

Emotions and disease - understanding, influencing and assessing The biopsychosocial model put into practice – Sexual Medicine

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What is an emotion?

The Ekman Study – 6 „international“ emotions

- Anger
- Disgust
- Happiness
- Sadness
- Fear
- Surprise



Source: Ekman, 1978.



Anger



Happiness



Disgust



Surprise



Sadness



Fear

United States	97%	92%	95%	84%	85%
South America	96%	94%	92%	72%	63%
Japan	100%	90%	100%	62%	66%

The percentage of subjects from three different cultures who identified each facial expression as an instance of the label shown.

Source: Ekman, 1973.

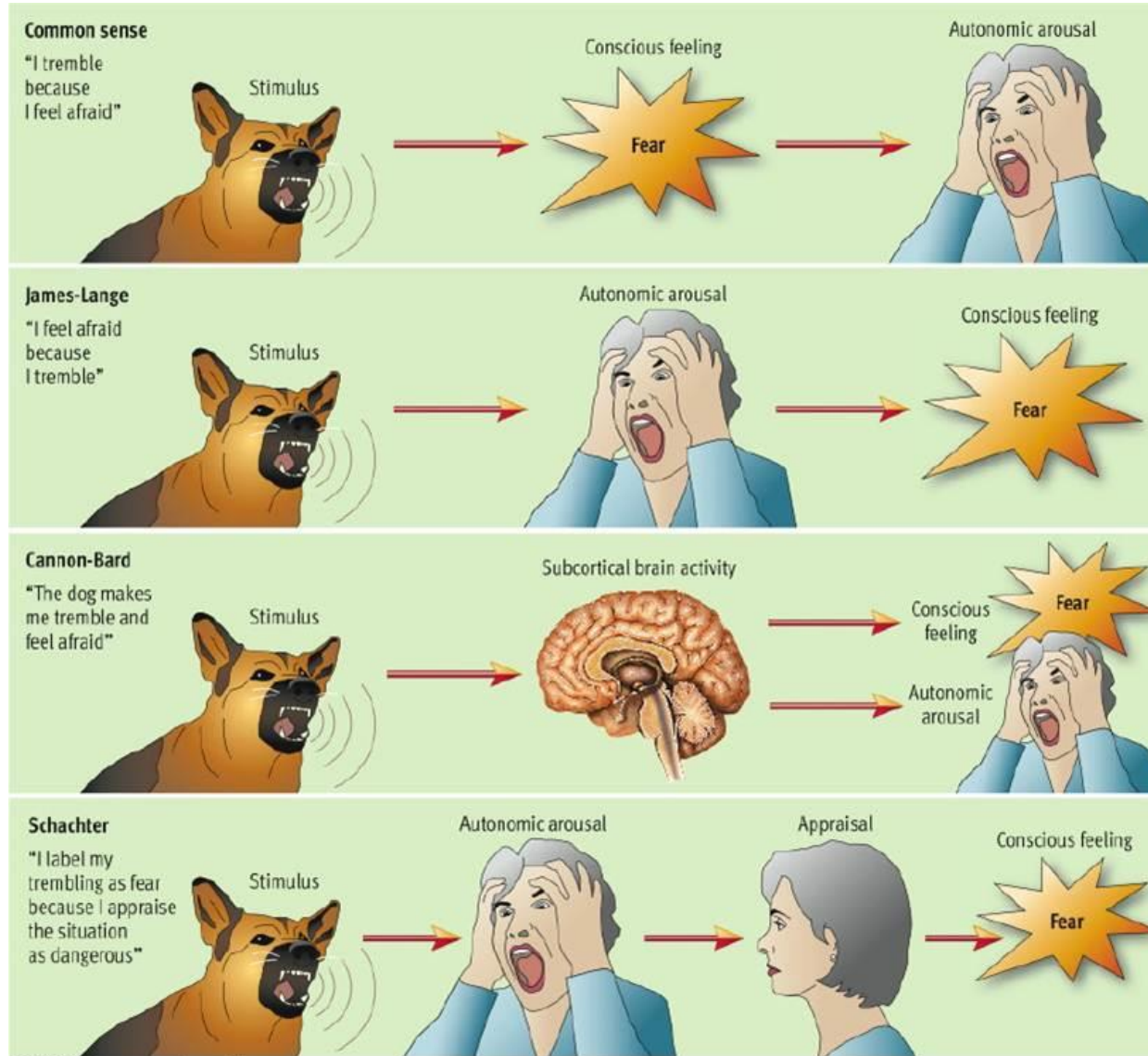
Izard Study with newborns from birth to 4 months

- Interest
- Social smiling
- Anger
- Surprise
- Sadness

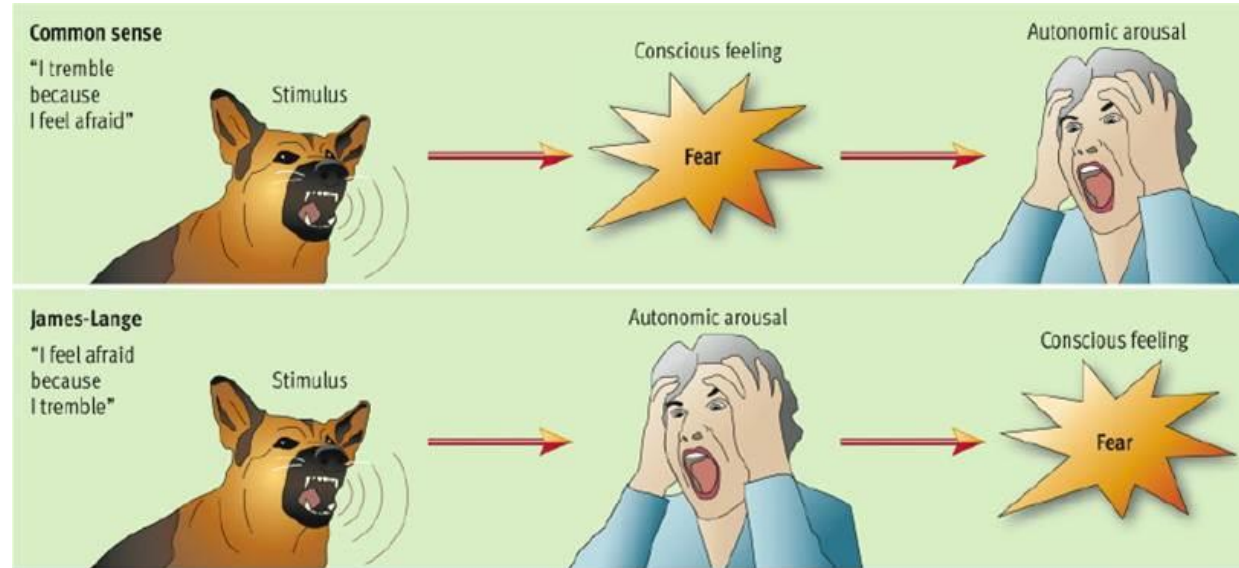
Functions of emotions

- **Rapid perception of danger and activation for action**
- **Perception of inner state (I feel good)**
- **Perception of „atmosphere“**
- **Perception of inner state of others (I can feel that you are sad)**
- **Establishing and forming relationships**
- **Having an impact and influence on others**

Emotion Theories

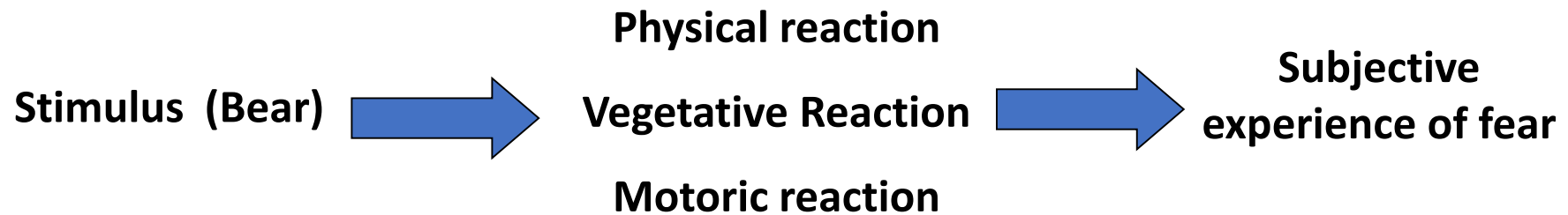


Emotion Theories



Emotion theories

James Lange Theorie

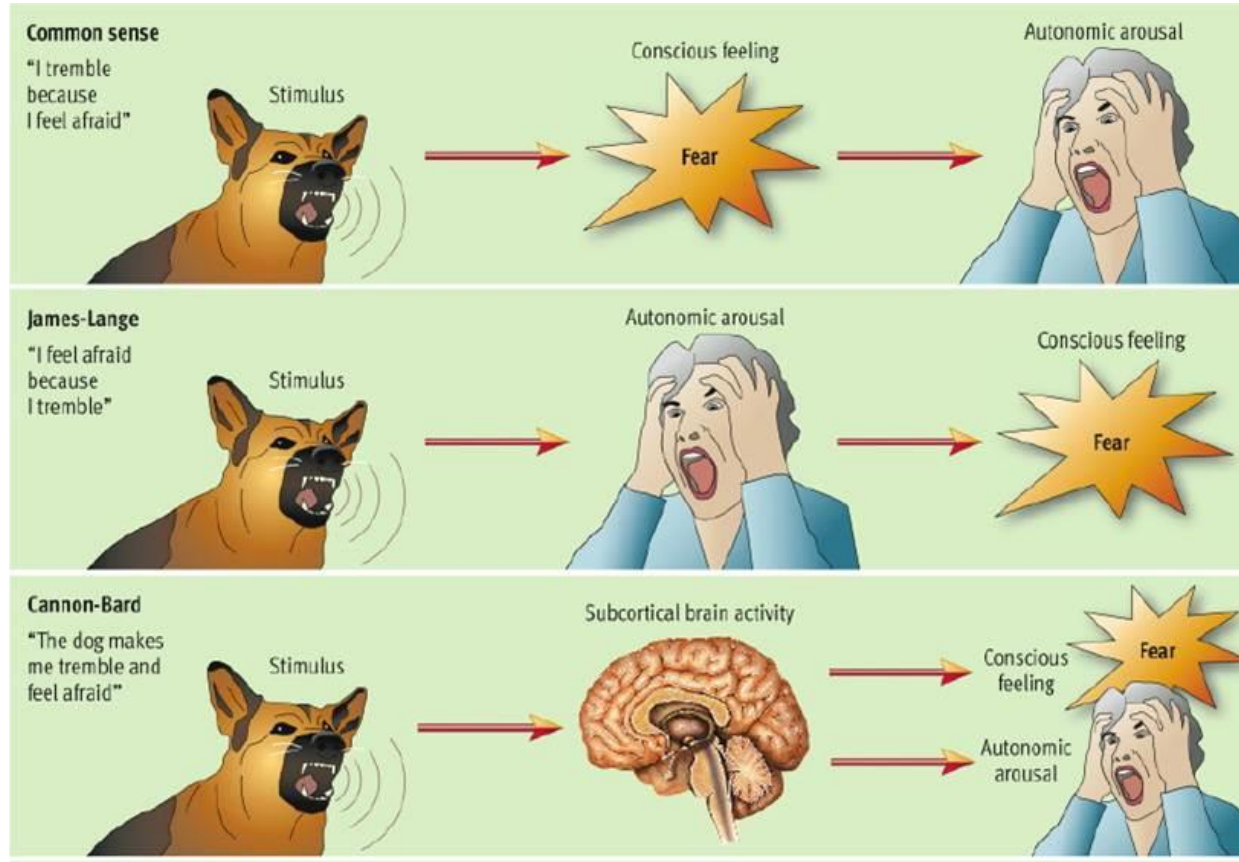


Each emotion is characterized by
a **specific physiological pattern**

Cannon's arguments

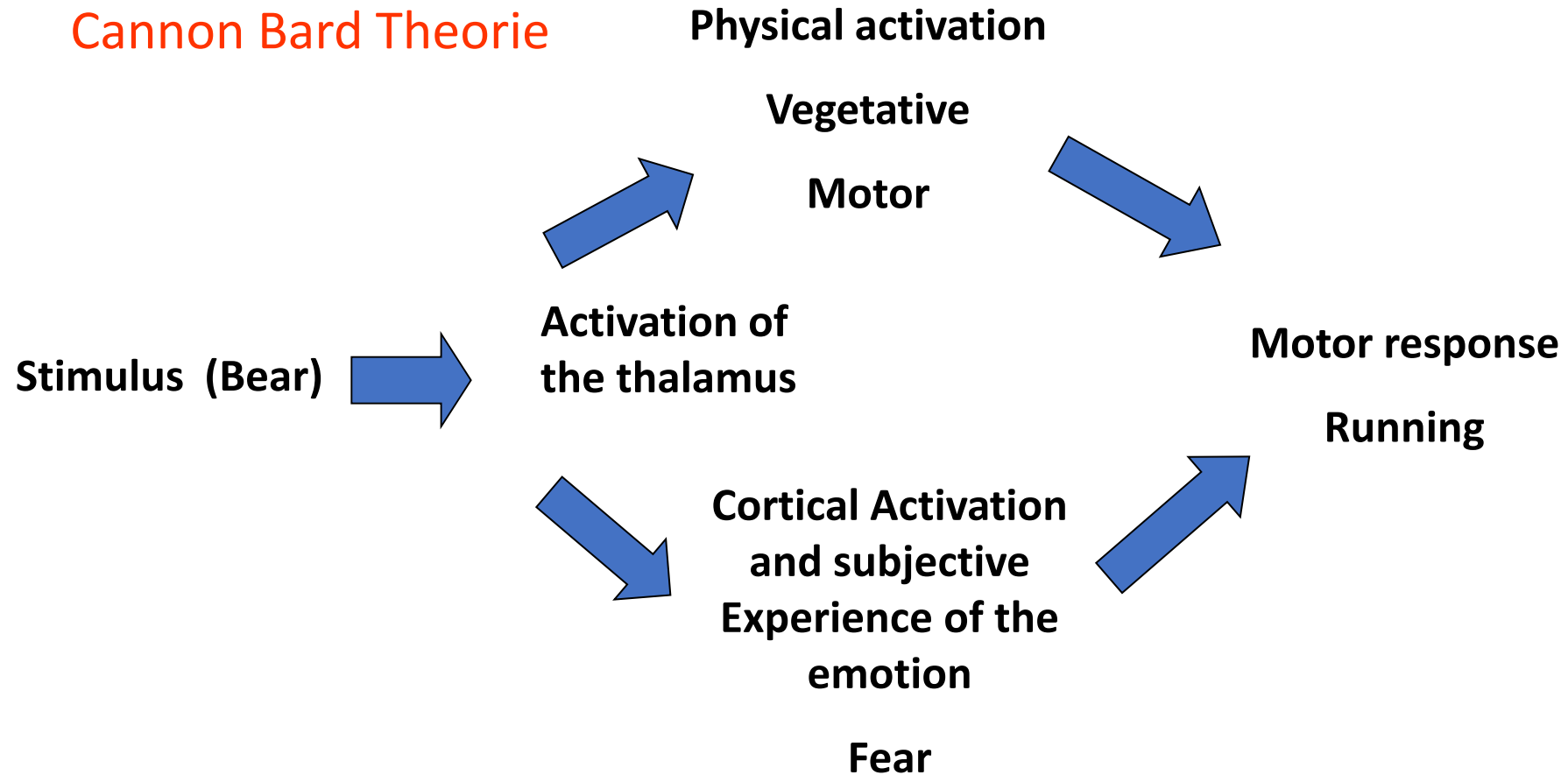
- Affects are faster than physical reaction
- If the vegetative system is blocked by surgery in cats and dogs the animals still show emotional reactions like fear and anger

Emotion Theories



Emotionstheorien

Cannon Bard Theorie



The physiological arousal pattern is the same in all emotions

The Facial Feedback Hypothesis

Ekman, Nathanson et al

- Make as much as possible a
 - Sad Face
 - Happy Face
 - Surprised Face
 - Angry Face
 - Worried Face
 - Disgust Face

Measurement of
physiologic and face
motoric reactions

Look in the mirror in
the morning and
smile



The 2 factor Theory

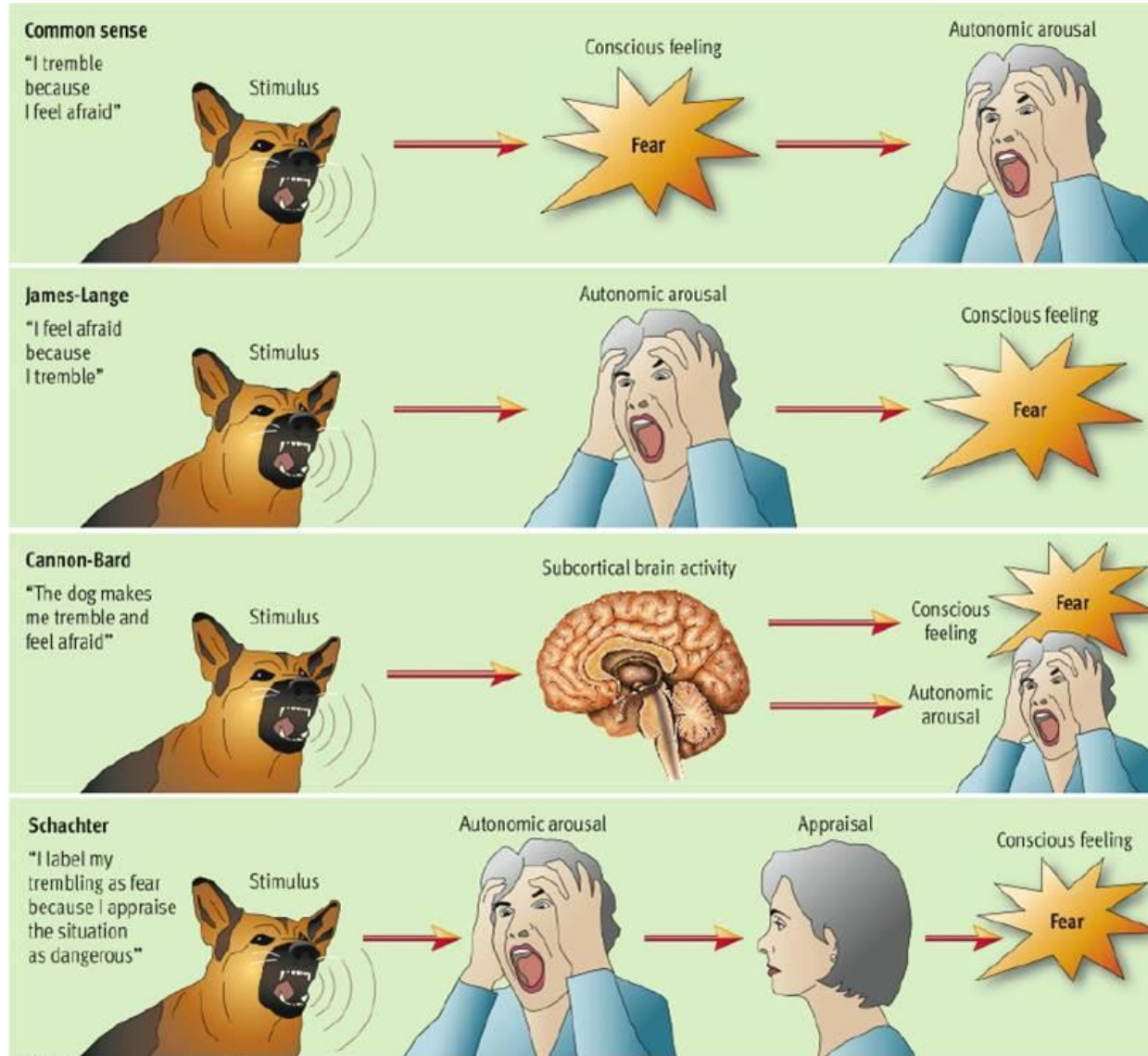
- The experience of an emotion can be subdivided into 2 parts:
 - A general physiological arousal
 - Cognitive attribution
- **Arousal provides the energy of an emotion**
- **Cognition provides the meaning/content of an emotion**
- Physical arousal signals that something is happening; Cognitive processes give an emotional name to this arousal which corresponds best to the actual situation

The Schechter and Singer Experiment

Priming

- The participant receive an Adrenalin injection and they are informed that the injection contains a vitamin,
- Then they are divided into 2 groups.
- Group 1: Each participant comes into a waiting room in which he/she meets somebody who behaves aggressive and angry (as instructed by the investigator without knowledge of the participant)
- Group 2: Each participant comes into a waiting room in which he/she meets somebody who behaves happy and content (as instructed by the investigator without knowledge of the participant)
- The participants of group 1 reported that the injection had lead to feelings of anger while the participants of group 2 said that they felt happy and content after the injection
- A control group received a placebo injection with the same experimental context. They neither reported anger nor happiness

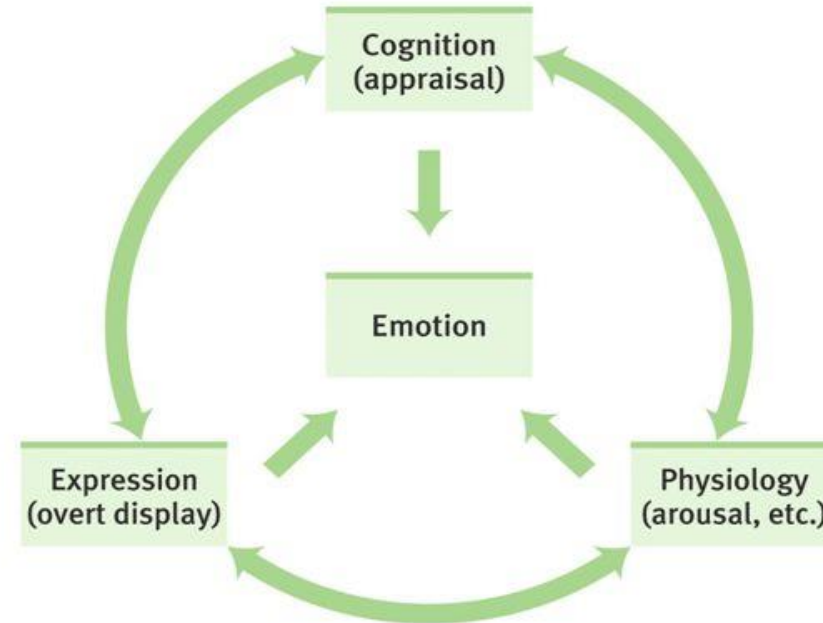
Emotion Theories



The body - mind link

What is emotion?

- Emotions are a **mix** of:
 - *Physiological activation* of sympathetic nervous system (heart rate, blood pressure, breathing, pupil dilation) and various parts of the brain (amygdala; frontal cortex)
 - *Expressive behaviors* (quicken pace clenched fists, smile, frown)
 - *Conscious experience*, including thoughts /cognitive interpretation (“are they going to attack me?”) and subjective feelings (a sense of fear).



