a stimulus can be perceived as a positive challenge (i.e. a novelty, a stimulus that needs a response) are creative sexual practices such as:

- vibrotactile stimulation (Rowland, 2010, Panagiotopoulou et al., 2018) (e.g. innovative genital touching and masturbation, inventive use of vibrators or other devices, orgasmic meditation)
- visual erotic (Huynh et al., 2012, Wu et al., 2017) (e.g. legal pornography, motivating videos or voyeurism, 'top shelf' magazines, artistic sexual 'selfies')
- sex games (Faccio et al., 2014, Carlström, 2018) (e.g. mock Sadomasochism, cross dressing, inspiring sexual fantasies)
- uncommon sexual positions (Reynolds et al., 2015) (such as face sitting, or others inspired from Kama Sutra for instance), and
- use of novelty aids (Rehor, 2015) (e.g. ridged condoms, rings, 'love balls', G-spot stimulators etc).

In this respect it is possible to create situations whereby a sexually-charged challenge increases sensory and mental activity. The novelty of the stimulation is perceived as a challenge by neurons and this may improve adaptation of neuronal function, and endorphin, dopamine and serotonin modulation (Uphouse, 2014, Hull et al., 2004).

A study of intrapersonal erotic touch has shown (Jönsson et al., 2015) that this can communicate emotions and erotic feelings when it is perceived as relatively weak (i.e. not unpleasant and not rough). This evokes notions of hormesis whereby the most benefit is derived from an application of a stimulus of a certain strength – not too much and not too little. In another study (Jiao et al., 2007) of 30 heterosexual males with no sexual dysfunction, it was shown that vibrotactile detection thresholds were reduced after watching erotic videos. In other words, sexual arousal was associated with increased sensitivity to vibrotactile stimulation which indicates a synergistic effect. Thus, multiple sexual inputs must be taken into account because the hormetic threshold may be surpassed.

Both physical and imagined erotic stimulation may have a sexual effect. It was shown that both imagined and tactile self-stimulation of erotic areas such as the clitoris and the nipple, activate several brain areas, whereas non-erotic stimulation (with a speculum) did not have such an effect (Wise et al., 2016). This underlines the importance of imagination in erotic stimulation and that there are various ways to achieve a desired effect, something that may be of relevance to older people who lack a sexual partner.

2.4. Sexuality and cognition

There is some evidence suggesting that sexual activity is associated with improved cognition (Wright and Jenks, 2016, Freak-Poli et al., 2018), such as improved memory and executive function. Processing erotic information involves several realms, including memory, brain activation and coordination of signals, circulatory system and hormonal response (Parada et al., 2016). Erotic and non-erotic information involves different processing patterns in men compared to women. For instance, men are inclined to look for longer at female erotic pictures, whereas women do not have such a bias: their preference is equal and uniform between opposite and same sex pictures (Lykins, 2008). This underlines the difficulties in suggesting erotic stimulation to males who respond differently to the same stimulus compared to females.

Within an increasingly cognitive technological environment, it becomes necessary to examine ways to enhance cognitive function. One such way is through sexuality augmentation. For instance, it is known that Dehydroepiandrosterone (DHEA) improves neural function and this is intimately connected to sexuality (Pluchino et al., 2015). Although sexuality and cognition are distinct functions, these are interrelated both peripherally and centrally in the brain (Motofei, 2011). Several cognitive processes are connected with sexuality, and it is known that novel external stimulation (visual, tactile, etc.) as well as abstract/social stimuli are integrated through the ascending reticular activating system to reach several neuronal structures including the thalamus, hypothalamus and cortex (Motofei and Rowland, 2014) coupling the sexual and the cognitive systems. Another example underlying the common frontiers between sexuality and cognition can be appreciated by studying the dynamics of tibolone treatment (Genazzani et al., 2006). Tibolone is used for the management of menopausal symptoms, has progestogenic and androgenic effects, as well as affecting mood, libido and cognition. It protects against cognitive decline in postmenopausal women even during short-term treatment (Pinto-Almazán, et al., 2017). The relationship between cognition and sexuality is further highlighted by the example of the drug Modafinil. This is used as a general cognitive enhancer (Murillo-Rodríguez et al., 2018), but it has also been reported that it enhances sexuality (Swapnajeet et al., 2016). Therefore, hormetic sexual stimulation may be another form for achieving cognitive enhancement.

2.5. 'Sex hormetins'

Hormetins are chemical substances that initiate the stress response, in the sense that they invoke the phenomenon of hormesis (Rattan, 2012). Compounds which may mimic certain physiological aspects of sexuality may be classified as 'sex hormetins'. The study of sex hormetins (or 'sex mimetics') is based on the concept of a pharmacological extension of the hormetic sexual techniques discussed above.

A candidate sex hormetin is the pluripotent agonist of the serotonin 5-HT1A receptor, Flibanserin. This is approved specifically for use in HSDD (Hypoactive Sexual Desire Disorder) which is the most common form of female sexual dysfunction (Jaspers et al., 2016). Flibanserin increases the number of gratifying sexual events in pre and post- menopausal women (Stahl, 2015). Its functions exhibit a 'U-shaped', clinical dose-response pattern: its and pharmacological effects depend on the dose used in each situation. Another sex mimetic is Anandamide, an endocannabinoid which modulates neurotransmitter release, and has been linked to an improvement of sexual behaviour in animals (Canseco-Alba and Rodríguez-Manzo, 2013). It increases mounting episodes, intromission, ejaculation and resumption of copulation following ejaculation (Rodríguez-Manzo and Canseco-Alba, 2015). We know that there is cross-talk between the endocannabinoid and the immune systems (Boorman et al., 2016) where this multifaceted relationship may affect inflammation response, depression and immunocompetence. This is an example of biological amplification mentioned above. A third sex hormetin is Dapoxetine, a selective serotonin reuptake inhibitor and antidepressant, which is also used in the treatment of premature ejaculation. In a typical hormetic fashion, a moderate dose of Dapoxetine is clinically useful, while a higher dosage is harmful, and a very low dose is ineffective (El Mazoudi et al, 2015). This highlights the hormetic, dose-response action of Dapoxetine, and reminds us once more of the importance of regulating the degree of challenging stimulation. Moderately low doses of these compounds is sensed as a pharmacological challenge by the target organs. This upregulates the stress response and improves cross-talk between different domains such as the immune system, neuronal structures and endocrine organs.

3. Conclusions

Hormesis plays a role in sexual function and this has effects that are amplified in order to influence other organs and tissues. In terms of practical conclusions, a reasonable advice stemming from the above discussion could be to encourage personal expression of sexuality in ageing, accept and encourage other older people to express their own sexuality, and pursue a sexual life which is at the outer limit of one's comfort zone (i.e. challenging but pleasant) (Skalacka and Gerymski, 2018). In order for the hormetic effect to take place, routine and boredom must be avoided, and the activities should be creative, rousing, novel, and able to elicit a biological response. Sexuality and eroticism may be used as tools which can enhance not only sexual health in later life, but also brain function, cognition, and overall clinical health.

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