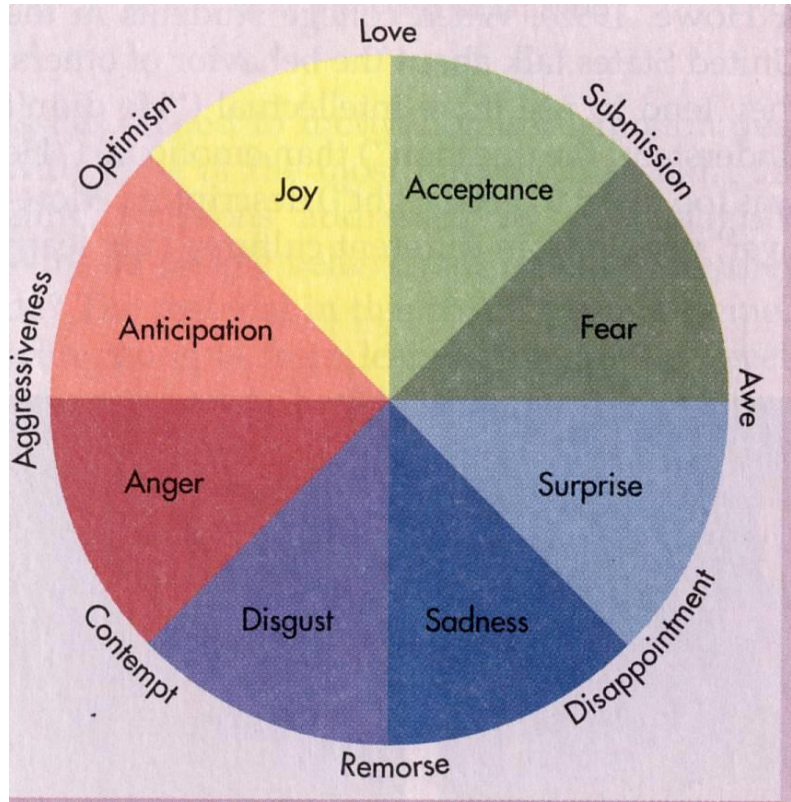
Autonomic Nervous System Controls Physiological Arousal		
Sympathetic division (arousing)		Parasympathetic division (calming)
Pupils dilate	EYES	Pupils contract
Decreases	SALIVATION	Increases
Perspires	SKIN	Dries
Increases	RESPIRATION	Decreases
Accelerates	HEART	Slows
Inhibits	DIGESTION	Activates
Secrete stress hormones	ADRENAL GLANDS	Decrease secretion of stress hormones



Phenomenology of emotions

Plutchik's List

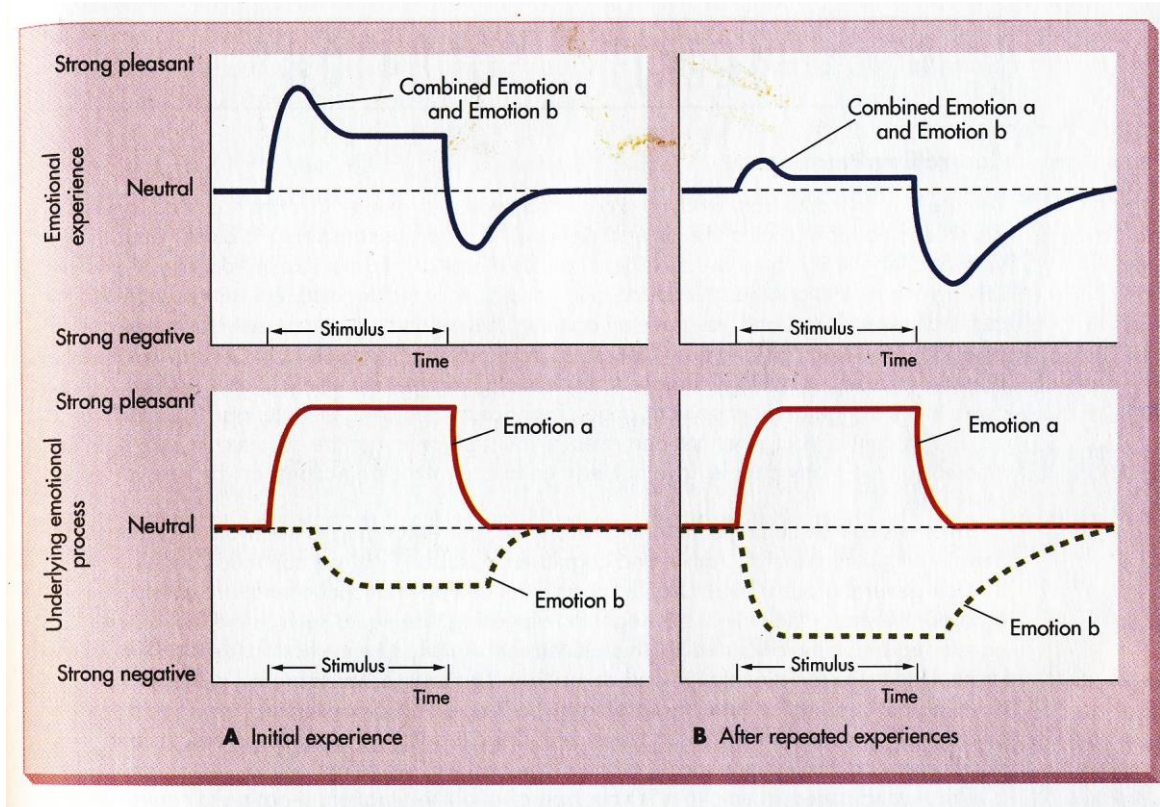
- Joy
- Acceptance
- Fear
- Surprise
- Sadness
- Disgust
- Anger
- Anticipation



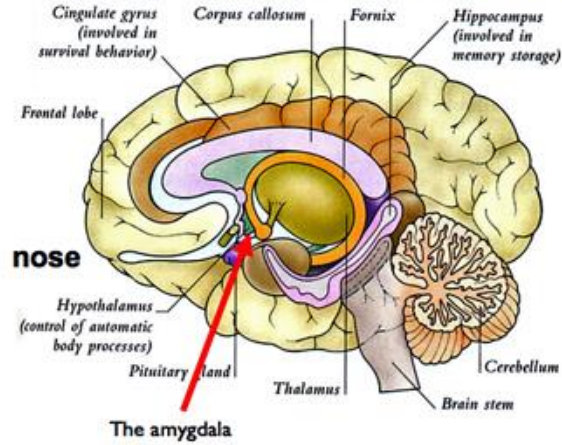
Concomitant activation of opposite emotions

- **There is a mechanism of emotional hemostasis** meaning the extreme emotional reactions into positive or negative direction are downregulated (negative feedback) to come back to an optimal level of arousal

Emotional Hemostasis



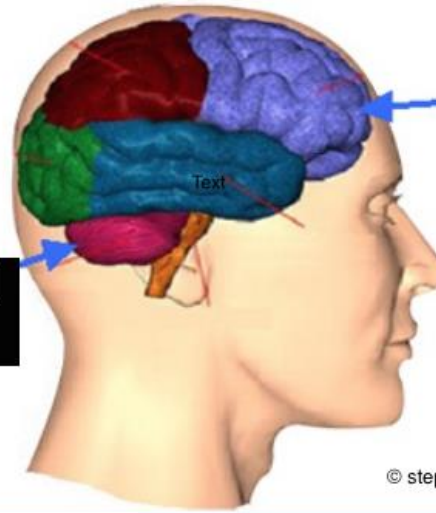
The limbic system – the emotional brain



Fast
5x more
powerful

**Emotional
Brain**

Irrational
Emotional
Illogical



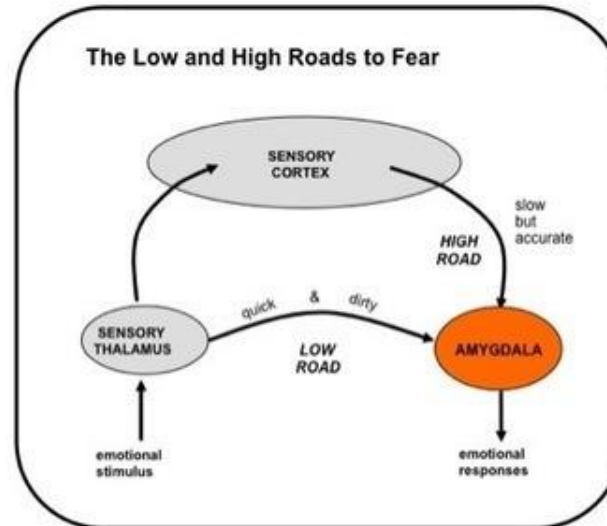
**Thinking
Brain**

Rational
Thinking
Logical

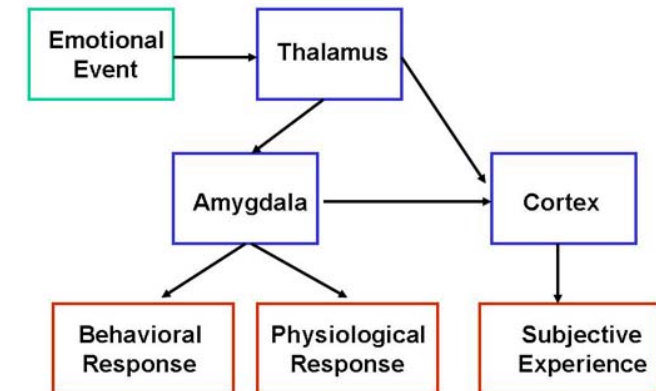
Slow
5x weaker

© stephenlongcoaching

The Low and High Roads to Fear



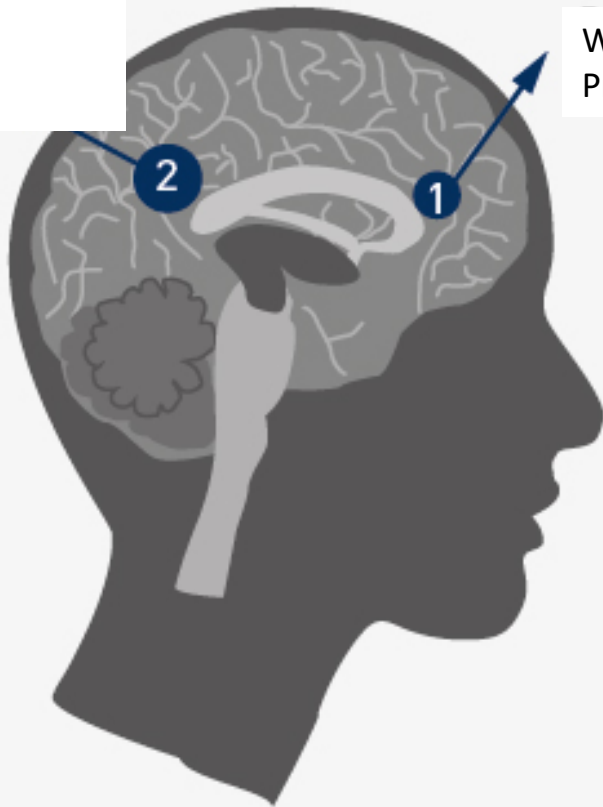
Emotional Systems of the Brain After LeDoux (1996)



Activated brain regions

.....listening to facts

Wernicke Areal
Understanding
language

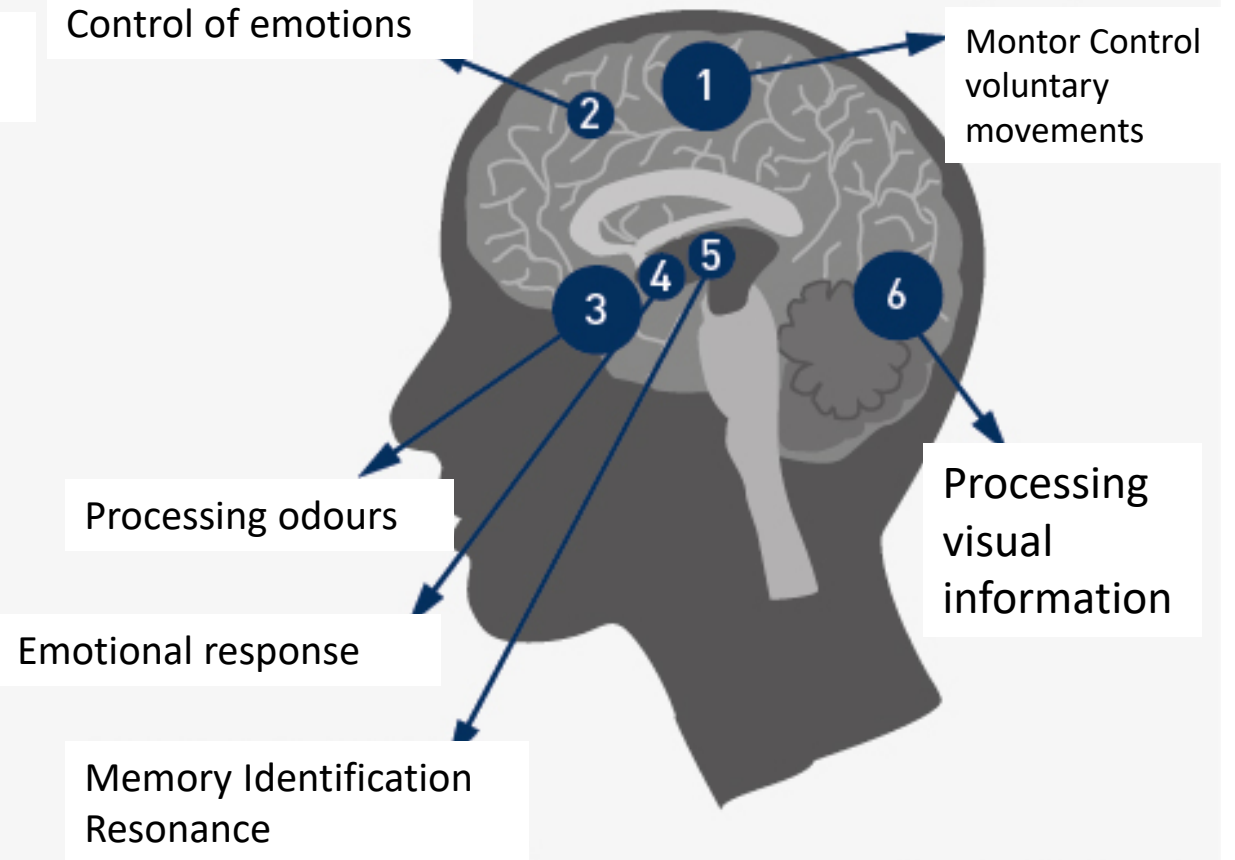


Wernicke Areal
Processing Language

.....when we hear stories

Control of emotions

Motor Control
voluntary
movements



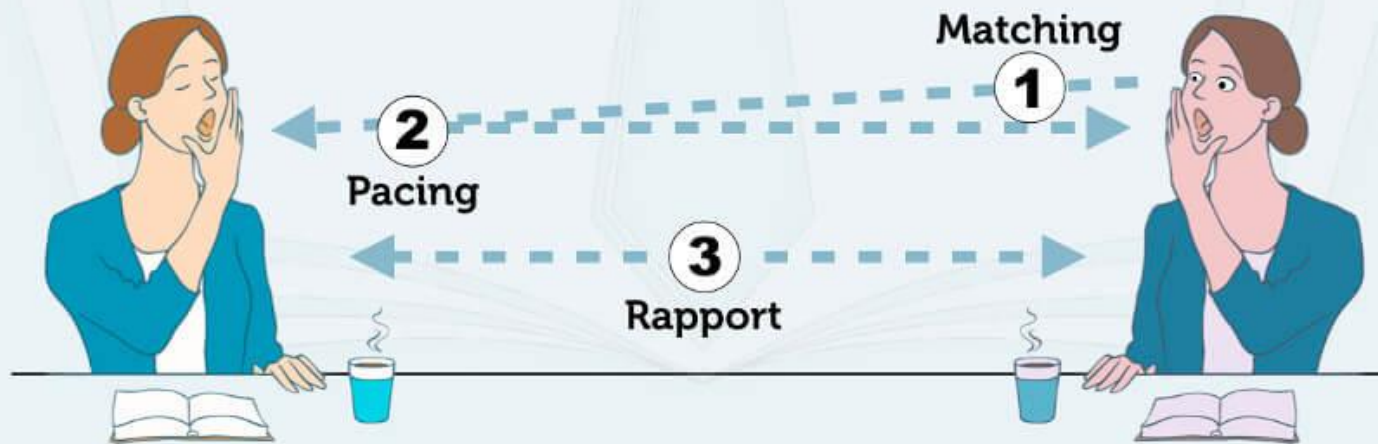
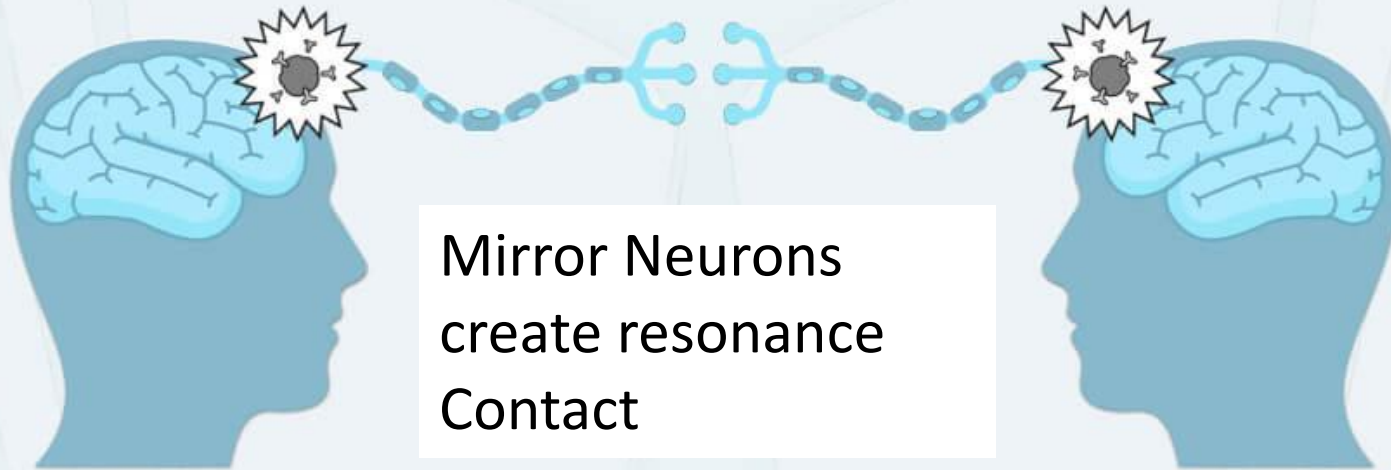
Processing odours

Emotional response

Memory Identification
Resonance

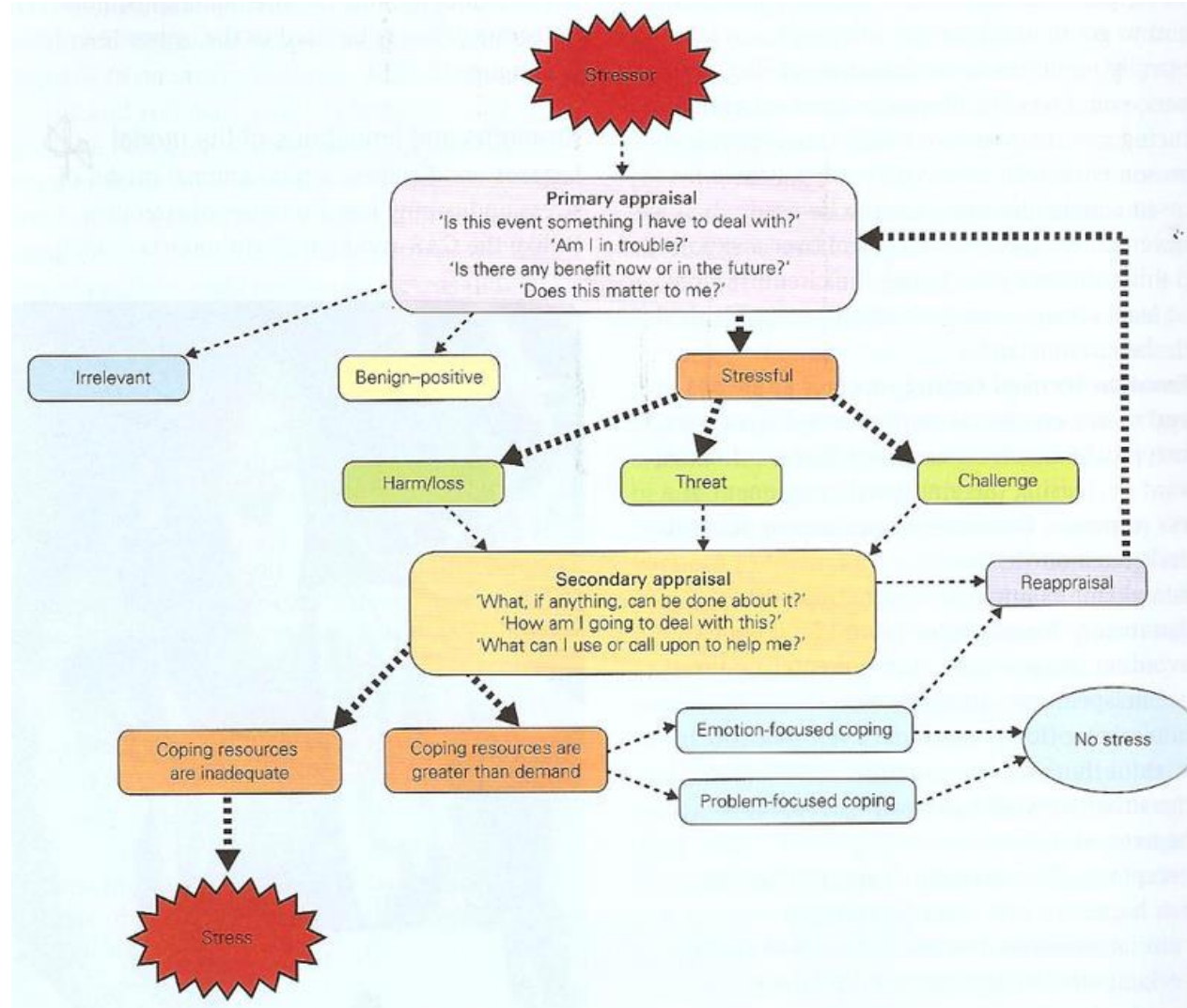
Processing
visual
information

Mirror Neurons how do they work

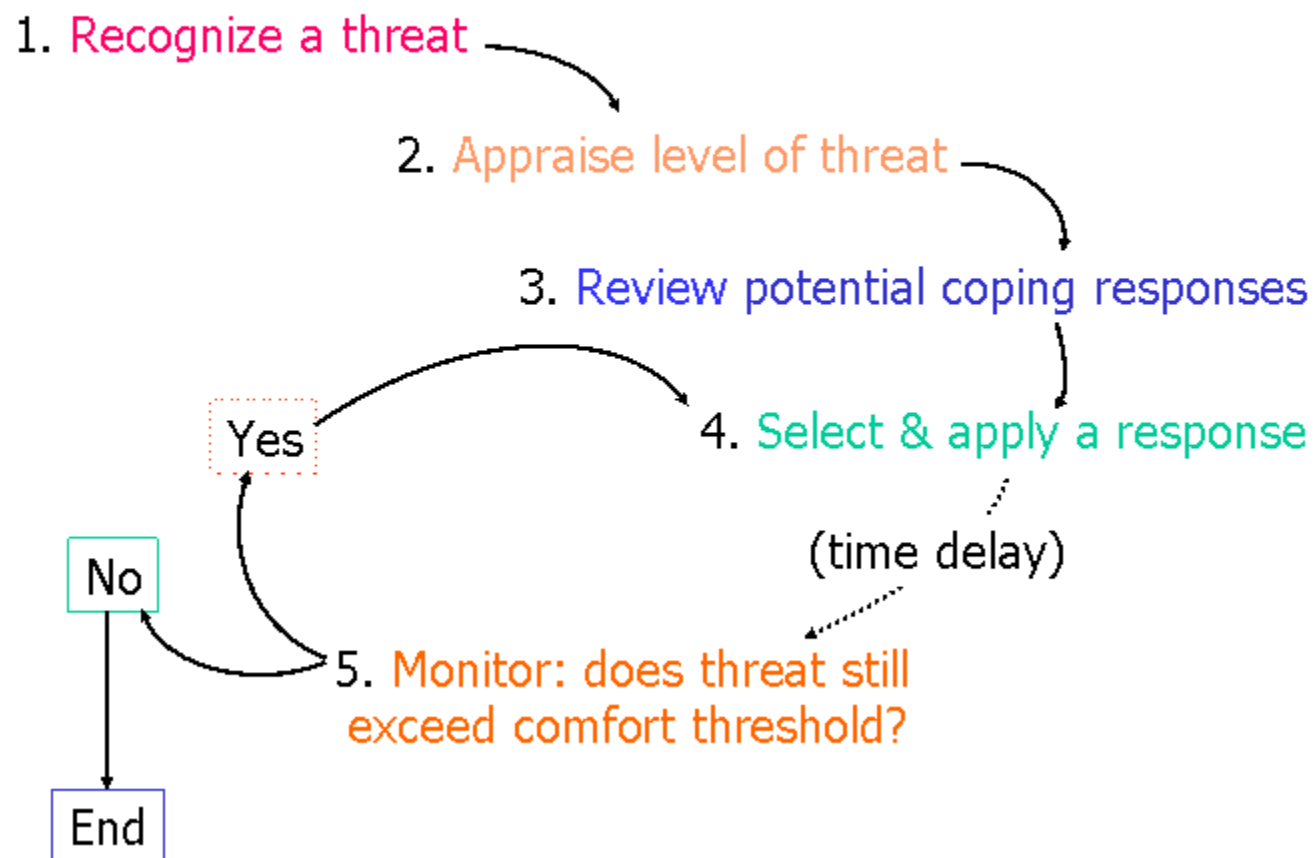


The psychology of the stress response

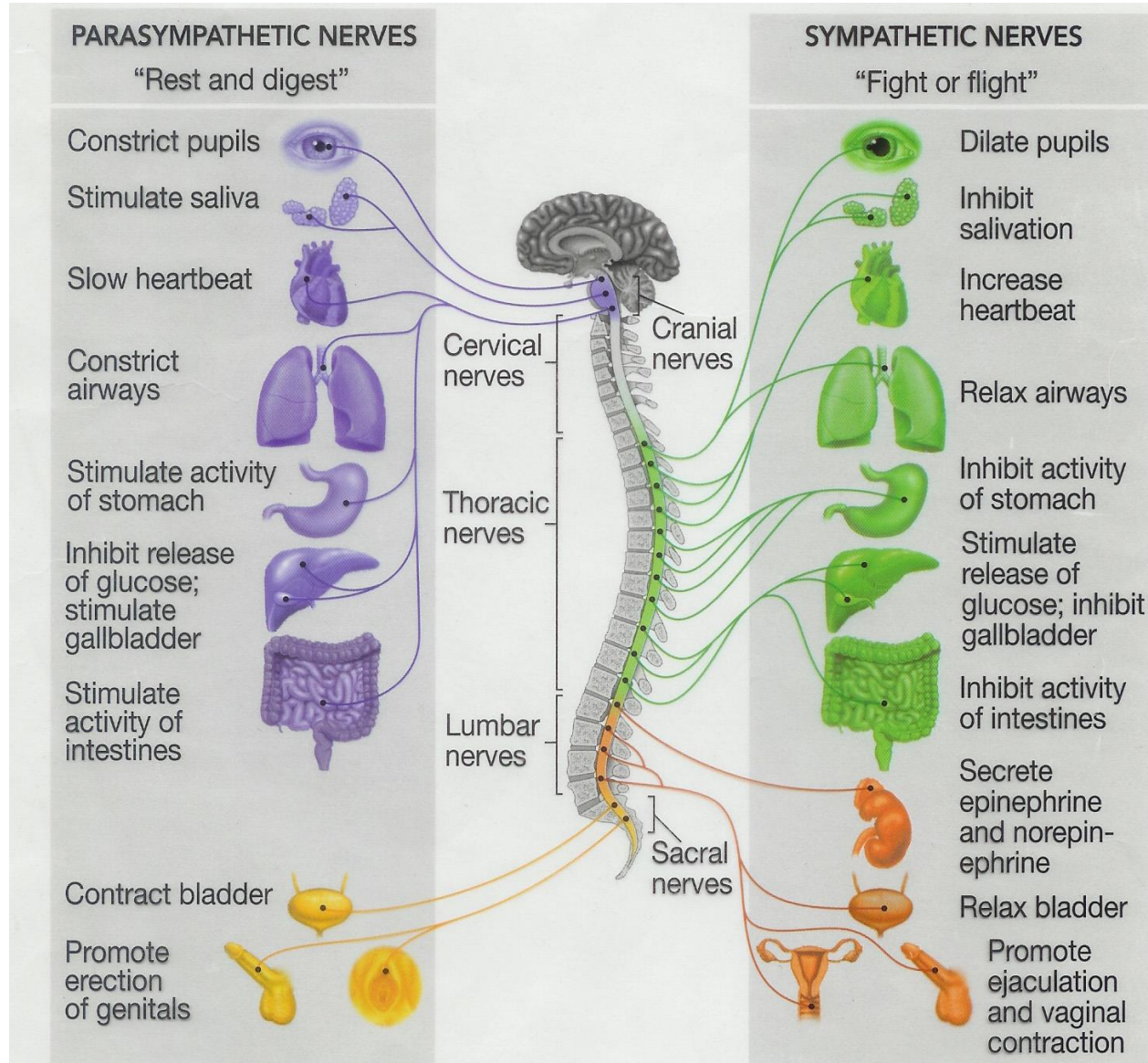
Lazarus



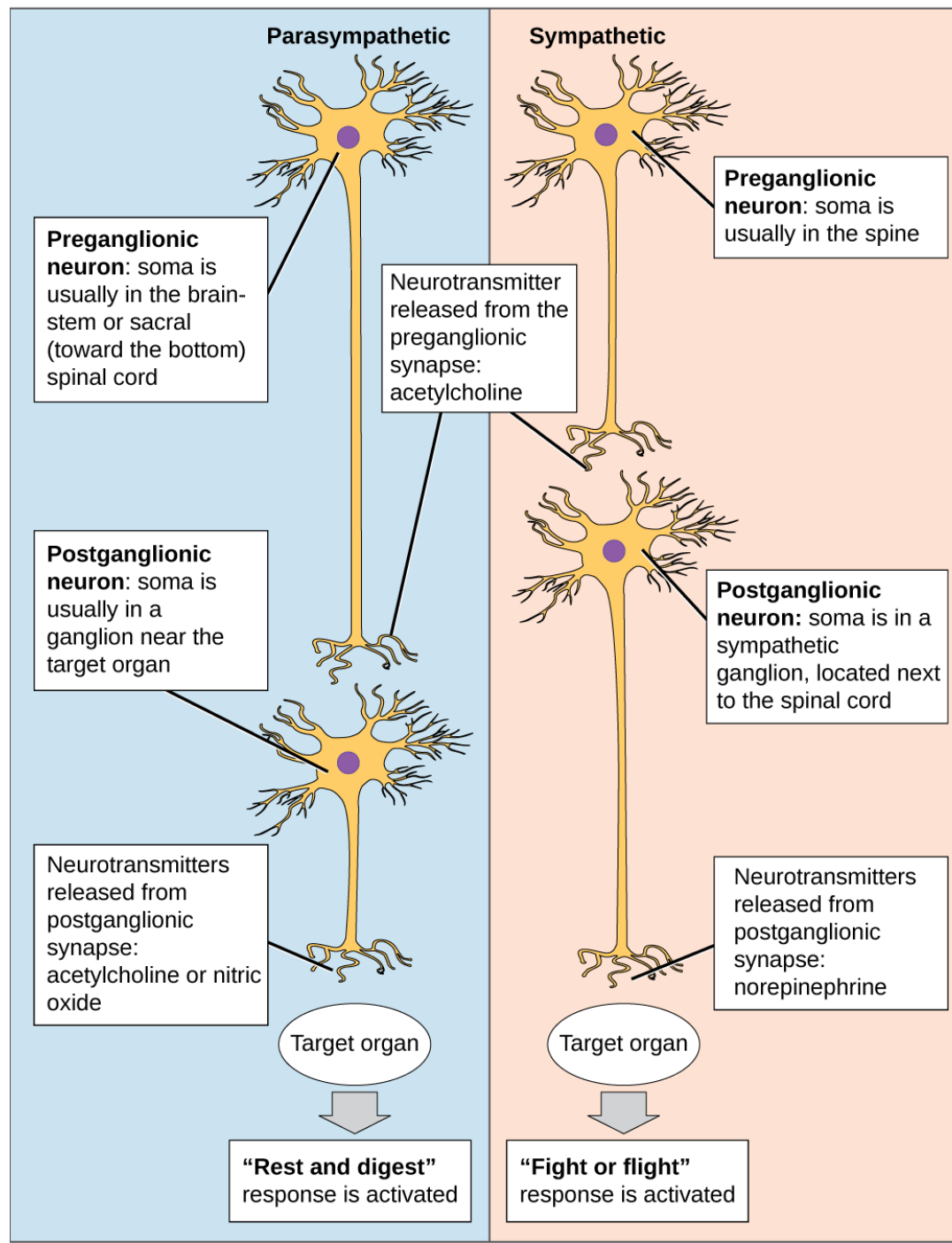
Coping Model (I)



The psychovegetative stress response

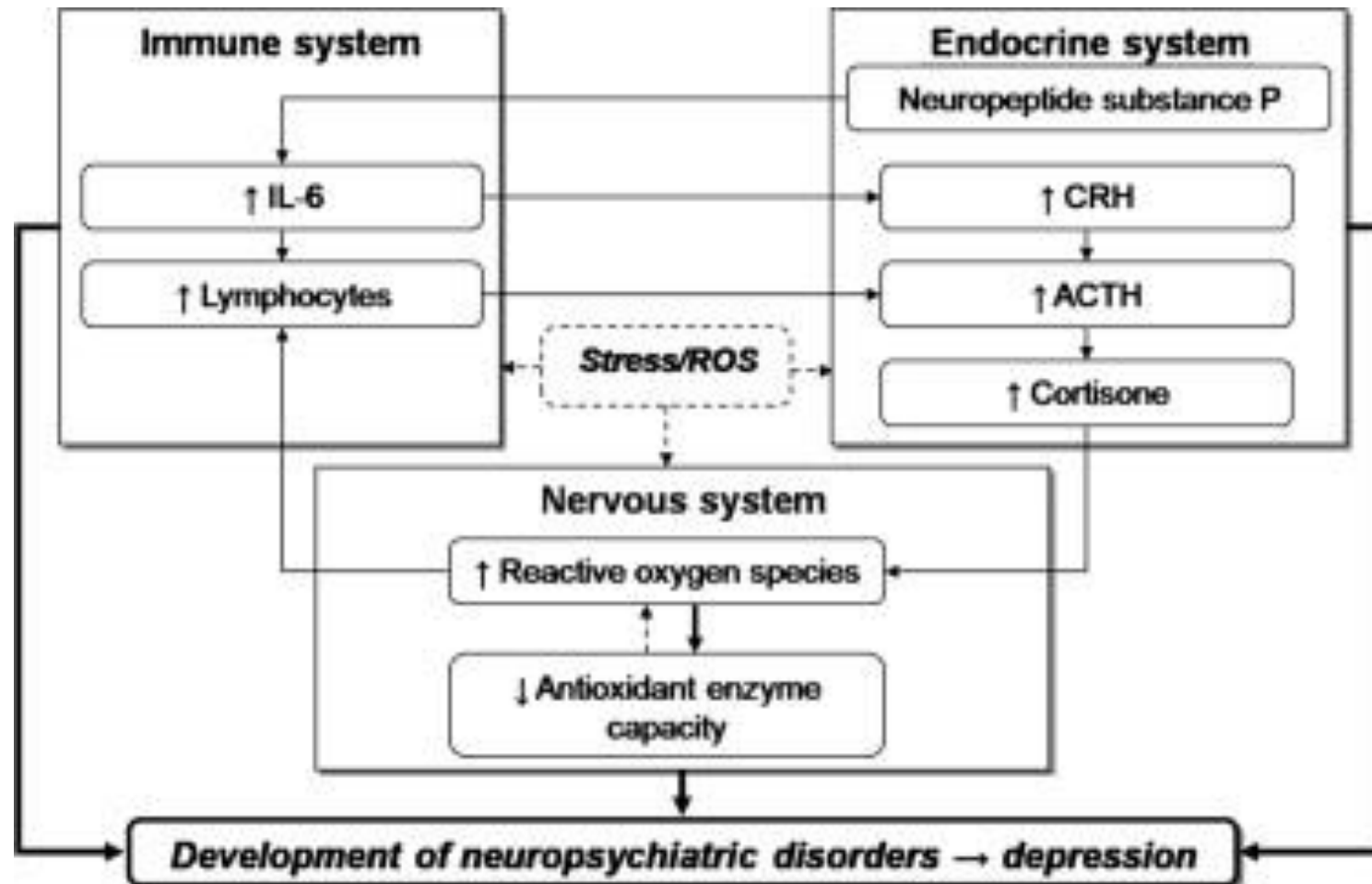


Autonomic Nervous System

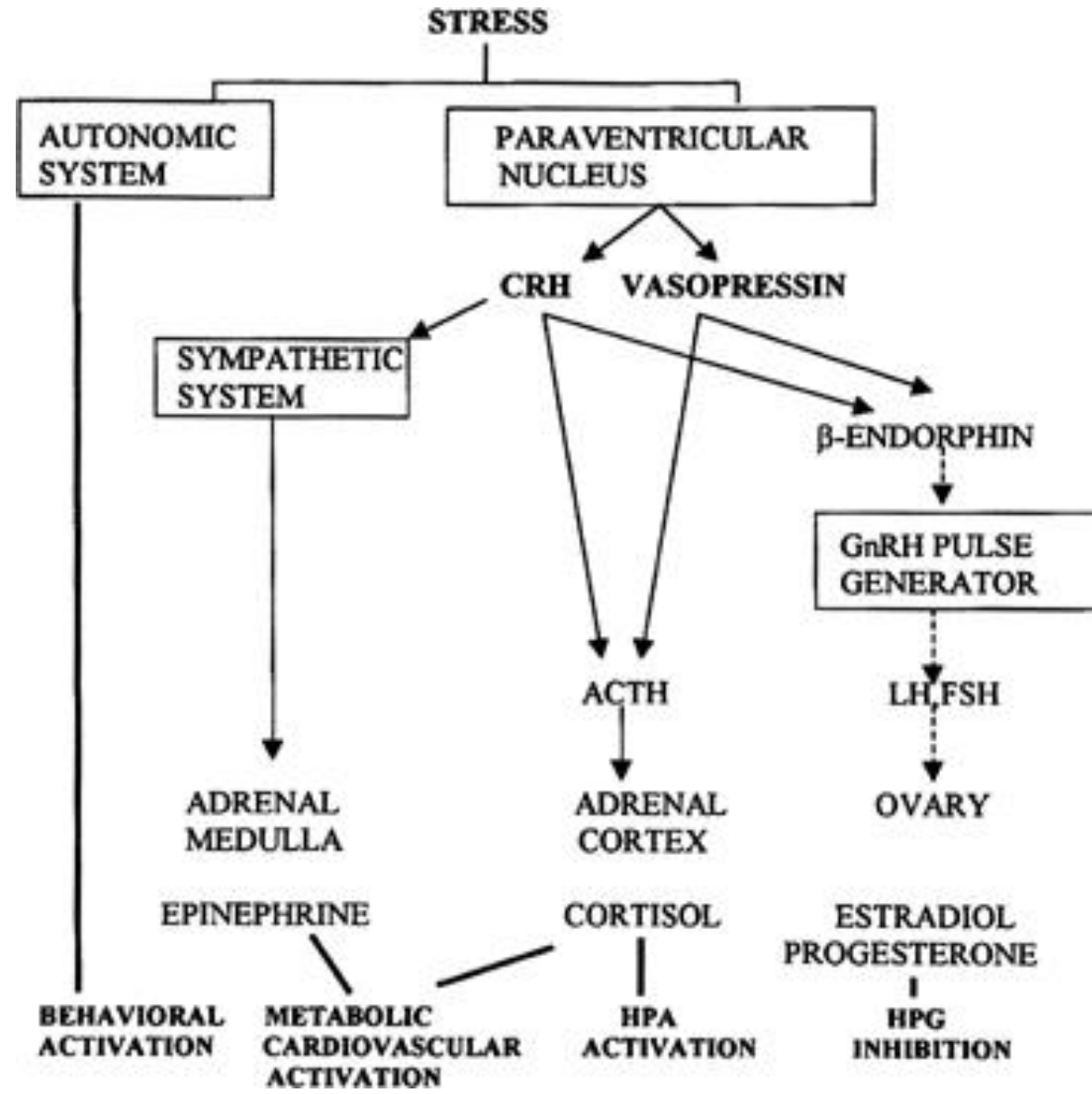


The psychovegetative stress response

The **neuroendocrine** and **neuro-immunological** stress response combined

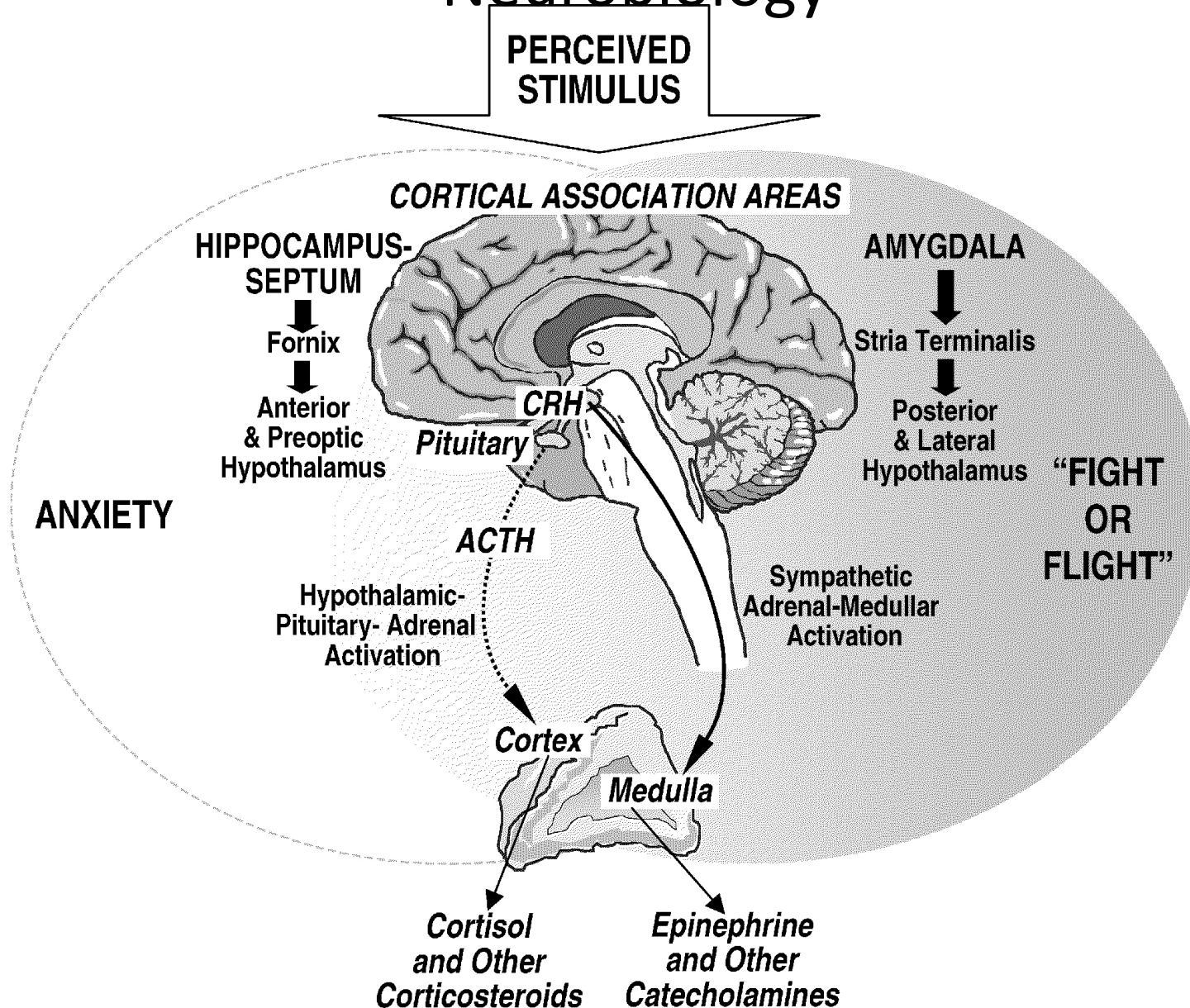


The **psycho-endocrine**, **psycho-vegetative** response combined

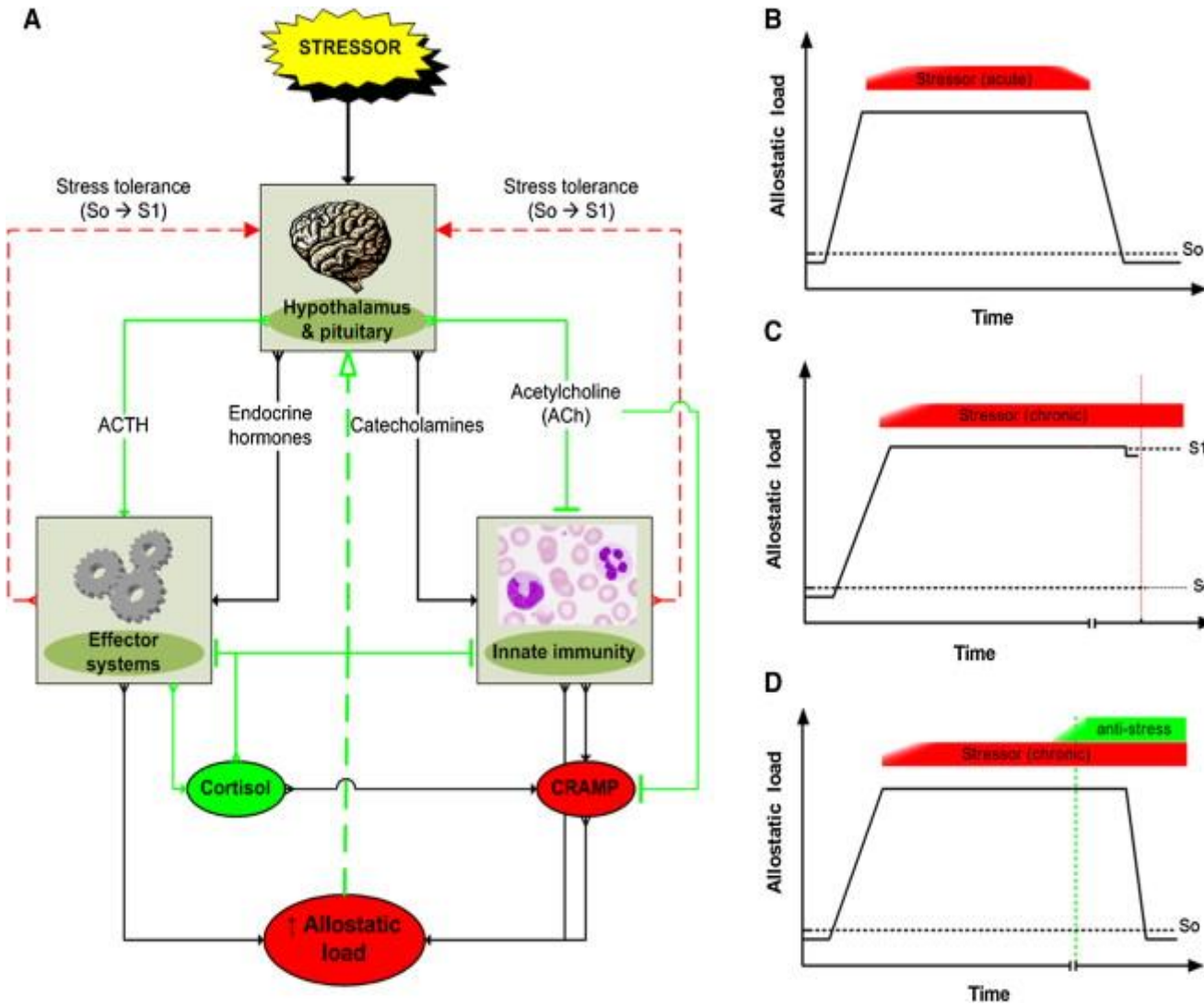


The main brain structures involved

Neurobiology



The psycho-endocrine stress response



Activation of
Stress
Response

Activation of
Anti Stress
Response

What is emotional health

- Capacity of emotional regulation
 - Understanding one's own emotions
- Empathy
 - Understanding the emotions of the other person
- Emotional literacy

Sexuality – the paradigm of body/mind/environment interaction

The body sexual response

The subjective sexual experience
Thoughts, emotions, behavior

**The sexual interaction with
another individual**

The sexual culture

The biopsychosocial model

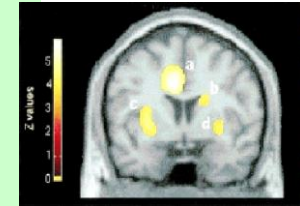


The partner

Relationship dynamics
Sexual Health/Disorder
Conflicts and Resources

The mind

Feeling
Thinking
Behavior
Mental health
Sexual biography



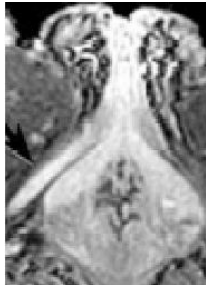
The environment

Socio cultural norms and
ideals
Education and Information
Laws and Politics



The body

Organs
Hormones
Diseases
Drugs



Sexual health - a delicate balance between „hell and heaven“

Hell

**Unwanted
pregnancies**

STI

**Sexual
trauma**

**Sexual
violence**

Sexual health

Heaven

Pleasure

Attachment

Intimacy

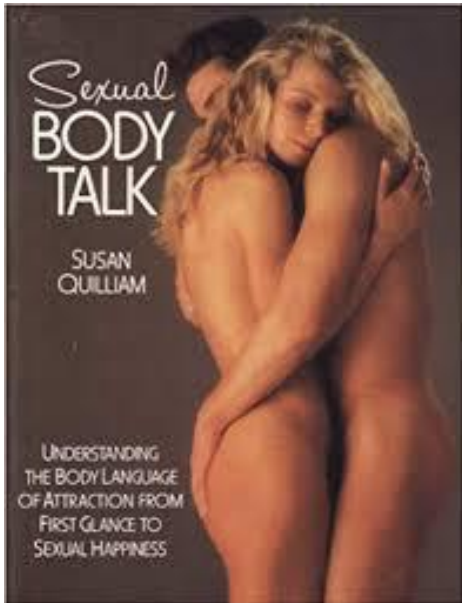
**Gender
Identity**

What is the challenge to sexual health (heaven)

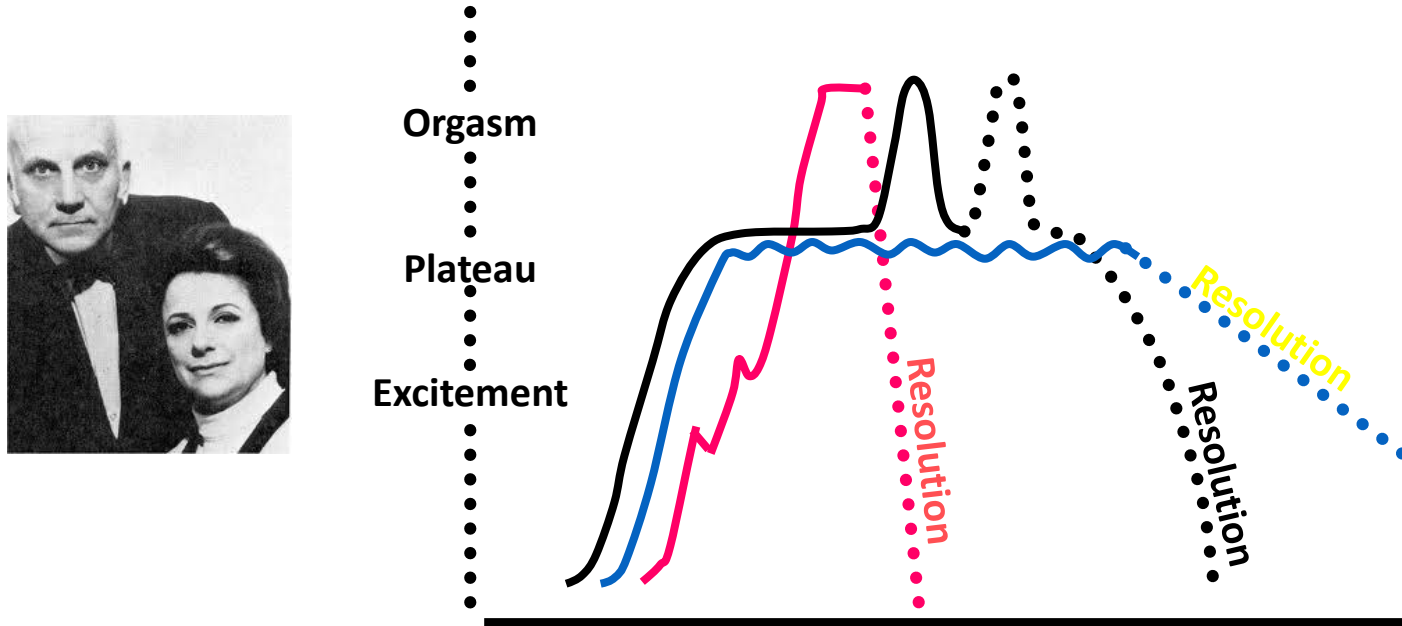
- Women and men suffer from lack or loss of **motivation** for sex
 - No desire, no interest
- Women and men suffer from lack or loss of **pleasure** from sexual activity
 - No arousal, no satisfaction
- Women and men suffer from lack of **function**
 - No Erection, no lubrication, no orgasm, mistimed orgasm
- Women and men suffer from **pain** when the want to be sexually active
 - My vulva, penis, vagina.....it hurts

The 2 classical perspectives

- The sexual body
 - Observation
 - Visualization
 - Measurement
 - Experiment
 - Biomedical objective model
 - The anatomy and physiology of the sexual response
- The sexual mind
 - Listening and Identifying
 - Patient reports, narratives
 - Understand patients' beliefs
 - Observe their behavior
 - The psychology of the sexual person



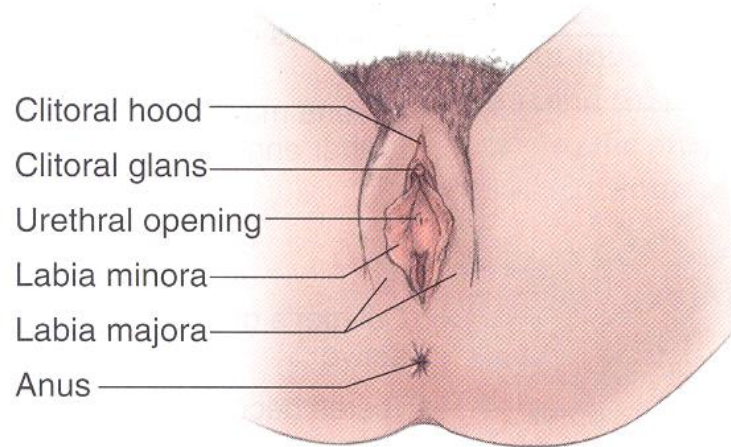
Masters and Johnson's model of female sexual response



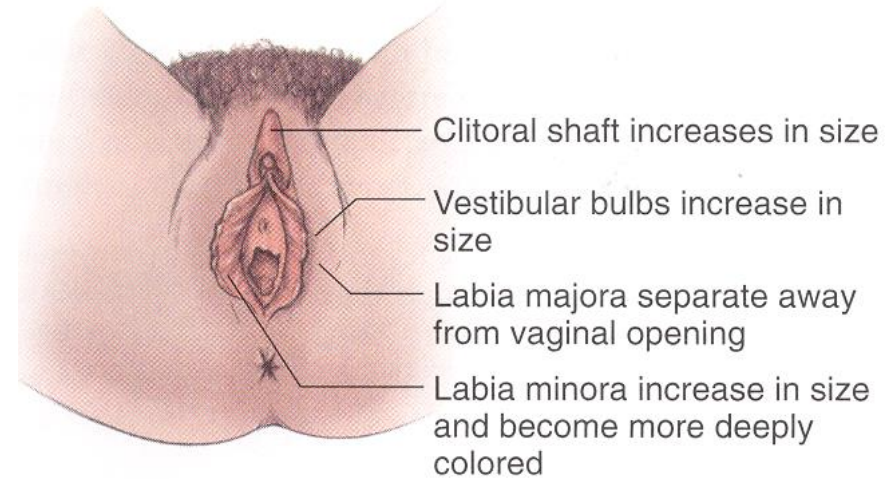
- The lines reflect the distinct responses that different women may have, or that an individual woman may have on separate occasions

Sexualität und Medizin

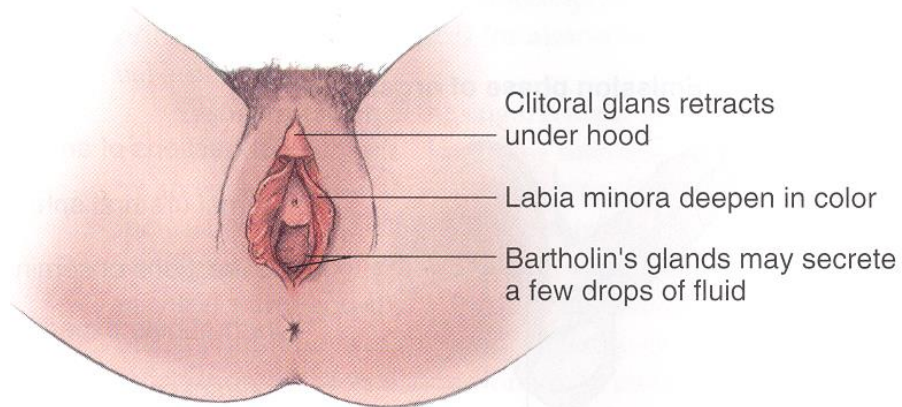
(a) **Unaroused state**



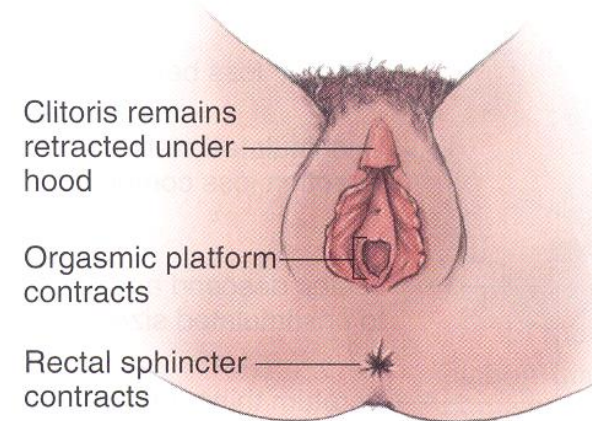
(b) **Excitement phase**



(c) **Plateau**

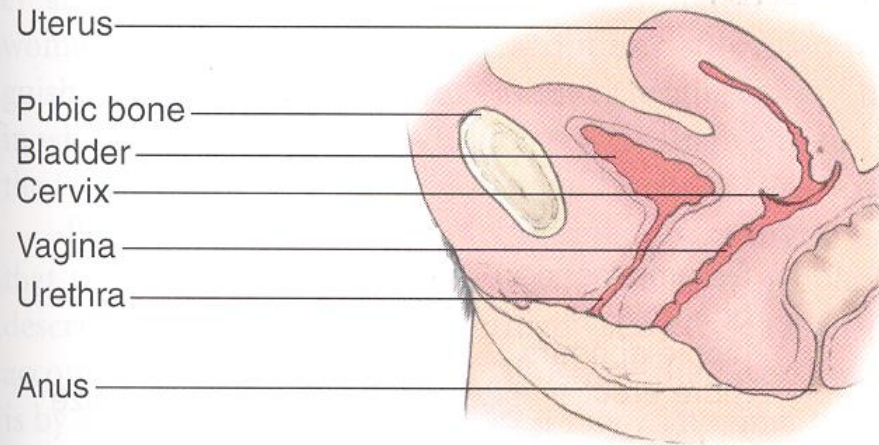


(d) **Orgasm**

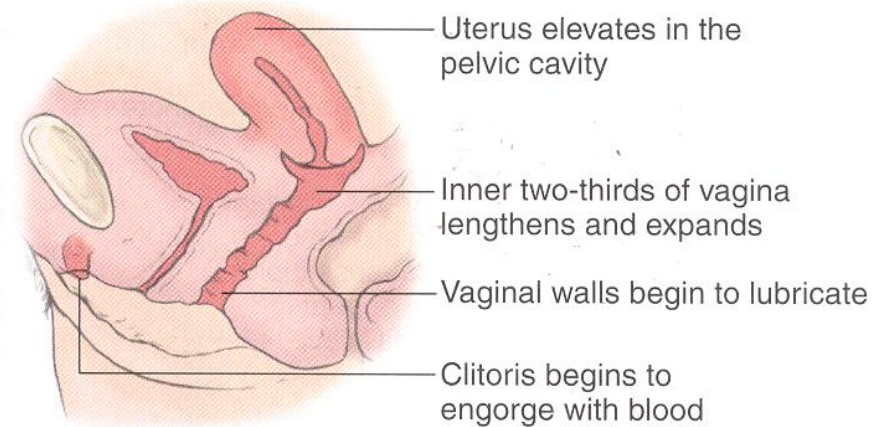


Sexualität und Medizin

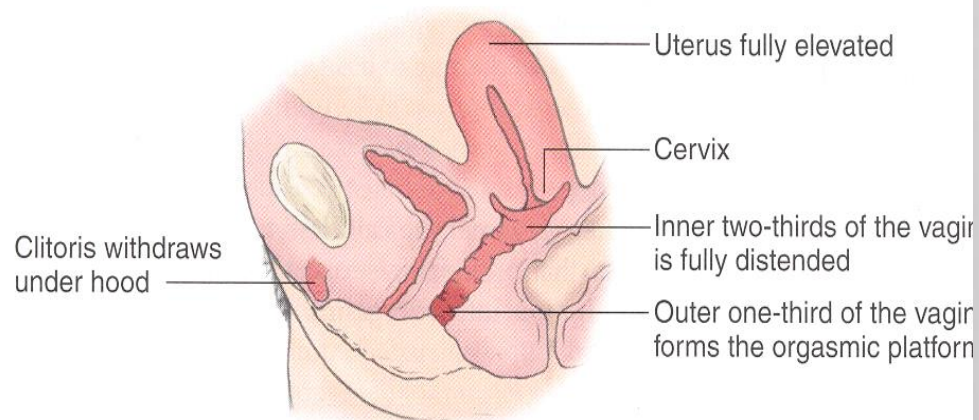
(a) **Unaroused state**



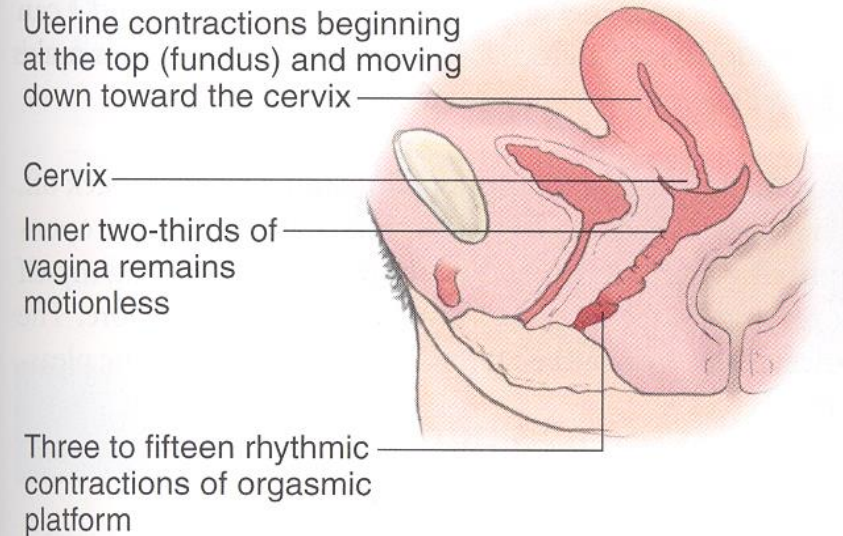
(b) **Excitement phase**



(c) **Plateau phase**



(d) **Orgasm**



Signs of orgasm

- Prospective signs
 - Change of the colour of the labia minora from red to pink.
 - Increase of the vascular congestion of the labia minora. The labia majora separate more.
 - Many women develop red spots at different parts of the body due to increased blood flow in all parts of the body

Signs of orgasm

- Actual signs
 - Rhythmic, involuntary contractions with a rhythm of about 0,8 sec. of the distal part of the vagina through the activation of the striated muscles surrounding the vagina (pelvic floor, bulbospongiosus, ischiocavernosus (
 - Mild orgasm 3-5 contractions 2.4 to 5 seconds
 - Normal 5-8 contractions 4 to 6.4 seconds
 - Intensive orgasm 8-12 contractions 4 to 9.6 seconds
 - There is no correlation between the contractions and the subjective intensity of orgasm
 - Uterine contractions (smooth muscle).
 - Contractions of the anal sphincter

Signs of orgasm

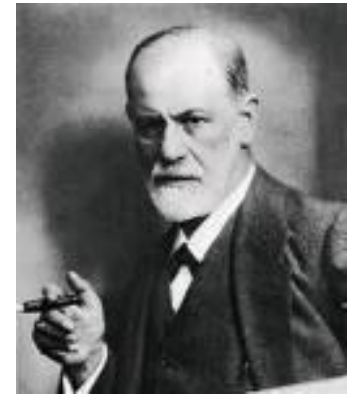
- Retrospective signs
 - Areola congestion and decongestion
 - Increase of the VPA en la photophlethysmography
 - Elevated prolactin
 - Oxytocin

The „drive“

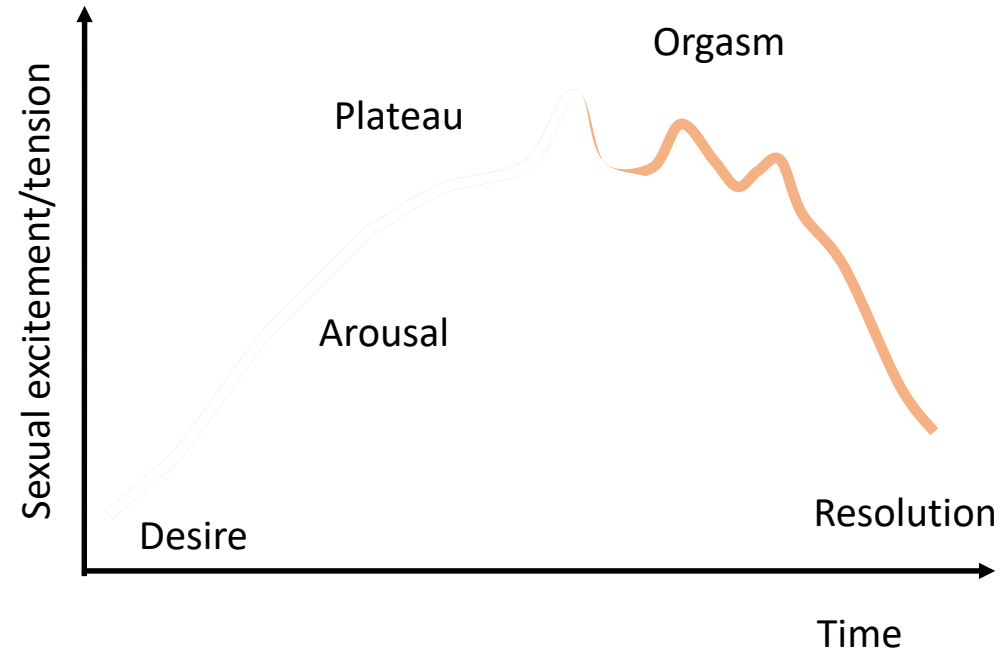
- Biologically determined need (hunger)
- Appetite
- „Sexual Food“
- Satiety



- Biologically determined energy (tension)
- Internal pressure
- „Acting out“
- Relief



Kaplan's model of female sexual response



- Kaplan added the concept of desire to the Masters and Johnson model and condensed the response into three phases: desire, arousal, orgasm

Current understanding of Sexual desire

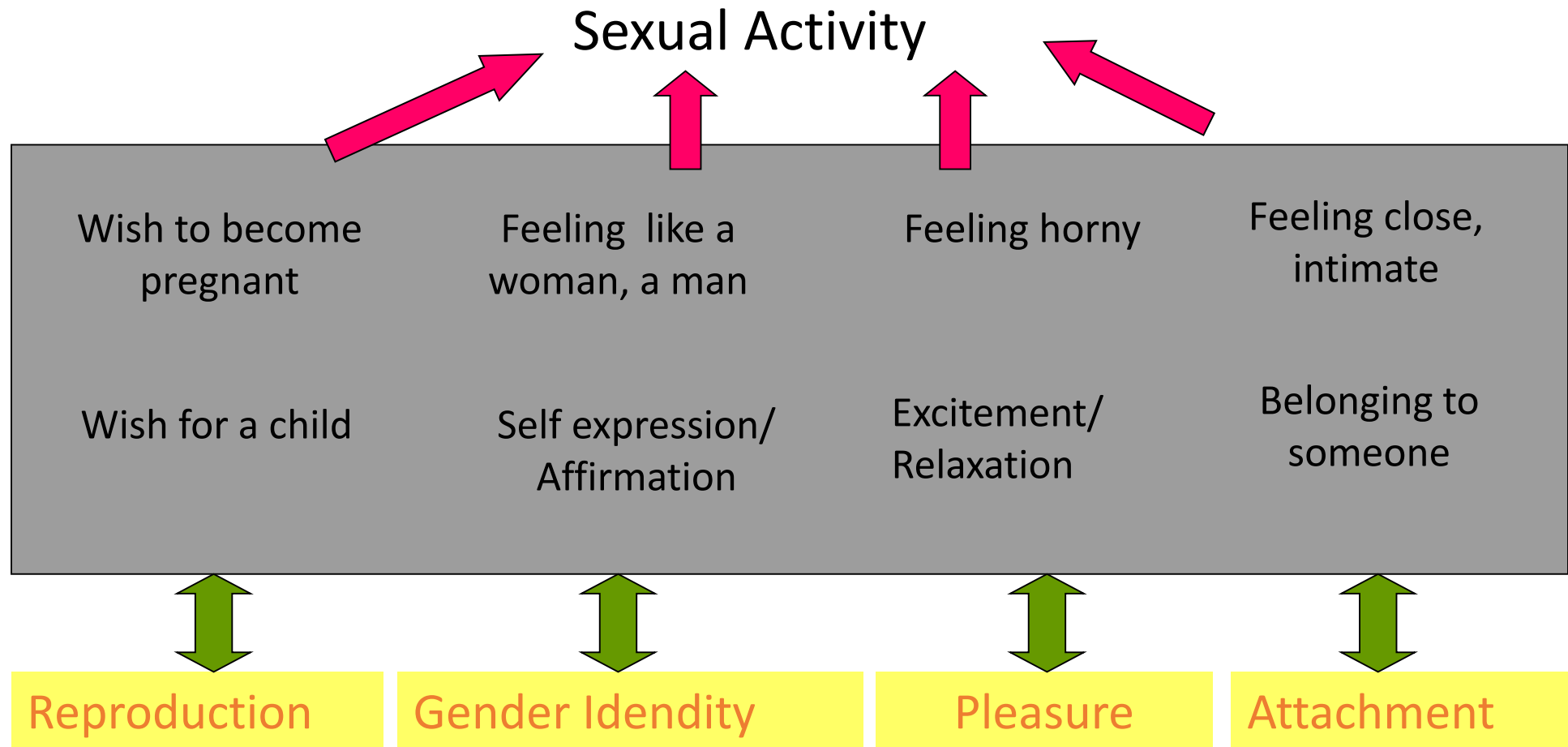
*Multifaceted, multidimensional
phenomenone, modified during the lifespan*

Drive (feeling sexy)

Motivation (sexual objectives)

**Willingness to let the body respond to
sexual stimuli**

The motivation for people to become sexually active



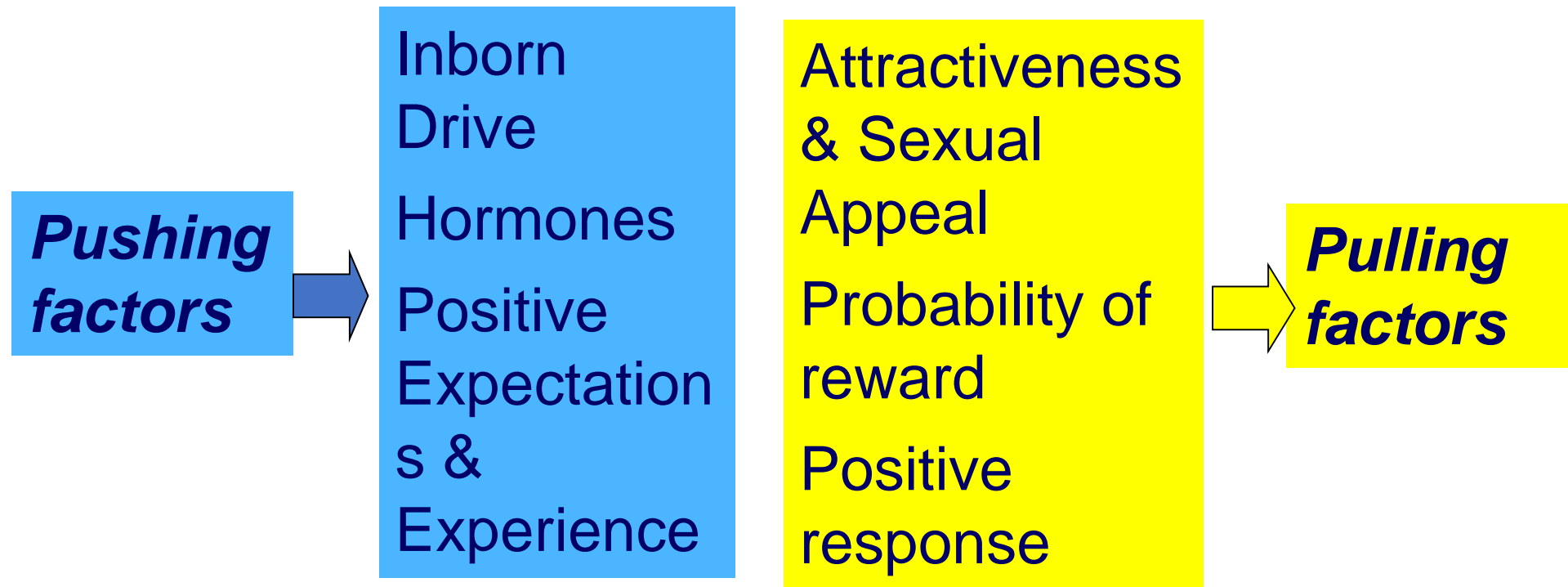
Incentive Motivation Model

- The Internal Drive model is outdated (some internal pressure builds up that must be acted upon)
- Thus, there must be other driving forces for the sexual system

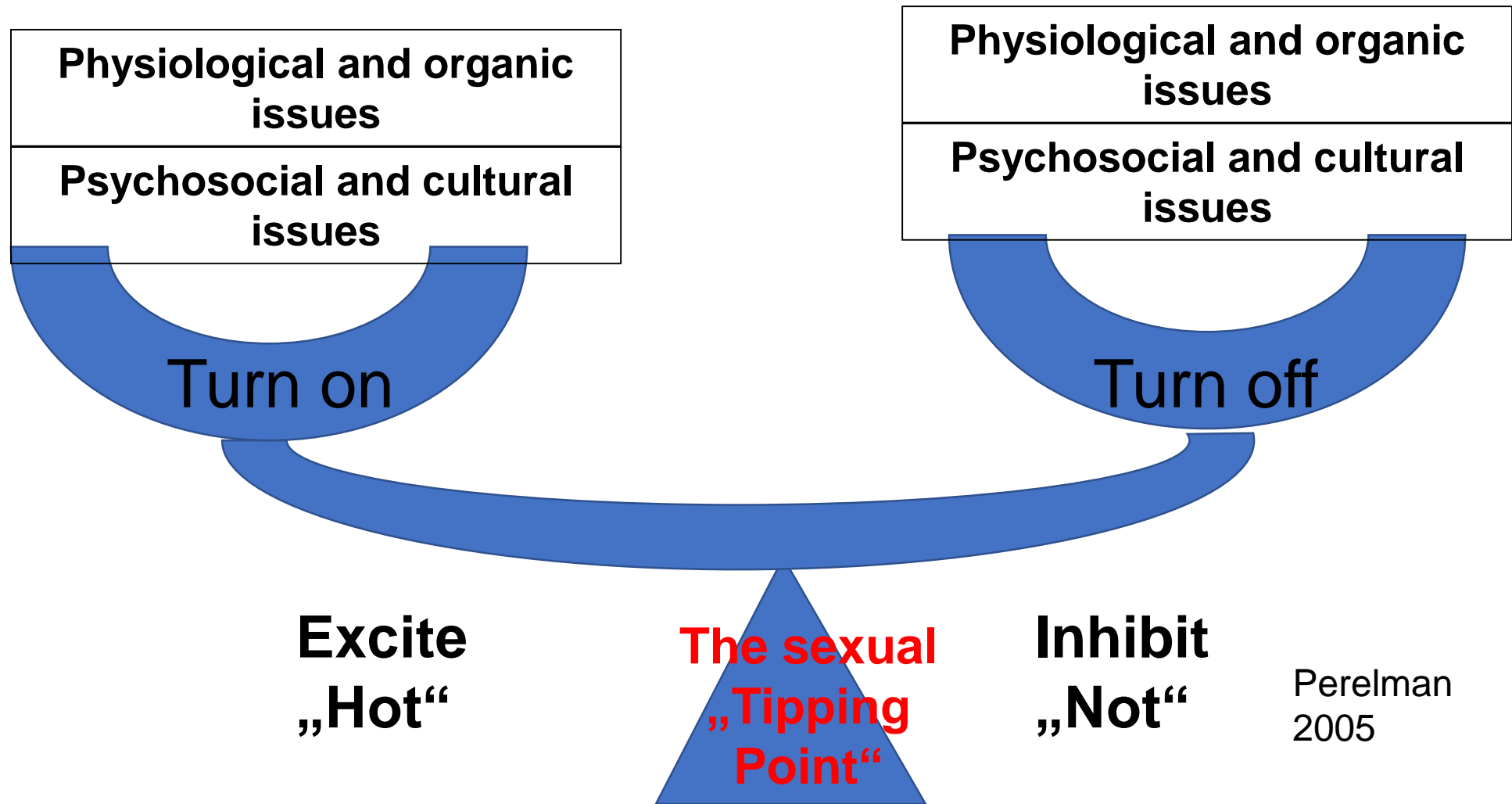


Everaerd, Laan. J Sex Marital Ther 1995;21: 255-263

The „Pushing and Pulling“ Model



The „tipping point“ Model



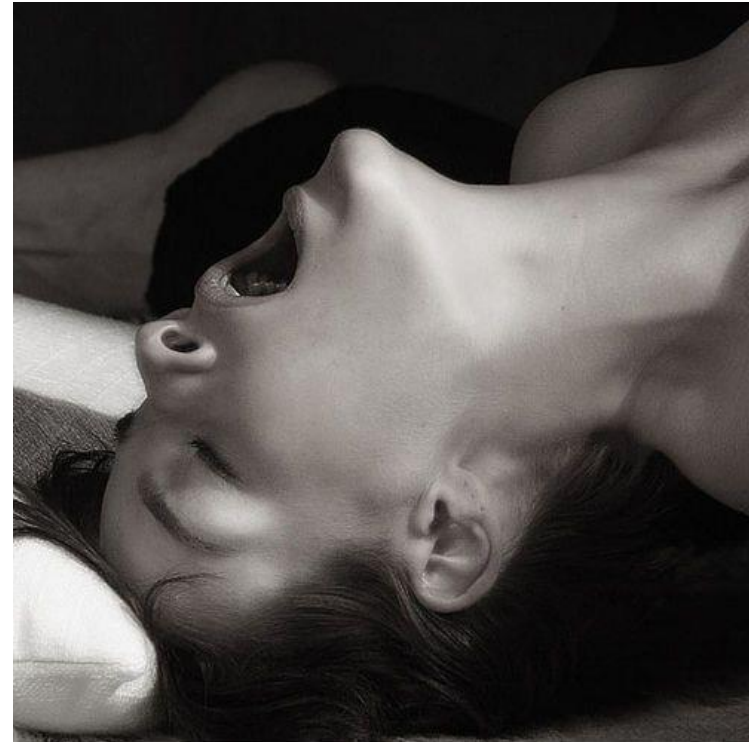
The sexual experience

Description of
pleasure, orgasm,
excitement,
relaxation,
frustration,
pain.....

Patient
reported
outcome

What is an orgasm?

“An orgasm in the human female is a variable, transient peak sensation of intense pleasure, creating an altered state of consciousness, usually accompanied by involuntary, rhythmic contractions of the pelvic striated circumvaginal musculature, often with concomitant uterine and anal contractions and myotonia that resolves the sexually-induced vasocongestion, usually with an induction of well-being and contentment” (Meston et al., 2004).



Ellen Laan Cortesy

Why do women have orgasm ?

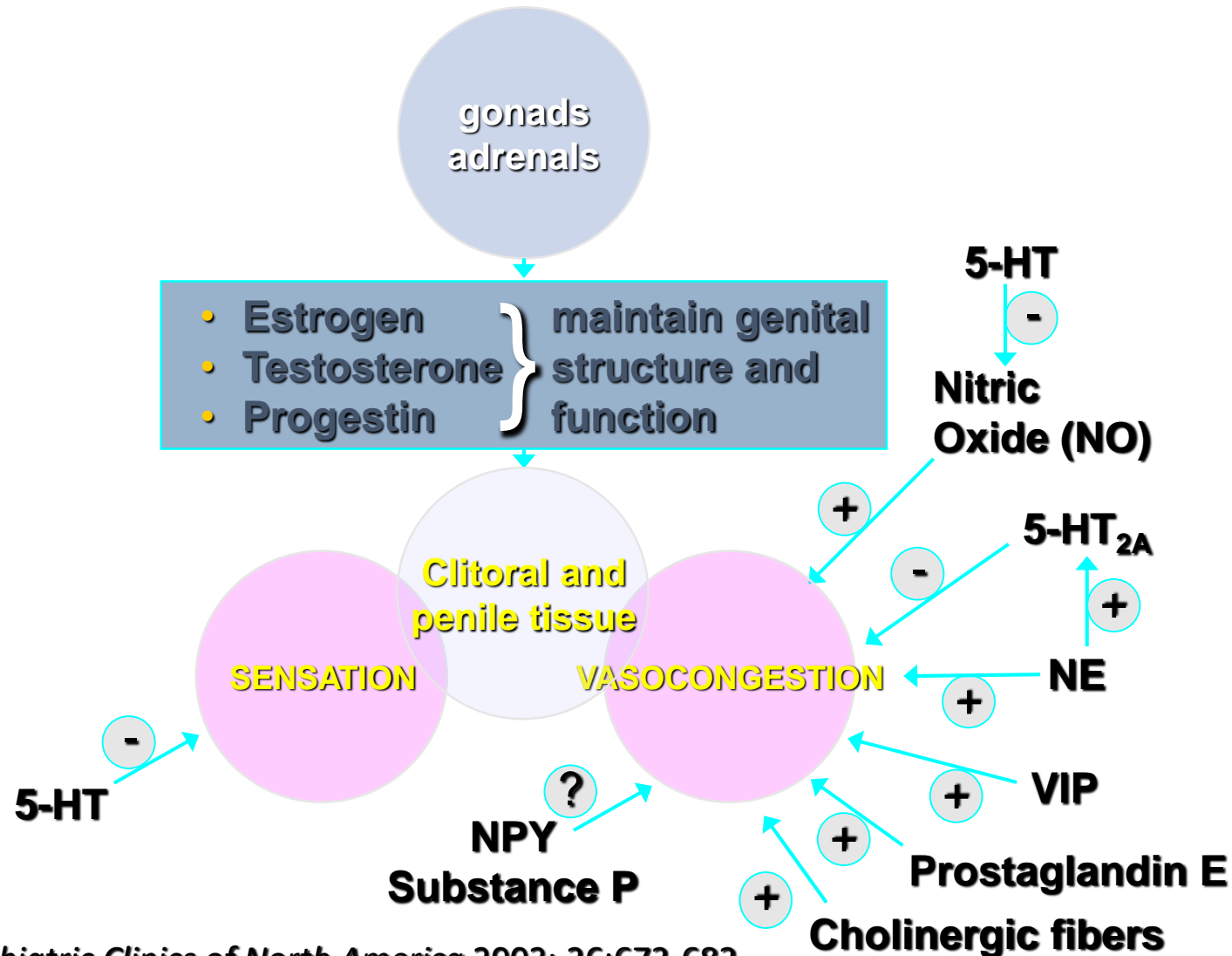
- The reward of intense pleasure for acceptance of the danger of coitus with its possibility of pregnancy (and of possible death in childbirth)
- To end coitus
- For resolving pelvic congestion
- Orgasmic uterine contractions may create a possible sperm upsuck
- To create arousal in the male by felt vaginal contractions on the penis and cause ejaculation
- Because of the difficulty in attaining orgasm, orgasm acts as a Mr. Right indicator and aids the creation of a strong pair bond
- To release oxytocin which affects motility of the uterus and fallopian tubes and to induce bonding feelings and emotions
- To release ADH for the possible contraction of the uterine musculature and to inhibit urination and delay sperm losses

We must have 2 perspectives

- We look at the sexual body
 - History of diseases and treatment
 - Physical examination
 - Imaging (Ultrasound, MRI, ECG)
 - Laboratory (Hormones, Metabolic parameters)
- We look at the sexual mind
 - Biographic history (major life events) and sexual history
 - Questions (interview, questionnaires)
 - Scenic, interactive information

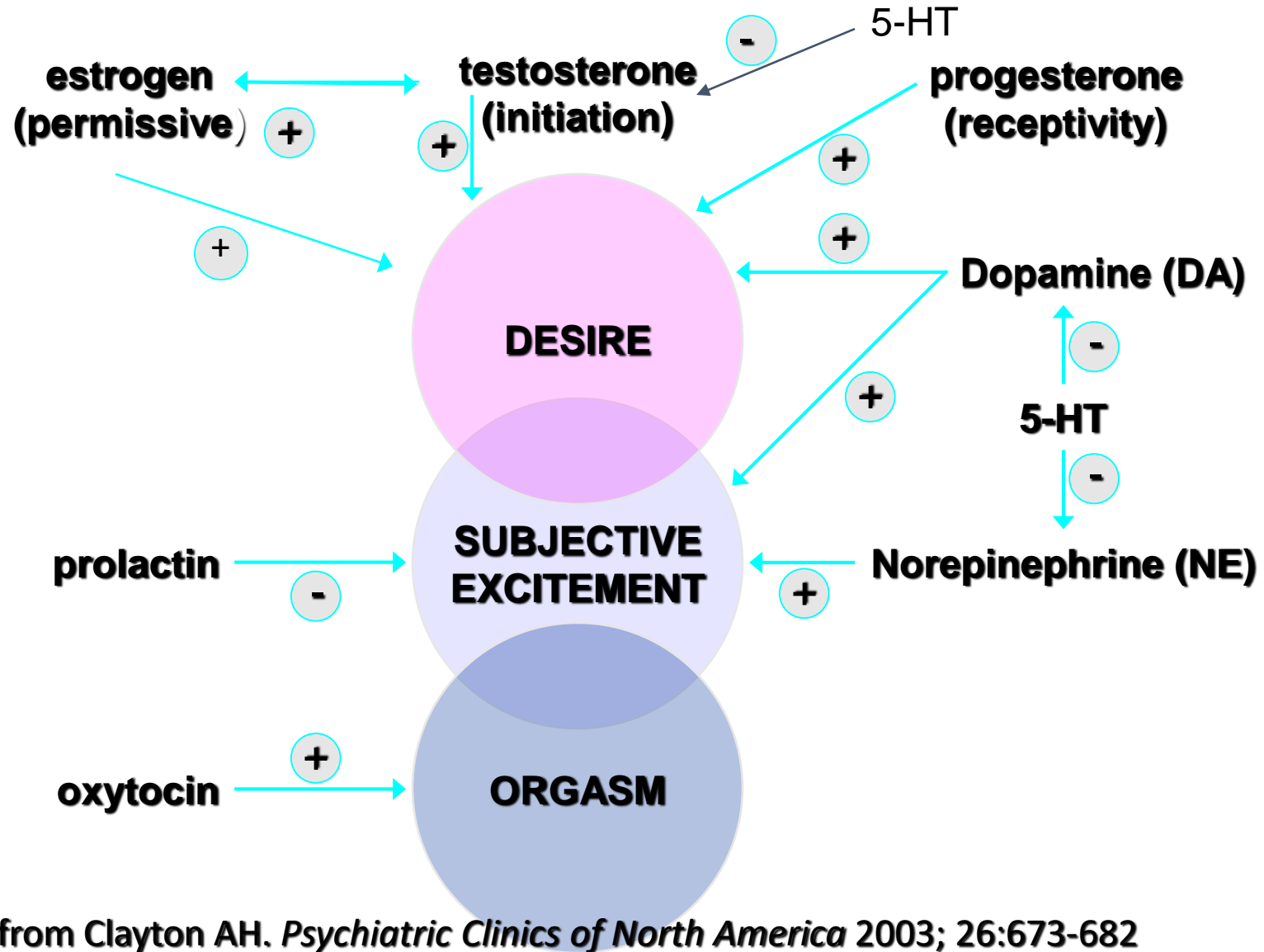


Hormones and neurotransmitters and Female Sexual Function - Peripheral effects



Hormones and Female Sexual Function

Central effects



Modified from Clayton AH. *Psychiatric Clinics of North America* 2003; 26:673-682

Psychosocial Factors having a positive or negative impact on sexual health /Individual Factors

Caring and supporting
early development

Sexual education

Self developed sexual
script

Stable body image

Satisfying self
confirming experiences

Conflict resolution capacity
Sexual communication skills

Coping with changes

**I know myself
what I like
what I want**

Early neglect

**Abuse
Traumatization**

**Lack of knowledge
and sexual
education**

**Insecure
negative sexual
script**

**Performance
Anxiety**

Psychosocial Factors having a positive or negative impact on sexual health /Relationship Factors

Good communication
about needs (yes/no)

Shared values and aims

Shared life
experience
Attachment

Sexual autonomy and
identity

Conflict resolution capacity
Sexual communication skills

Coping with changes

**We
Can listen,
talk,
understand
and respect
and love each
other
Find
compromise**

**Lack of communication,
Denial Avoidance**

**Loss of trust
Harm experienced**

**Lack of knowledge
and sexual
education in both**

**Loss of
attractiveness.
stimulation**

**Difference in
personal
development**

We must have 2 perspectives

- We look at the sexual body
 - Surgery
 - Drugs
 - Physiotherapy



Change the body
(structure, function,
regulation) from outside

- We look at the sexual person
 - Different forms of Psychotherapy
 - Individual and couple Therapy



Change the mind
(Thoughts, feelings,
behavior) from inside

We must have 2 perspectives

- We look at the sexual body

- Surgery
- Drugs
- Physiotherapy



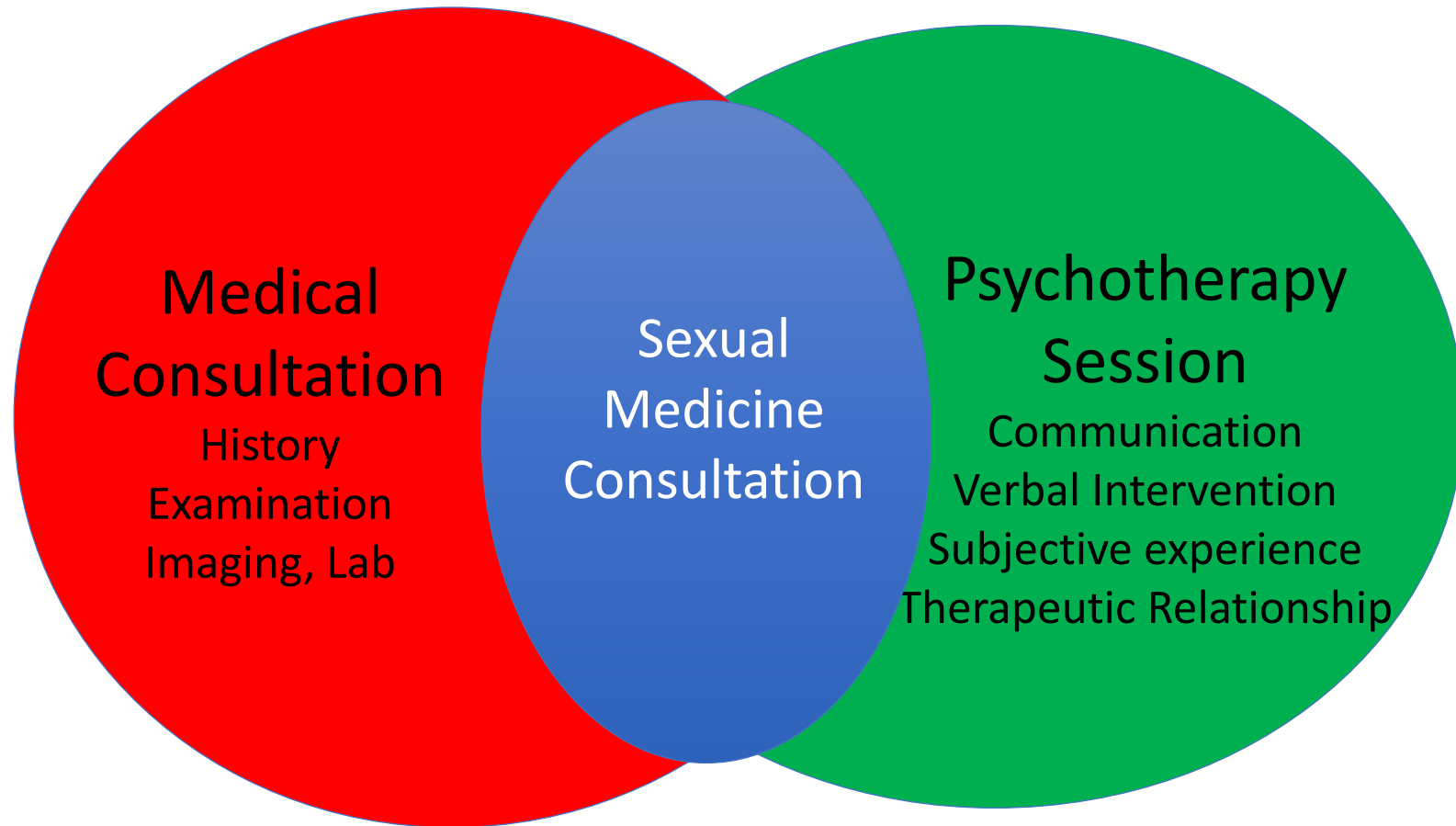
Therapist uses a tool on
the body and the patient
is a passive recipient
Expert model

- We look at the sexual person
 - Different forms of Psychotherapy
 - Individual and couple Therapy

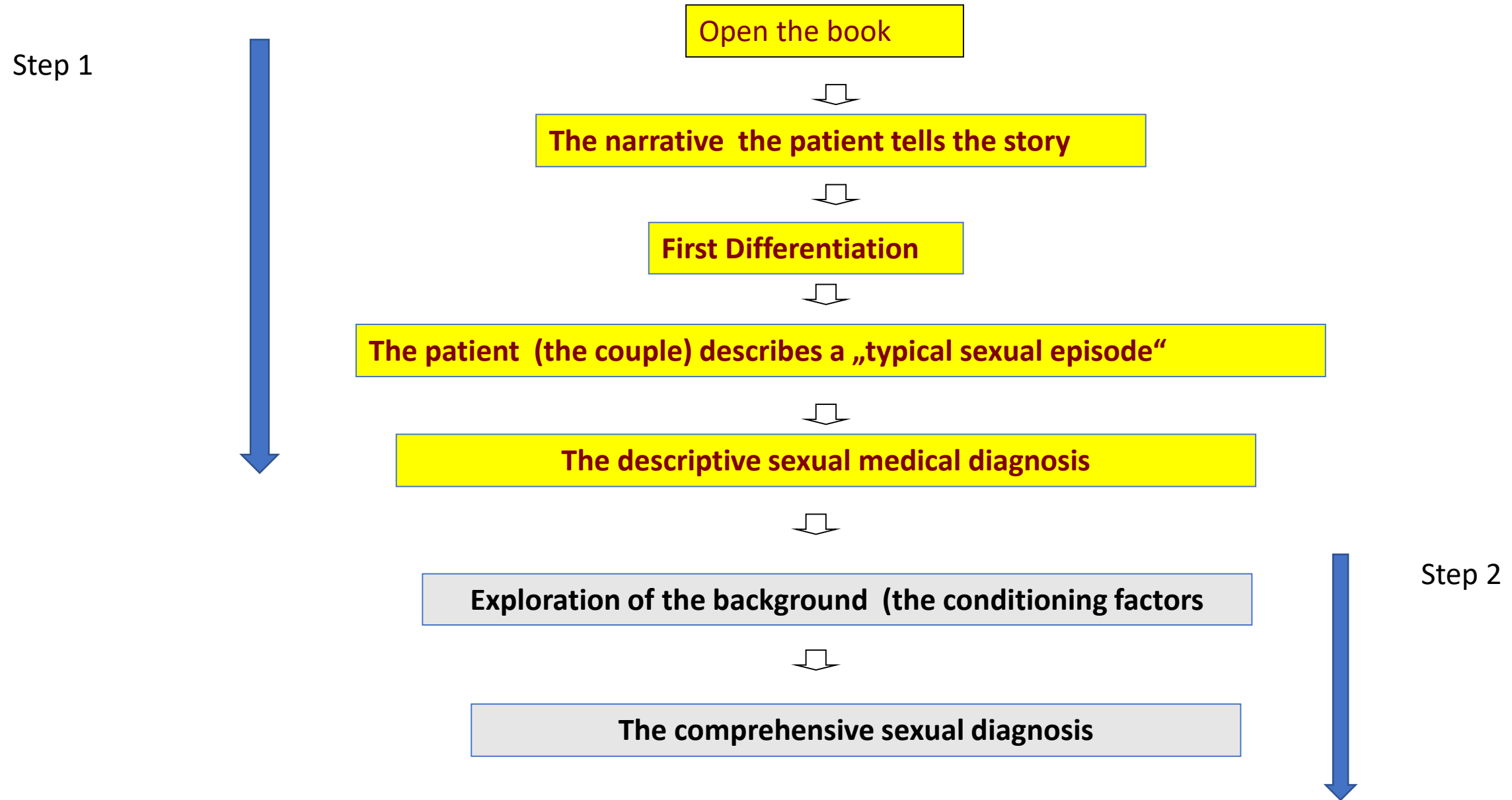


The therapist helps the
patient to understand and
learn
Teacher, Coach model

How to put this into practice



The diagnostic process – a dialogue



The Challenge of Talking About Sex

- The physician-patient discussion about sexual problems is very different from the one about (for example) blood pressure:
 - It can be uncomfortable for both physician and patient
 - No learned example of an 'ideal' conversation
 - Lack of clarity regarding definition, assessment and objective measures
- The challenge of talking appropriately with patients about sex needs to be met because sexual problems:
 - Are highly prevalent
 - May affect overall well-being & self-image more than other conditions
- It can be a relief to patients when they understand their sexual problems are common
- It is the responsibility of the physician to initiate the conversation

Initiating The Sexual Conversation

- Don't be too focused on finding a solution during the first visit; sexual problems can be complex
- Don't think that talking about sexual health problems needs more time than talking about other health problems
- Don't put yourself or the woman under time pressure, it's better to arrange a second visit

An example:

Q: "By the way, I just wanted to mention that if you find yourself having any sexual problems at any point, don't be afraid to tell me."

A: "Well...yes...I do actually have a problem."

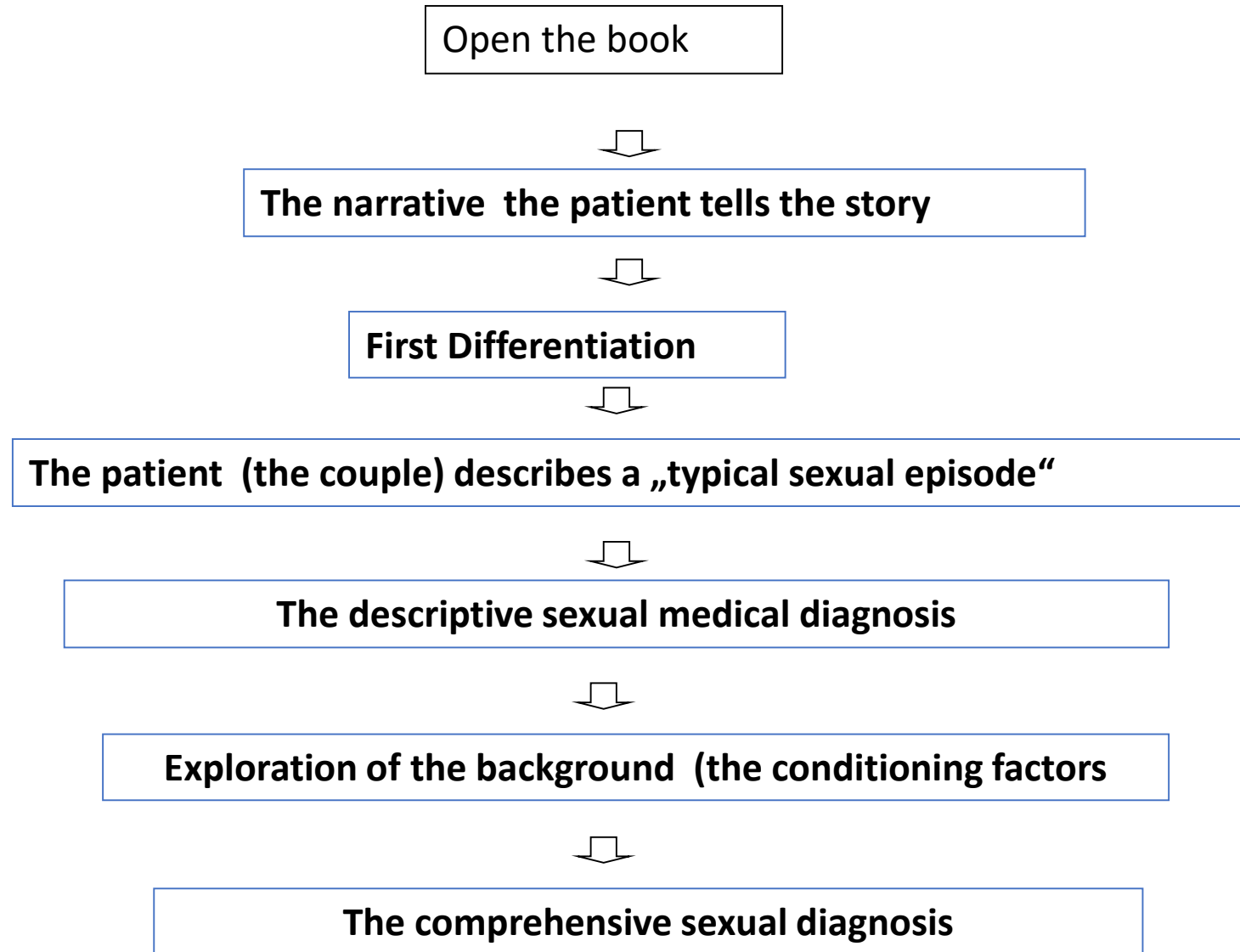
Q: "OK then, tell me about it."

Examples of Screening Questions for Sexual Disorders

- **Sexual Desire Disorder:**
“Have you noticed any change in your desire for sex?”
- **Sexual Arousal Disorder:**
“Have you noticed any change in your ability to get sexually excited?”
- **Orgasmic Disorder:**
“What about your orgasm experiences?”
- **Sexual Pain Disorder:**
“Is anything ever painful with sex?”

All of these questions need to be followed with the question:
“Are you distressed/bothered about this”

The diagnostic process



The Narrative

Listen actively, open questions:

You lost your interest, tell me more about it

*You do not feel aroused – how do you realize
that you are aroused*

First Differentiation

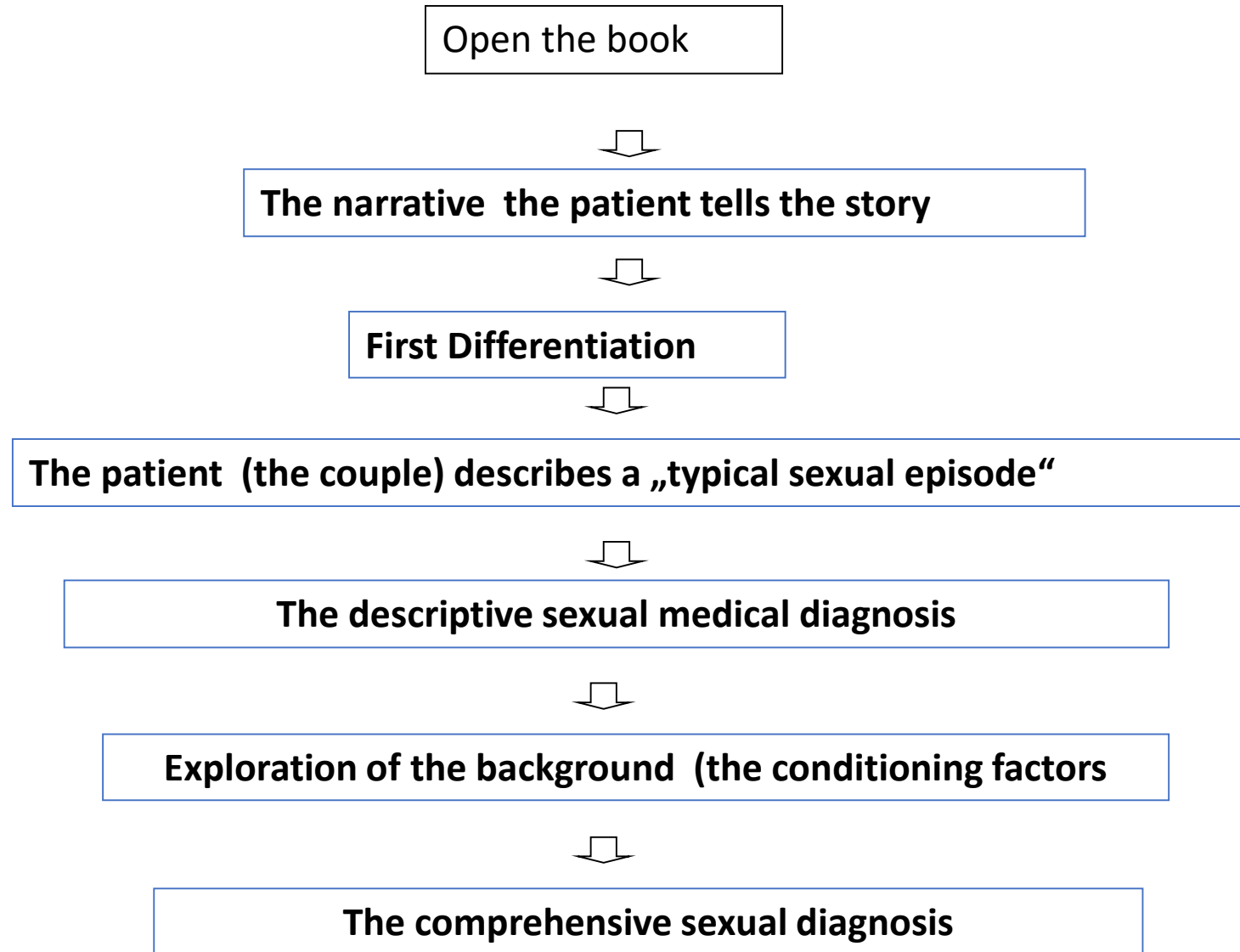
Directed questions:

- *Since when do you have this problem?*
- *Was there a time when you were enjoying your sexuality?*
- *When was that ?*
- *Do you think that the actual problem has something to do with your partner, his appearance or his behavior towards you?*
- *Do you think it has something to do with specific situations like family or professional stress etc. ?*

The typical episode

- Please remember the last time when you were sexually active. (masturbation, intercourse) What happened ?
- Who started the activity ? How did you react ? What thoughts did you have ? What were your feelings ?

The diagnostic process



Classification of Sexual Disorders*

- Sexual Desire Disorders
 - Hypoactive sexual desire disorder
 - Sexual aversion disorder
- Sexual Arousal Disorder
- Orgasmic Disorder
- Sexual Pain Disorders
 - Dyspareunia
 - Vaginismus

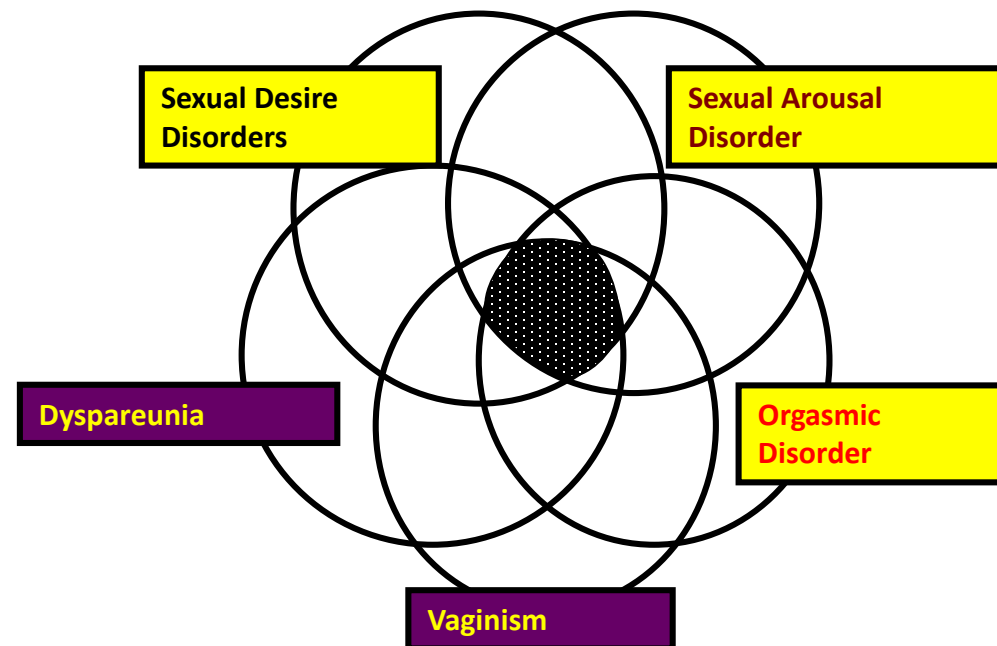
*This classification has been selected for practical purposes as it is the most simple

Sexual Dysfunctions are Comorbid

Comorbidity is frequent between:

- Different sexual dysfunctions
- Different sexual dysfunctions and medical conditions
- Different sexual dysfunctions and relationship problems

It is clinically important to assess which component is primary and how it evolved over time



Considerations in The Diagnosis of Sexual Disorders

Clinical diagnosis of all FSD sub-types should take into consideration the following information:

Duration

- Lifelong
- Acquired

Onset

- Gradual
- Rapid

Context

- Generalised
- Situational

The descriptive diagnosis of FSD

Global or
situational

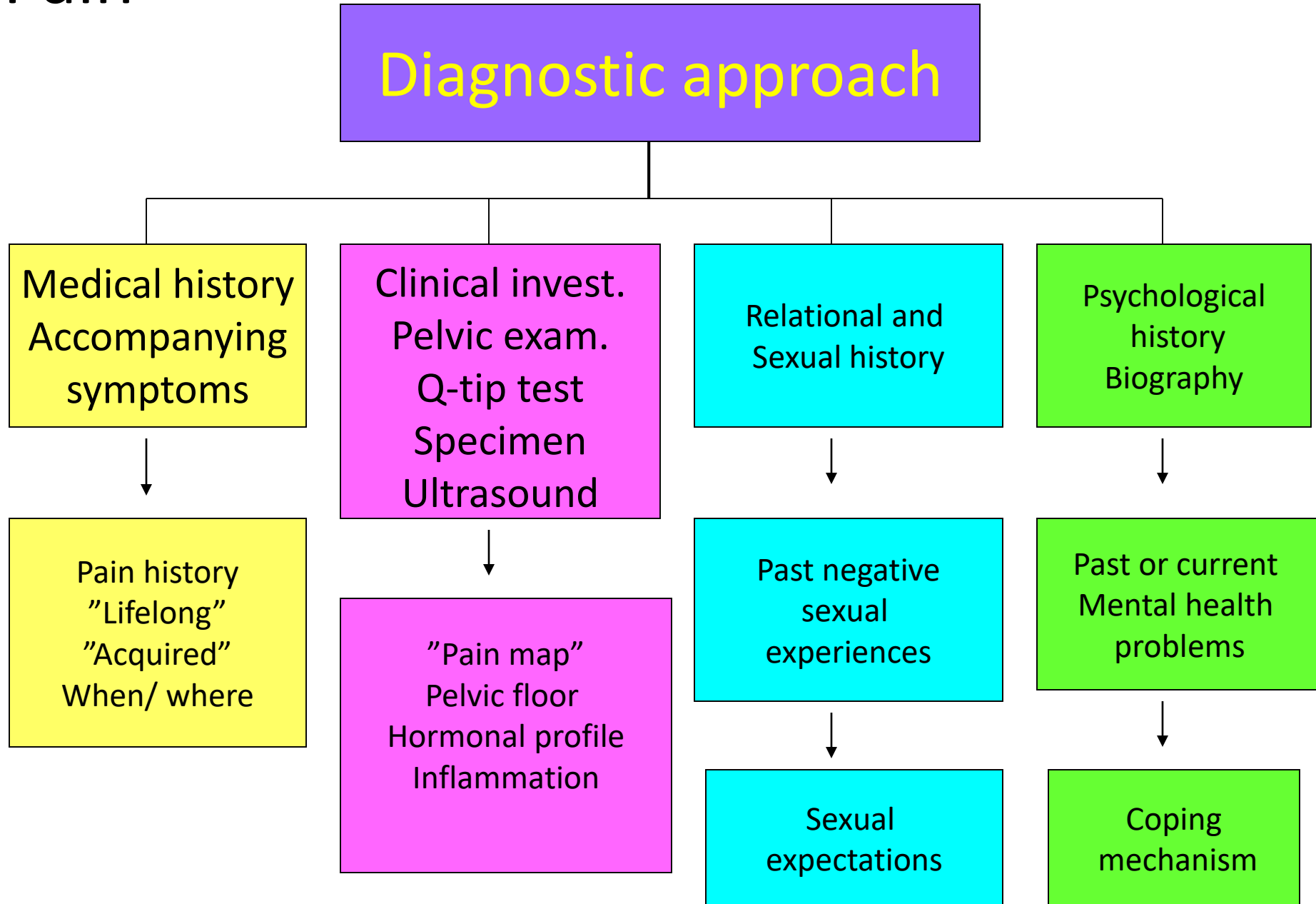
- **Desire Disorder**
 - Lack of desire causing distress
 - Sexual aversion
- **Arousal Disorder**
 - Lubrication
 - Mental
- **Orgasmic Disorder**
- **Sexual pain Disorder**
 - Dyspareunia
 - Vaginism

Primary or
secondary

Slowly
developping
versus abrupt
beginning

Single or
combined
disorder

Sexual Pain



Exploration of the background- Conditioning factors

Biomedical

Psychosocial

Diseases
and Drugs

Hormones

Individual
psychological
factors

Relationship
Factors

Sociocultural
economic
factors

How do I assess medical factors

- A detailed medical and sexual history
 - Past and present assessment of sexual desire, arousal, orgasm and pain
 - Psychosocial context
 - Diseases & drugs
- Physical examination
 - Vulva
 - Clitoris
 - Vagina
 - Pelvic floor
 - Pelvic organs

- . Laboratory testing
- . Specialised diagnostic testing

How do I assess individual psychological factors ?

An example:

Q: “How important is sexual happiness in your life?”

Q: “Did you have any negative experience that may impact your sexual life, for example neglect as a child, restricted education, unwanted pregnancy, abandonment...?”

Q: “How do you feel about your body (any body image concern)?”

Q: “Have you had any negative sexual experience, such as harassment or sexual abuse?”

Q: “Do you feel comfortable enough to talk about these experiences?”

How do I assess relationship factors ?

An example:

Q: “Do you have a stable relationship?”

Q: “Does your partner have any health or sexual problems?”

Q: “In your opinion, is the quality of your relationship impacting your sexual life?”

If the answer is YES:

Q: “Do you still have a desire to have sex with your partner?”

Causes of Hypoactive Sexual Desire Disorder (HSDD)

Major Biological Causes

- Hormones
 - Low androgens (e.g. oophorectomy)
 - Hypothyroidism
- Psychiatric disorders
- Medications
 - SSRI
 - Anti-hormones
 - Anti-hypertensive
 - Chemotherapy
- Chronic diseases and related treatment
- Alcohol and recreational drugs (opiates)

Psychological Causes

- Relationship issues
 - Communication problems
 - Partner Conflict
 - Loss of attractiveness
- Intrapersonal issues
 - Early life experiences Abuse, Neglect
 - Sexual Education

Sociocultural Causes

- Poverty/Low income
- Working conditions
- Sexual norms

Secondary to or co-morbid with any other sexual disorder (self or partner)

There may be overlap and interaction between all these factors

Causes of Sexual Arousal Disorder (SAD)

Major Biological Causes¹

- Sex hormone deficiency
- Diabetes/Vascular factors
- Smoking
- Pelvic floor disorders
- Lower urinary tract symptoms (LUTS)
- Pelvic surgery
- Neurological diseases
- Drugs: Anti-hormones, chemotherapy

Psychological Causes

- Relationship issues
 - Communication problems
 - Partner Conflict
 - Loss of attractiveness
- Intrapersonal issues
 - Early life experiences Abuse, Neglect
 - Sexual Education

Sociocultural Causes

- Poverty/Low income
- Working conditions
- Sexual norms

¹For clinical purposes the biological focus is on factors affecting genital arousal

Causes of Orgasmic Disorder

Major Biological Causes

- Pelvic floor disorder
- Pelvic surgery
- Neurological diseases
- Medication (SSRI and other antidepressants)

Psychological Causes

- Relationship issues
 - Communication problems
 - Partner Conflict
 - Loss of attractiveness
- Intrapersonal issues
 - Early life experiences Abuse, Neglect
 - Sexual Education

Sociocultural Causes

- Sexual norms
- Lack of erotic skills
- Misbeliefs

Causes of Sexual Pain Disorders

Major Biological Causes

- Sex Hormone deficiency
- Vulvovaginal dystrophy
- Vulvovaginitis
- Hyperactive Pelvic floor
- Vulvodynia / Vulvovestibulitis
- Post surgery / Scarring
- Dermatitis
- Endometriosis
- Pelvic Inflammatory disease
- Chronic pelvic pain

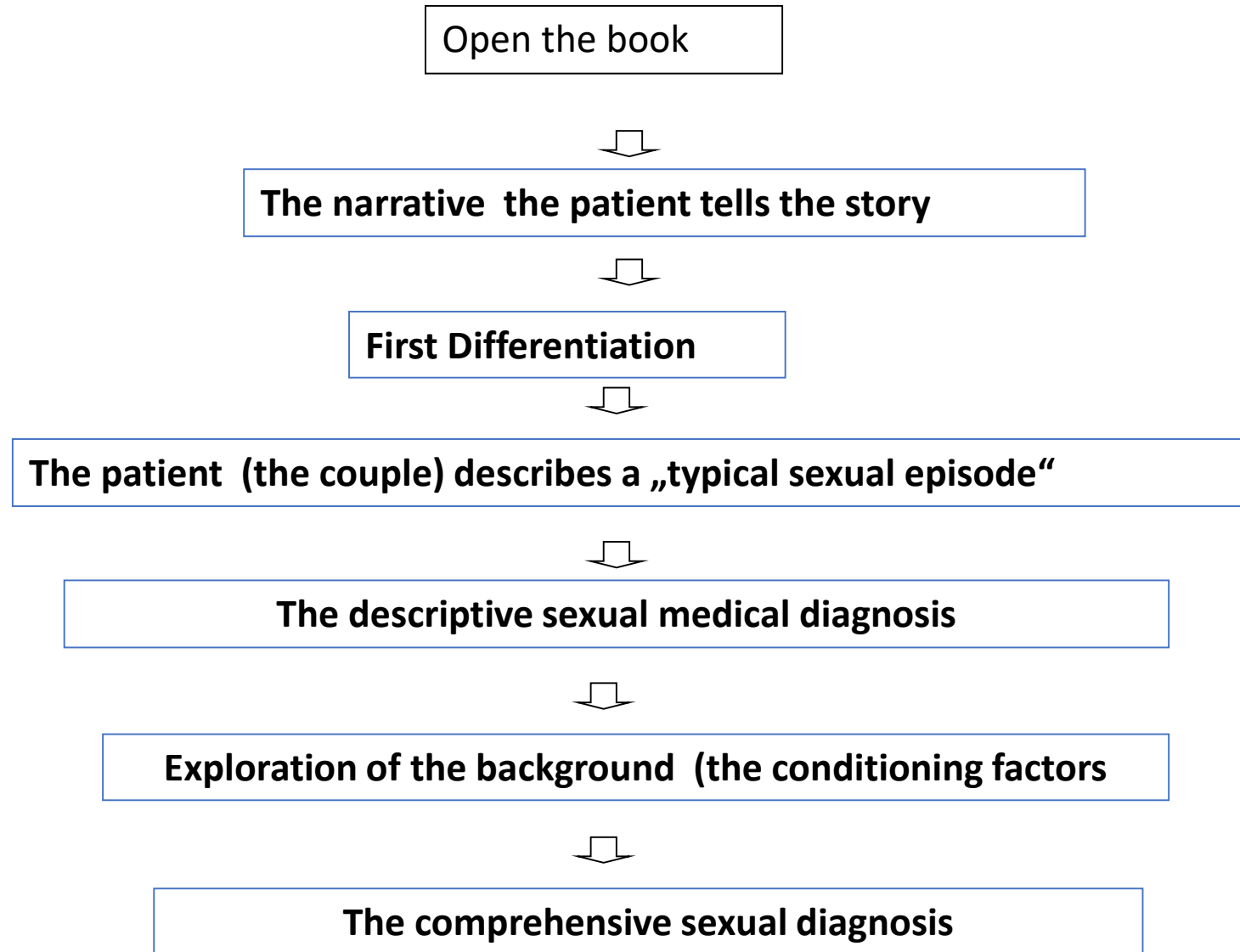
Psychological Causes

- Relationship issues
 - Communication problems
 - Partner Conflict
 - Loss of attractiveness
- Intrapersonal issues
 - Early life experiences Abuse, Neglect
 - Sexual Education

Sociocultural Causes

- Sexual norms
- Lack of erotic skills
- Culturally based genital modifications (mutilation)

The diagnostic process



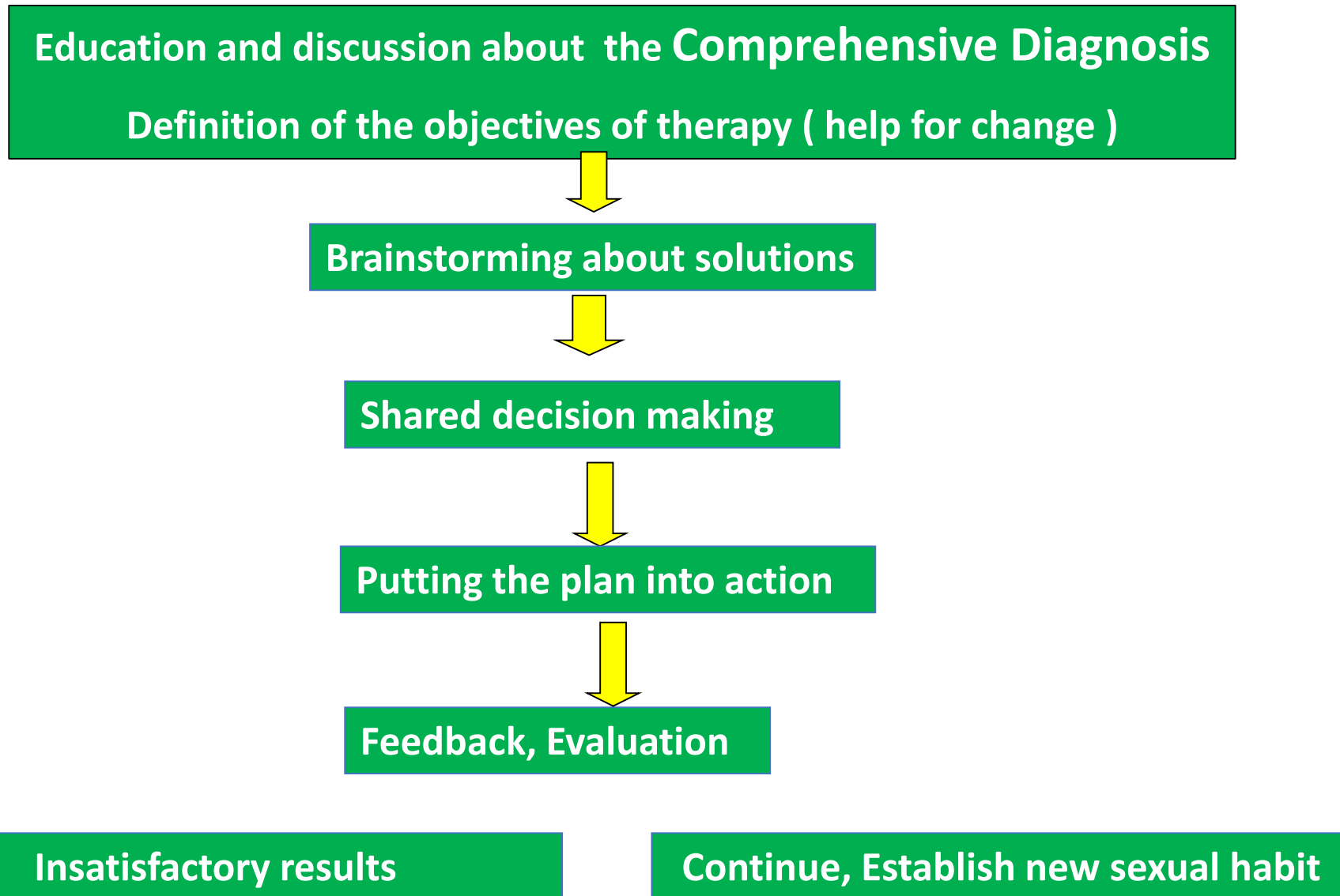
The comprehensive explanatory diagnosis

	Biomedical		Psychological		Sociocultural
	Chronic diseases and Drugs	Hormonal factors	Intra-individual	Inter-personal	
Predisposing Distant Indirect					
Precipitating Factors Trigger					
Maintaining Proximate Direct					

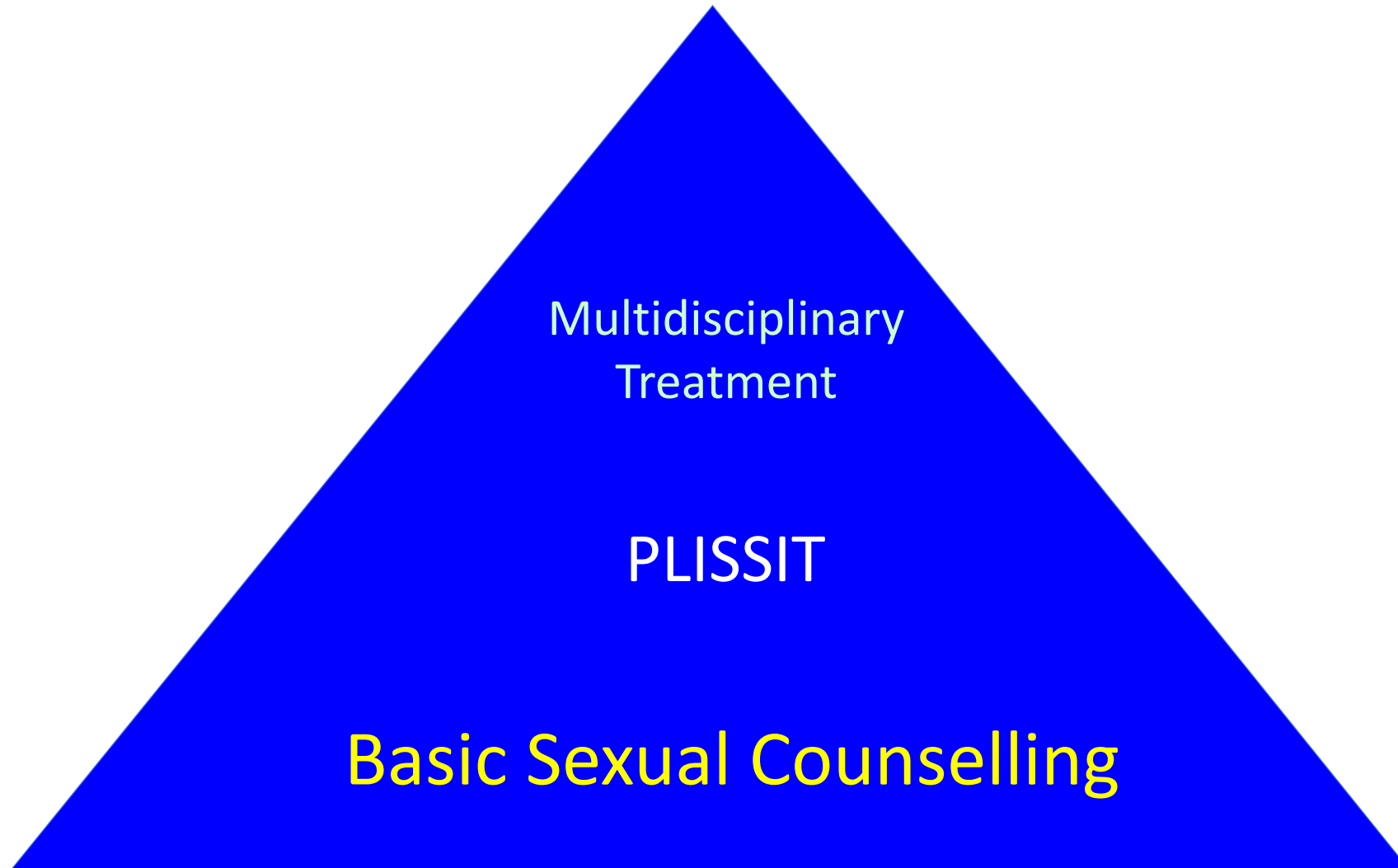
How does the woman herself rate the importance of these factors in contributing to her low desire ?

Go back to
listening

The therapeutic process



The “Sexual Medicine Toolbox”



Basic Sexual Counselling

The Integral part of all therapeutic approaches

- Give the patient opportunity to talk about her own sexuality
- Listen actively
 - Patient feels accepted and understood
 - Emotional relief
- Inform about the reality of human sexuality
 - Put the variety of personal experiences into perspective
 - Frequency of problems
 - Differences between female and male sexuality
 - Knowledge
 - Empowerment
- Dispel myths about male and female sexuality

The “Sexual Medicine Toolbox”

Multidisciplinary Treatment

Hormones

Estrogen, Testosterone,
DHEA

Drugs

Vasodilators
Centrally acting
drugs

Physical Therapy

Operations
Devices

Basic Sexual
Counseling

Individual Sex
Therapy

Body awareness
Focal Therapy

Couple Sex
Therapy

Sensate Focus
Systemic Therapy

Physiotherapy

Typical “Myths”

- A healthy woman always has an orgasm
- Sex must lead to orgasm
- Masturbation is only for singles
- No sex leads to health problems
- A man always wants sex and can always have sex
- Passion equals love
- Sex is fulfilling only when spontaneous
- Sex needs no help
- Women want less sex than men
- Women always need long foreplay
- Pornography / Erotic material is only for men (if at all)
- Menopausal women are not interested in sex any more
- Etc.

Pharmacological / Hormonal treatment approaches

- Oestrogen therapy
- Oestrogen + Testosterone therapy
- Tibolone
- DHEA

Sex hormones and female sexual function

- Sex steroids increase the sensitivity of an individual towards sexual stimuli
- Oestrogens, androgens and progestins modify the “motivational” state towards or against sexual activity
- The decline in sexual function at menopause is associated with oestradiol levels
- Oestrogens seem to play an important role in the process of arousal
- T-levels decrease from the 20s onwards, stabilizing around menopause
- Testosterone seem to play an important part in sexual desire, arousal and receptivity towards sexual stimuli
- The interplay between the various sex steroids appears to be important
- The distinct effects of oestrogens and androgens on desire are still not completely understood

Hormonal treatment – Oestrogen I

- The primary treatment for general menopausal and sexual symptoms (i.e. vaginal dryness and atrophy) is either systemic and/or local oestrogen depending on symptoms
- Optimise hormonal administration with oestrogen (and progestin in women with intact uterus; be aware that the different progestins may have different actions)*
- Oestrogen alone may not be sufficient to treat FSD

*According to European and national recommendations and guidelines

Hormonal treatment – Oestrogen

- Oestrogens are important for the maintenance and function of the vaginal epithelium, stromal cells, smooth muscles and nerve trophism
 - Genital sexual symptoms are more frequent in women with Oestradiol levels < 50 pg/ml
- Oestrogens have vasodilatory effects and increase vaginal, clitoral and urethral blood flow via nitric oxide synthase (NOS) and vasoactive intestinal polypeptide (VIP) pathways leading to genital congestion and vaginal lubrication
- Oestrogens modulate sensory thresholds

RCTs* Assessing Effect of Systemic Oestrogen on Sexual Function in Naturally Menopausal Women

Sherwin BB, *et al.* (1991) *JCEM* **72**: 336–343

Wiklund I, *et al.* (1993) *Am J Obstet Gynecol* **168** (3Pt1): 824–830

Nathorst-Boos J, *et al.* (1993) *Obstet Gyencol Scand* **72**: 656–660

Castelo-Branco C, *et al.* (2000) *Maturitas* 34: 161–168

Hays J, *et al* (2003) *N Engl J Med.* 348: 1839-54

The large majority of studies show positive effects of estrogen therapy on different aspects of female sexual function and sexual satisfaction

Transdermal Testosterone Patch Program: Comprehensive & Robust

- 9 Pharmacokinetic Studies
 - Range of doses/dosing durations
- 3 Instrument Validation Studies
 - Followed by a Confirmatory Validation Study
- 3 Phase II studies
 - Dose-ranging, different routes of E administration
- 6 Phase III studies: well-controlled / comparable
 - 2 in surgical menopausal women (SM)
 - 2 in natural menopausal women (NM)
 - 1 Testosterone-only (SM & NM, no oestrogen)
 - 1 in natural menopausal women, transdermal oestrogen



Alcohol-free, translucent, matrix patch

Twice-a-week application to abdomen

Contains 8.4 mg testosterone

Delivers 300 mcg/day testosterone

Clinical Trials

Testosterone Therapy in Women with HSDD

**Surgical
Menopause plus
Estrogen/Prog**

**Natural Menopause
plus Estrogen/Prog**

+

Shifren JL et al. N Engl J Med 2000;343(10):682-8.

Buster JE et al . Obstet Gynecol 2005;105(5 Pt 1):944-52.

Simon J et al. J Clin Endocrinol Metab 2005;90(9):5226-33

Shifren JL et al. Menopause 2006;13(5):770-9.

Braunstein et al.. Arch Intern Med 2005 ;165(14):1582-9.

Davis SR et al. Menopause 2006;13(3):387-96.

Davis SR; APHRODITE Study Team. N Engl J Med. 2008

Nov 6;359(19):2005-17.

+

+

+

**Surgical and Natural
Menopause without
E/P**

**Premenopausal
Women**

Hormonal treatment

Tibolone

- Tibolone is a synthetic steroid
- It has oestrogenic, androgenic and progestogenic properties
- Tibolone is indicated for the relief of climacteric symptoms and prevention of osteoporosis in postmenopausal women
- Data suggest a positive effect on sexual symptoms comparable to hormonal therapy
- Good overall tolerability with low incidence of vaginal bleeding and breast tenderness
- Current available data on breast cancer risk are inconclusive

Hormonal Therapy – DHEA

- It is an androgen
- A pro-hormone converted to a variety of biologically active steroids
- The specific action and safety of the final metabolites have not been clarified yet
- Conflicting data exists on the specific role of DHEA on sexual function
- DHEA is a non-licensed substance. Caution should be exercised, the content is not always adequately quality controlled (substance and dosage)

The patient should be asked if she is taking DHEA, since concomitant use interferes with hormonal treatment

Blood vessel dilators under investigation

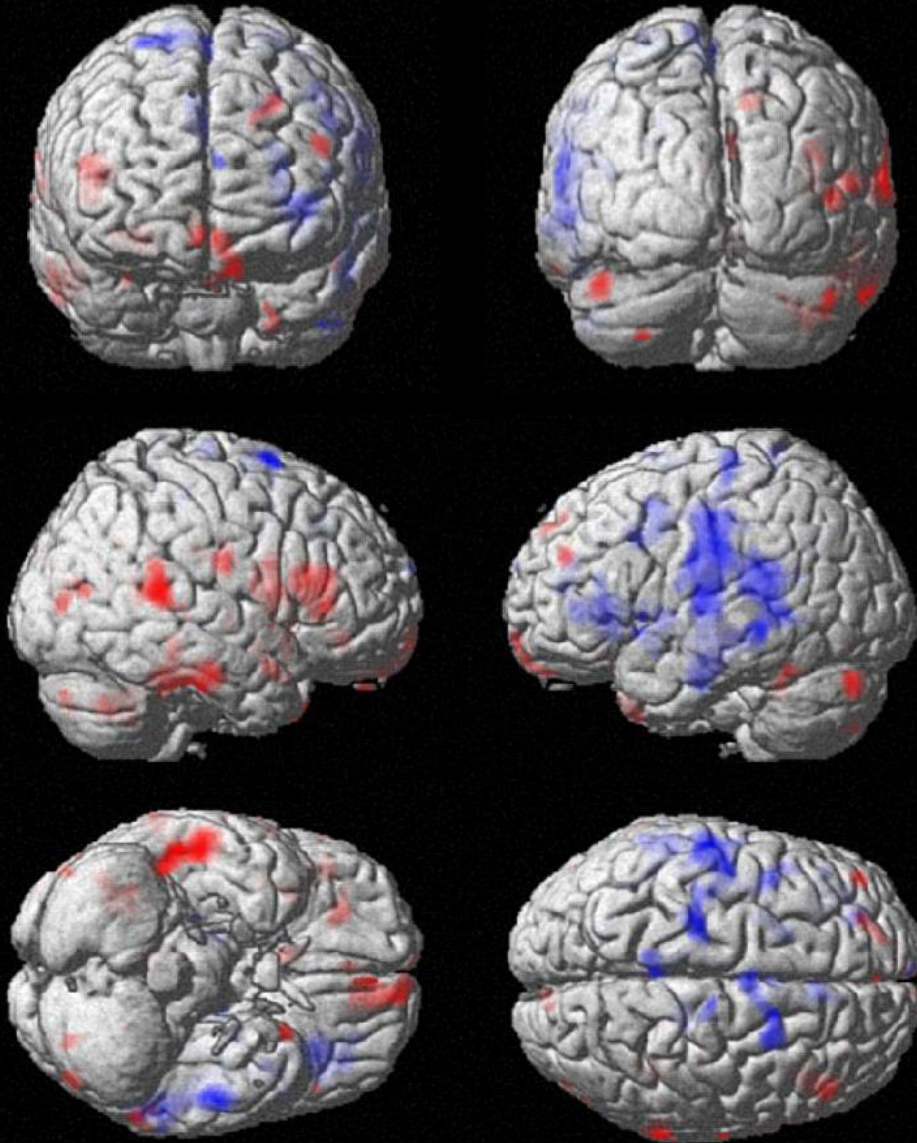
- **Prostaglandin E1 (PGE1) is a naturally occurring vasodilating agent**
 - **A topical formulation containing a synthetic version of PGE1 is under investigation**
- **Phentolamine is a competitive, nonselective alpha adrenergic receptor antagonist. It promotes vasodilation.**
 - **More data is needed on the efficacy and safety of an oral preparation**
- **A feminine massage oil (various, natural ingredients) is currently available. Clinical evidence is based on a study involving 20 patients.**

Centrally acting drugs

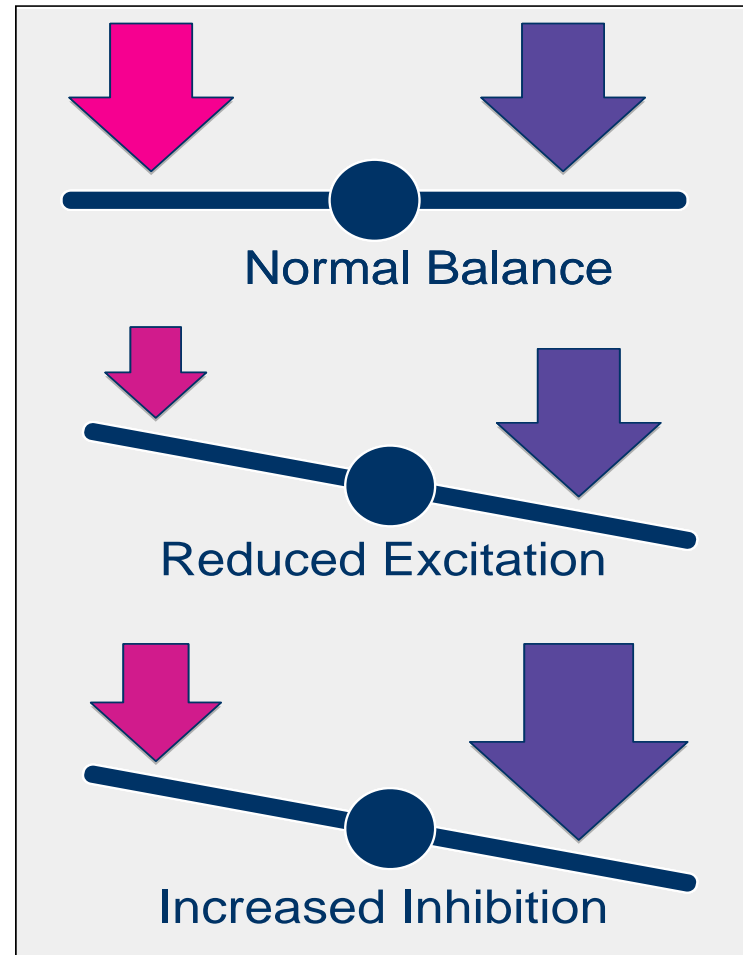
- Bupropion
 - Increases arousability and responsiveness. Increases desire in women with major depression treated with SSRIs (Clayton 2004; Segraves 2004)
- Flibanserin
 - Increases sexual desire in prämenopausal women. Improvement in all domains of FSFI, SSE, and diary (Goldfischer, 2008 ISSM)

Brain and HSDD

Higher activation (red) and de-activation (blue)
in non-HSDD than in HSDD volunteers watching
erotic movies compared to neutral movies



Pathophysiology of low sexual desire seen in HSDD: Hypothesis

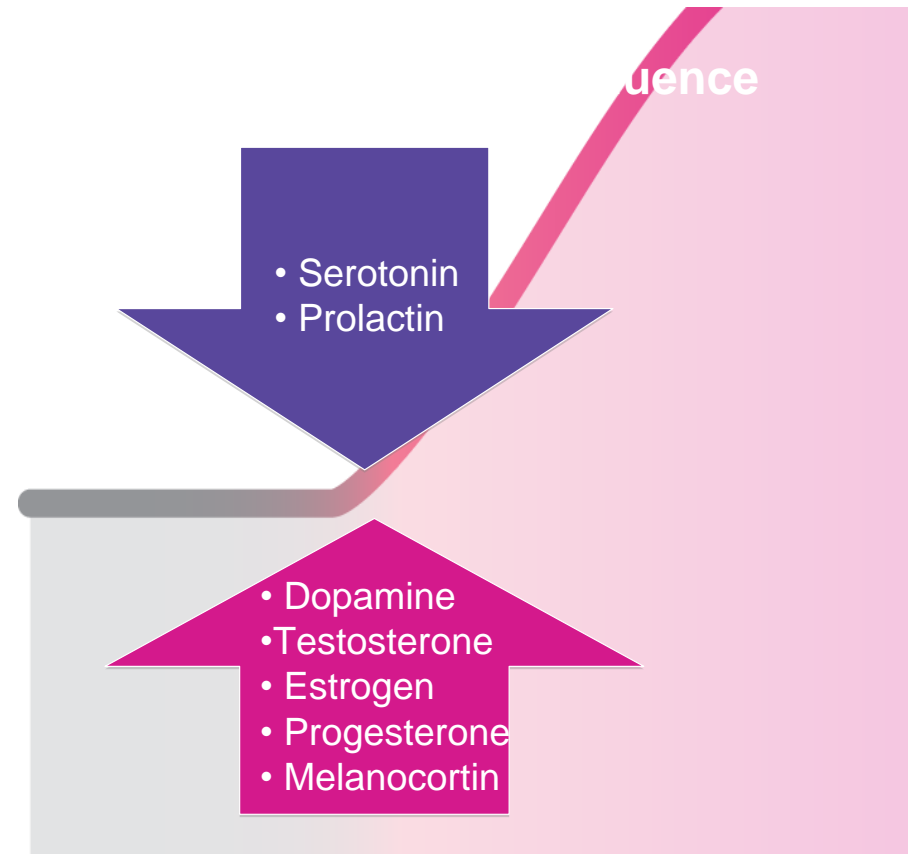


Female sexual desire: neurohormonal influence as the basis for pharmacological interventions

DESIRE

Neurohormonal

Influence

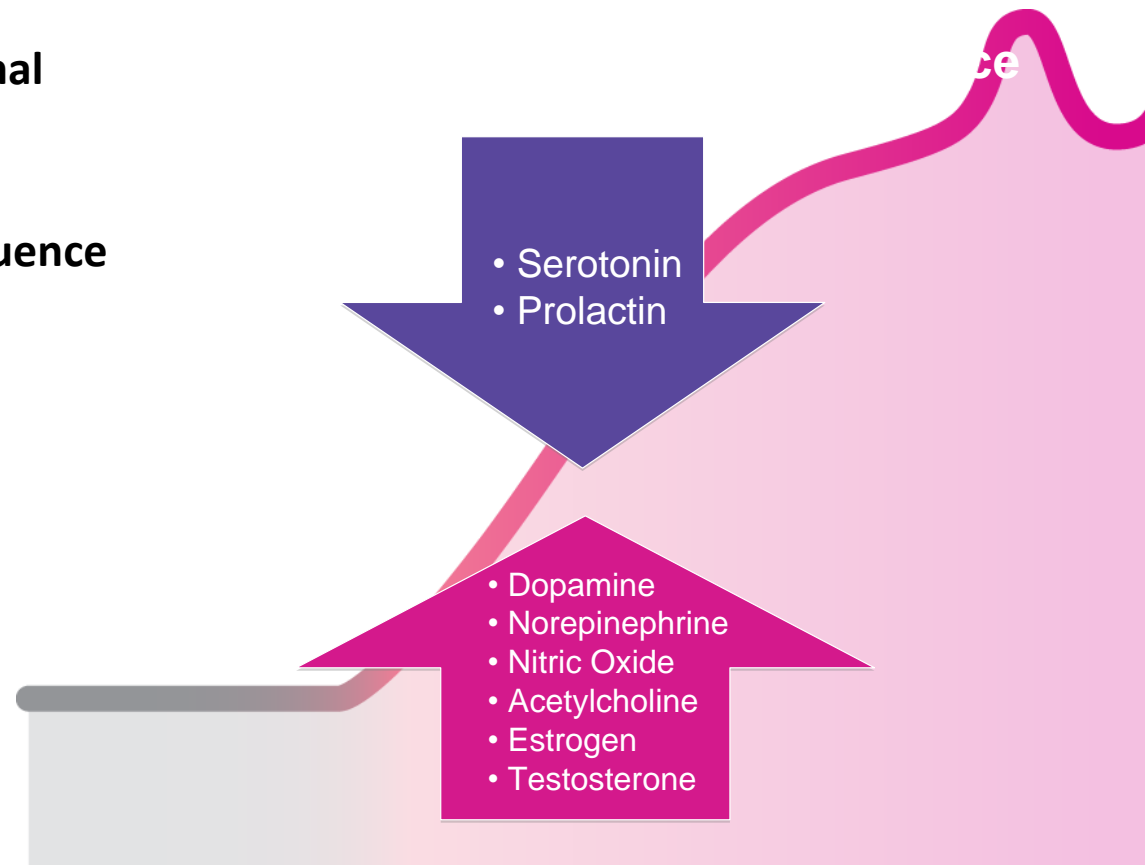


Female sexual desire: neurohormonal influence as the basis for pharmacological interventions

AROUSAL

Neurohormonal

Influence



Centrally acting drugs

- Drugs acting on central nervous dopaminergic and noradrenergic pathways
 - **Bupropion** – currently approved for smoking cessation and treatment of depression
 - Promising results in patients suffering from major depression and also non depressed patients
 - Ginzburg 2005
 - Clayton 2004

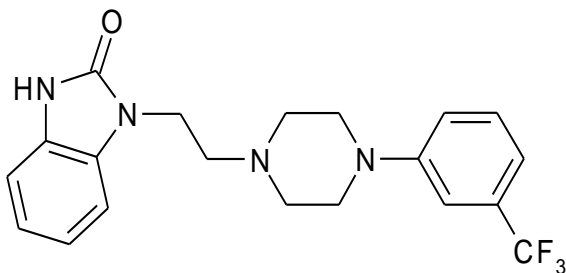
Centrally acting drugs

- Drugs acting on the Melatonin System
 - **Bremelanotide/PT-141** – MSH (Melatonin Stimulating Hormone) receptor agonist
- Bremelanotide is a cyclic hepta-peptide lactam analogue of alpha-melanocyte-stimulating hormone (alpha-MSH) that activates the melanocortin receptors MC3-R and MC4-R in the central nervous system.
- Originally, the peptide Melanotan II that bremelanotide was developed from was tested as a sunless tanning agent. In initial testing, Melanotan II did induce tanning but additionally caused sexual arousal and spontaneous erections as unexpected side effects in eight out of the ten original male volunteer test subjects. In clinical studies, bremelanotide has been shown to be effective in treating male sexual and erectile dysfunction as well as female sexual dysfunction.

Flibanserin: a brief history...

In 1992:

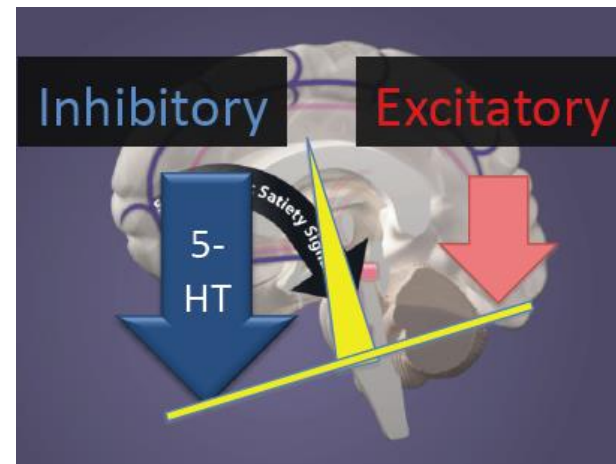
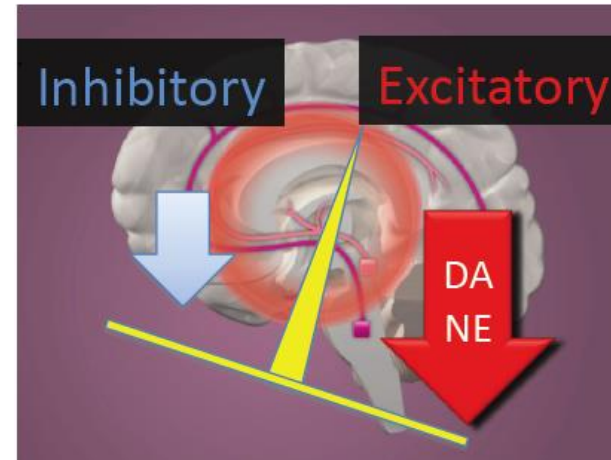
- BI initiated drug discovery for a combined 5-HT_{1A} agonist/5-HT_{2A} antagonist, produces BIMT 17 BS (flibanserin)



Systematic (IUPAC) name:
2H-Benzimidazol-2-one, 1,3-dihydro-1-[2-[4-[3-(tri-fluoromethyl)phenyl]-1-piperazinyl]ethyl]

How could Flibanserin work ?

- Balance between excitatory activity driven by DA (desire) and NE (arousal) and inhibitory activity driven by 5-HT (satiety) is necessary for a healthy sexual response.
- This balance may be disrupted in sexual dysfunction
- By selectively modulating these neurotransmitters in a regionally specific way, flibanserin may act to re-balance these systems in HSDD women



Flibanserin MOA – Key messages

- Flibanserin has two main pharmacological targets in the brain: post-synaptic 5-HT_{1A} receptors (agonism) and 5-HT_{2A} receptors (antagonism).
- Flibanserin administration leads to region-specific increases in the neurotransmitters dopamine and norepinephrine and decreases in serotonin
- The hypothesis of the mechanism of action of Flibanserin is that by modulating these neurotransmitters in selective brain areas flibanserin helps to restore a balance between inhibitory and excitatory factors leading to a healthy sexual response.

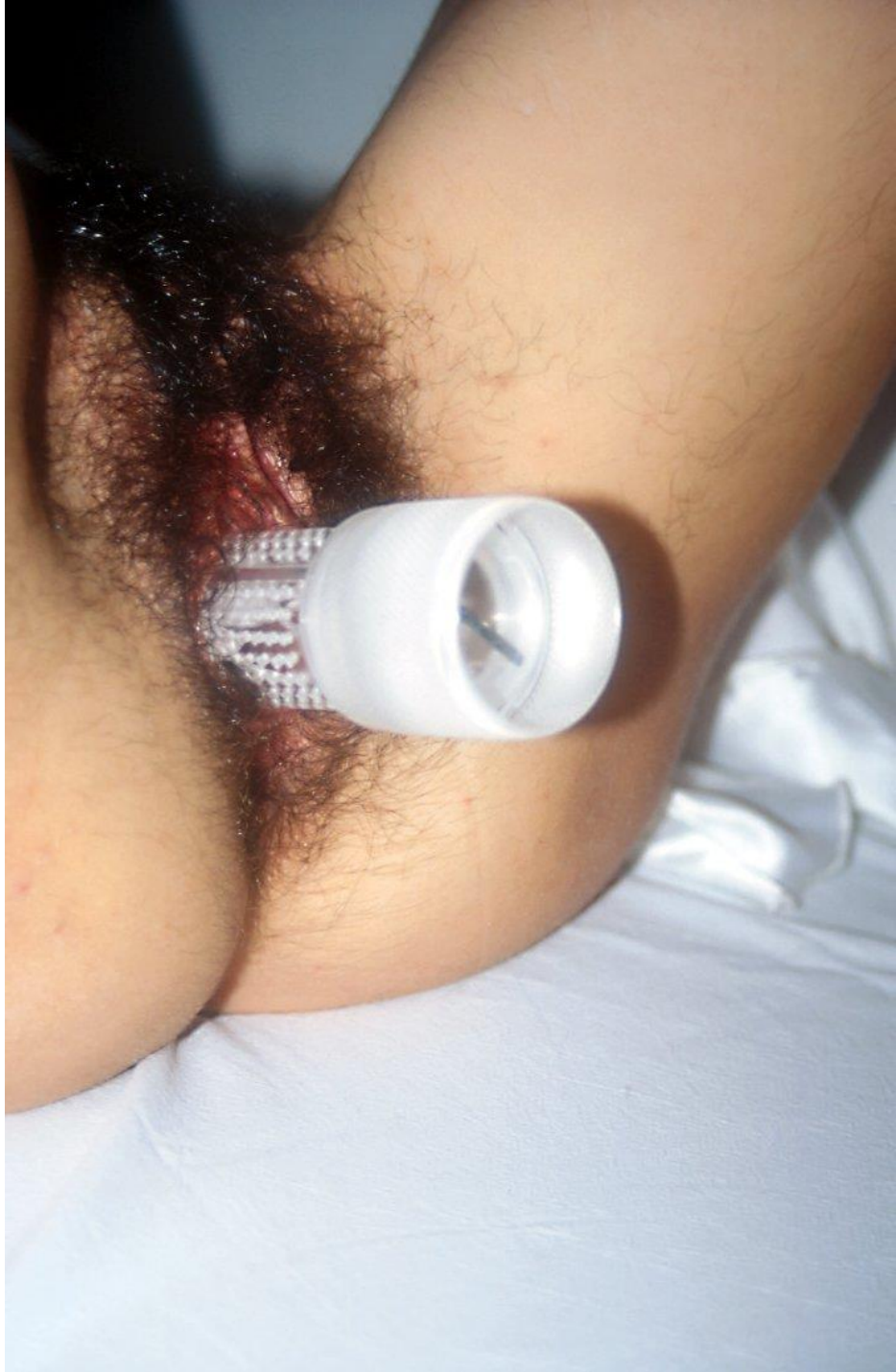


ZESTRA

(aceite vegetal)







Dilatators



Botox for vaginism

- First case study *by Brin*

Brin, Lancet 1997

- N=39 women
- standard cognitive-behavioral and medical treatment for vaginismus had failed
- electromyogram (EMG) recordings from the levator ani muscle showed hyperactivity at rest
- 63.2% of the patients completely recovered from vaginismus
- 15.4% still needed reinjections
- 15.4% had dropped out.

Bertolasi et al. Obstet Gynecol 2009

Surgery for patients with provoked vestibulodynia

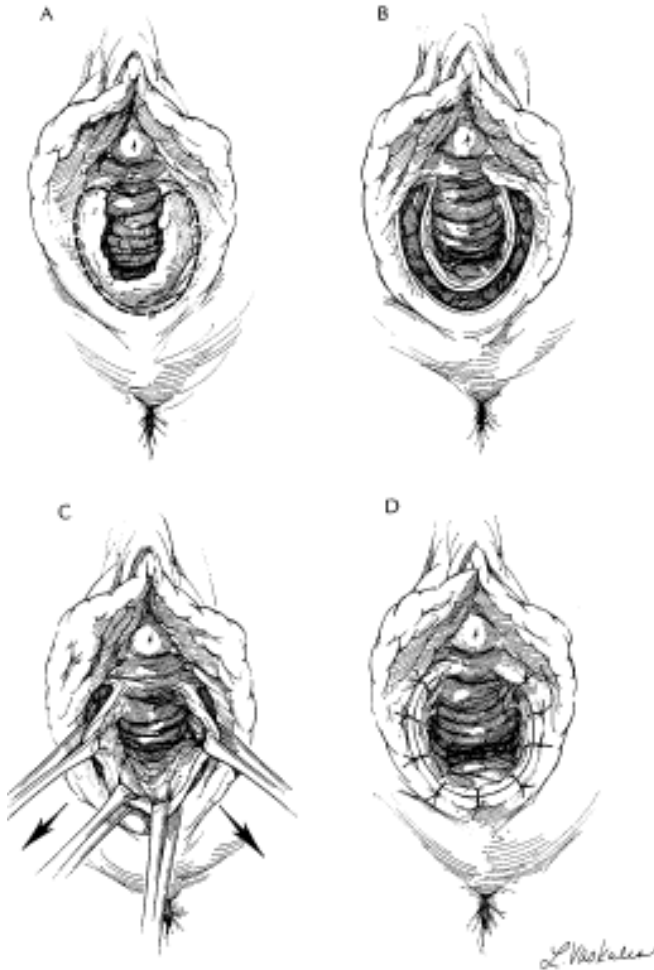


Table 1. Outcomes of Surgical Treatment Derived From the Responses to the Telephone Interview (N = 126)

Outcome After Surgery	n*	Yes	%	95% CI(%)
Intercourse possible	121	113	93	89-98
Intercourse painless	122	76	62	53-70
Satisfactory sexual life	117	85	73	65-81
Positive recommendation	121	108	89	84-95

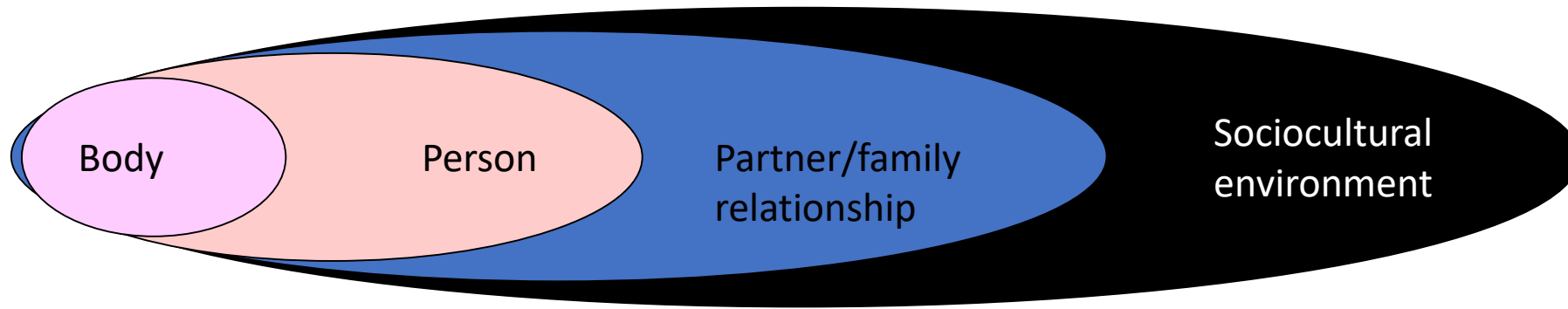
CI, confidence interval.

* Not all 126 women were able to answer all questions (if, for example, they did not have a sexual partner).

Traas, MAF et al. Surgical Treatment for the Vulvar Vestibulitis Syndrome. *Obstet Gynecol* 2006;107:256-62)

Psychosocial Interventions

B - Level of Interventions



Basic Counselling

**Body
Awareness
Education**

**Individual
Psycho-therapy**

**Couple
Therapy**

**Social
Interventions**

Psychosocial Interventions

General Principles

- Biomedical and psychosocial interventions **have to be combined frequently**
- The treatment of sexual dysfunction uses the individual and **couple resources** to solve the problem **(Salutogenetic approach)**
- Therapy is a step-by-step approach with continuous **adaptation of diagnosis and therapeutic strategies**
- Sexual symptoms may be conditioned and maintained as an **unconscious coping strategy for underlying problems** (treatment resistance)

Psychosocial Interventions

A - Determine Objectives of Therapy

- What should be changed?
- What should remain as it is?
- How important is change?
- Are there any concerns about change?
- How confident is the patient that sexuality can change?

Psychosocial Interventions

I. Basic Sexual Counselling

A - Integral part of all therapeutic approaches

B - Sexual education

II. Psychosexual Intervention

A - Body work

- Pelvic floor exercise
- Body awareness training

B - Individual psychotherapy

- Cognitive behavioral therapy
- Psychodynamic focal therapy

C - Couple therapy

- Communication training
- Psychodynamic therapy
- Sensate focus
 - Behavioral therapy
 - Cognitive therapy
 - Psychodynamic therapy
 - Systemic therapy

I. Basic Sexual Counselling

A - Integral Part of all Therapeutic Approaches

- **Give the patient the opportunity to talk about her own sexuality**
- **Listen actively**
 - Patient feels accepted and understood
 - Emotional relief
- **Assess patient's (and partner's) concepts and knowledge of sexuality, passion, intimacy, commitment and love**
 - Sexual biography / script
- **Inform about the reality of human sexuality**
 - Put the variety of personal experiences into perspective
 - Frequency of problems
 - Differences between female and male sexuality
 - Knowledge
 - Empowerment
- **Dispel myths about male and female sexuality**

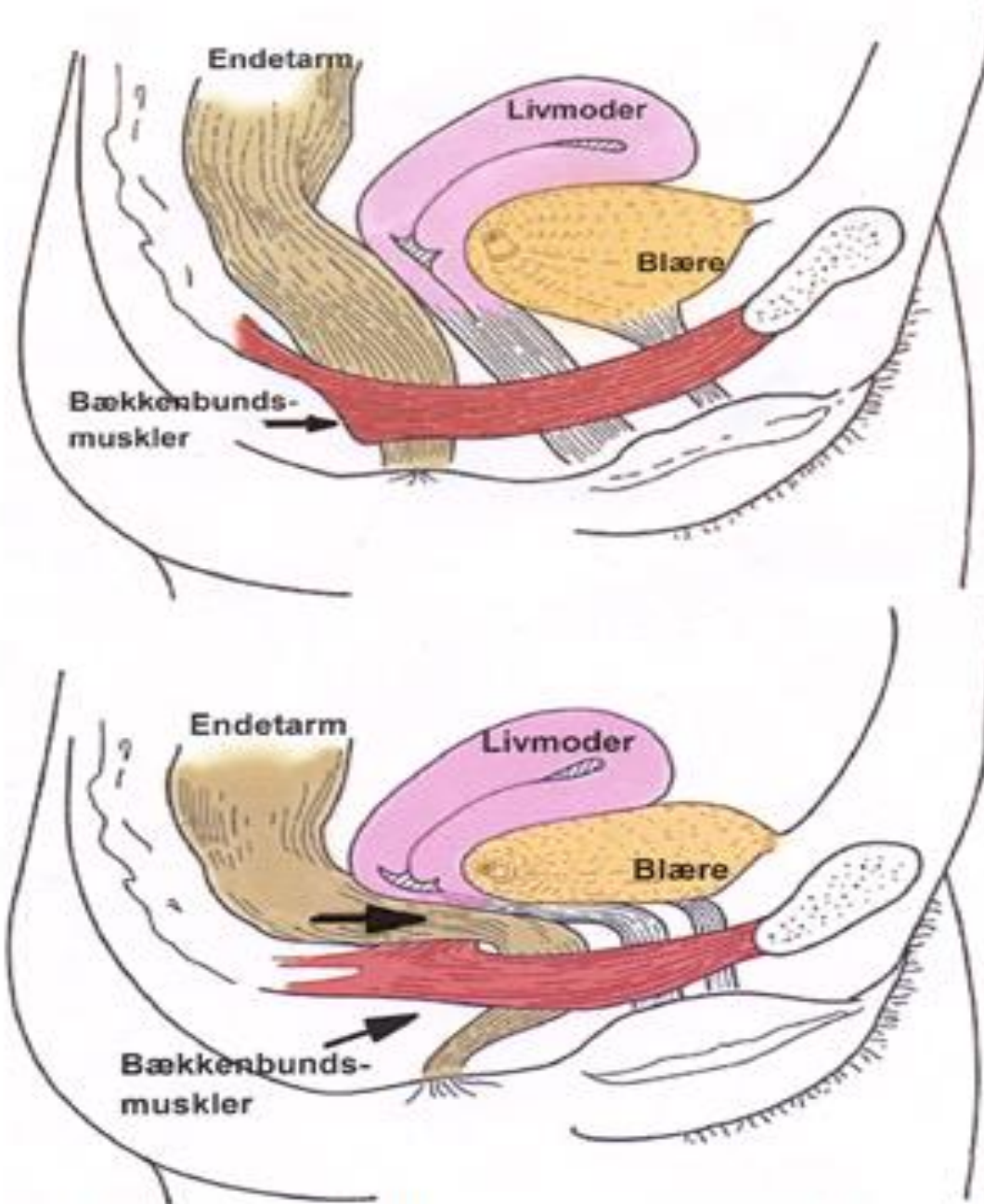
Myths about female sexuality

- A healthy woman has always an orgasm
- Sex must lead to orgasm
- Masturbation is only for singles
- To have no sex leads to health problems
- A man wants sex always and can have sex always
- Passion equals love
- Sex must be spontaneous
- Menopausal women loose interest in sex
- Women want less sex than men
- Women need always a long forplay
- Pornography is only for men (if at all)
- Etc.

II. Psychosexual Interventions

A Pelvic Floor Exercise

- **Instruction to practice pelvic floor contraction and relaxation at home:**
 - Interrupt the urine flow, core exercise, personal massage and stretching
- **Work with a physiotherapist eventually with bio-feedback**
 - **Differential perception** of different elements of the pelvic floor
 - **Becoming aware** of the **pelvic floor movements and respiration**
 - **Training of the muscles** of the torso (core)



Bækkenbunden ses i hvile øverst og under knib nederst.

Tegninger venligst udlånt af Fysioterapien, Hvidovre Hospital.

II. Psychosexual Intervention

A - Body Awareness Education

Exercises:

- Look at the naked body from all sides in a large mirror
 - Look at your body and compare it to drawings
- Look at the genitalia in a small mirror
 - Explore your genitalia with your hand
- Explore the genitalia for sensitive areas
 - Explore your body for sensitive areas
- Look for areas which stimulate
 - Try manual stimulation (where, how, how intensive?)
 - Increase intensity and duration
 - Think about using a vibrator
 - Manual stimulation in the presence of the partner
 - Partner should stimulate the woman
 - Partner stimulates manually during intercourse

II. Psychosexual Intervention

B - Individual Psychotherapy

Cognitive Behavioural Therapy

Indication:

- **Irrational Beliefs and Thoughts**, leading to emotional and physical dysfunction
- Ex: The generic thought “ I have no interest in sex” is accompanied by a **feeling of depression, frustration** and anger and will provoke innate reactions of defence or flight, which **inhibit physical reactions of pleasure, like vasodilation**.

Therapy

- **Learning to modify the belief** “I have no interest in sex” into “**Sometimes I have no interest in the usual way we have sex**” can help the person to feel better as a person, less depressed and hopeless and may encourage her to change behaviour which **could facilitate a pleasure response by the body**.

II. Psychosexual Intervention

B - Individual Psychotherapy

Psychodynamic Focal Therapy

Indication:

Some patients' sexuality is dominated **by norms** which make them **feel bad, dirty and inferior when spontaneous sexual fantasies and daydreams arise**, so that they learn to **suppress** this basic, instinctual part of their sexuality.

They **cut themselves off** from **the energetic part** of their sexuality

Therapy:

tries to help them overcome **this internal conflict and to encourage them to accept** the different elements of human sexuality including instincts and fantasies.

II. Psychosexual Intervention

B - Individual Psychotherapy

Psychodynamic Focal Therapy

Indication

Some patients have suffered **traumatic sexual or intimate experiences**, like being abandoned, being offended and humiliated, or being abused etc.

These experiences have **left scars in their emotional memory** which may be reopened each time a sexual encounter occurs.

Therapy

Therapy can help them **to integrate these experiences and separate the past from the present.**

II. Psychosexual Intervention

C - Couple Therapy

Communication Training

Indication:

- Partners frequently have **difficulties listening to each other** and to accept the views, feelings and thoughts of the other person **without interrupting, contradicting, judging etc.** thus making it impossible to create a platform of exchange and mutual understanding which would form the **basis of intimacy.**

Therapy

- **Listening to each other** (facts, emotions, relationship messages, etc.)
- How to **communicate yes and no**
- How to **communicate without hurting the other**
- How to **give feedback**
- How to **negotiate...**

II. Psychosexual Intervention

C - Couple Therapy

Psychodynamic Therapy

Indication:

Ex: **Both partners feel insecure and have low sexual self esteem.** One partner can take an active, dominant, self assertive role because the other takes the role of the admirer and follower. Both seem to have resolved their insecurity problem. During the course of time this strict separation of roles may hinder the personal development of one or both

Therapy

Partner 1 should learn to become independent of the submission and admiration of Partner 2 and **Partner 2 should become more self assertive** for himself or herself, without depending on the strength of partner 1, etc.

II. Psychosexual Intervention

C - Couple Therapy

Sensate Focus

Exercises at Home	Discussion and Reflection
Step 1: Caressing the body excluding the genital regions; changing active and passive roles – 2 times a week for 45 min.	What feels good? What feels bad or irritating or uncomfortable? How to talk about it? Negative feelings are important to report, they help to understand.
Step 2: Caressing the body including the genital regions; changing active and passive roles – 2 times a week for 45 min.	Exploring without the objective of stimulation; feelings and communication about the experience; feeling safe.
Step 3: Manual stimulation with changing roles. Build up excitement.	How does it feel to play with stimulation, to build it up and let it subside? How is each partner able to direct excitement? The joy of teasing.
Step 4: The man lies back and the woman sits on him introducing the penis into the vagina.	New experiences are possible; feeling close; the emotional significance of penetration; the woman has control.
Step 5: Movement and position experimentation.	Body movements and body expression as sexual stimulation can be experienced and shared.

Treatment of Hypoactive Sexual Desire Disorder

- Basic sexual counselling
- Lifestyle changes
- Hormone therapy in women with sex hormone deficiency
 - Androgen & Oestrogen
 - Oestrogen, Tibolone
- Addressing co-morbid depression
- Adjustment of medication e.g. psychotropic drugs
- Centrally acting drugs (Bupropion, Flibanserin)
- Psychosexual therapy
 - Individual (Fantasie work, Body exploration, Cognitive Behavioral Therapy)
 - Couple (Systemic Sex Therapy)
- Additional counselling of the partner is recommended

Treatment of Sexual Arousal Disorder

- Basic sexual counselling
- Lifestyle changes
- Hormonal therapy: Oestrogen systemic (combined with progestogen) or local
- Blood vessel dilators (Sildenafil)
- Lubricants
- Clitoral therapy device
- Physiotherapy of the pelvic floor
- Psychosexual therapy
 - Sensate Focus

Current evidence in the management of Arousal Disorder

- Results from various clinical trials show controversial results
- In some studies in women with sexual dysfunction and/or arousal or desire disorder using 10-100mg/d Sildenafil over a 12 week treatment period^{1,2,3} no effect could be shown
- However if only genital arousal disorder is present, Sildenafil showed some positive effect on arousal^{4,5}

1. Kaplan *et al*: *Urology* 1999 ; 53:481-486

2. Basson R *et al*: *Obstet Gynecol* 2000 ;95 (Suppl 1): S.54 (Abstract)

3. Basson R *et al*: *J Womens Health Gend Based Med* 2002; 11(4): 367 – 77

Berman JR *et al*: *J Sex Mar Ther* 2001; 27: 411-420

Caruso S *et al* *Br J Obstet Gynecol* 2001; 108 S 623-628

4.

5.

Treatment of Orgasmic Disorder

- Basic sexual counselling
- Lifestyle changes
- Optimize hormones
- Adjustment of orgasm inhibiting medications
- Oxytocin ?
- Physiotherapy of the pelvic floor
- Psychosexual Therapy
 - Masturbation
 - Sensate Focus (Masters and Johnson)

Treatment of Dyspareunia

- **Basic sexual counselling**
- **Normalize vulvar / vaginal tropism and pH** (may include hormonal therapy with Estrogen topical or systemic)
- **Treat concurrent diseases** (e.g. infections, dermatological conditions etc.)
- **Pain therapy**
 - **Systemic:** e.g. Antidepressants, Analgesic drugs
 - **Local:** e.g. Electro-analgesia, Ganglion Impar Block
 - **Vestibulectomie**
- **Lubricants**
- **Physiotherapy of the pelvic floor**
- **Psychosexual, Individual and Couple Therapy**

Treatment of Vaginism

- Basic sexual counselling
- Botox Injection
- Lubricants
- Physiotherapy of the pelvic floor
- CBT with dilators
- Group Therapy
- Individual psychotherapy
- (posttraumatic)

