

Psychobiology of Disease

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DAILY EXPRESS



THE WORLD'S GREATEST NEWSPAPER

- “Stress can cause cancer”

Jan 14, 2010

Comes from study:

Interaction between RasV12 and scribbled clones induces tumour growth and invasion

Looks at tumours in fruit flies

Caused biological stress to cells by damaging the developing eye tissue

What is Stress?

- Stress can be a *stimulus*
- Events that place strong demands on us are known as stressors
- For example, “I’ve got my exams coming up, I can’t pay my rent, and my girlfriend has run off with my dog”

Stressors

- **Stressors:** stimuli that place demands on us and require us to adapt in some manner
 - **Microstressors:** daily hassles and minor annoyances
 - Traffic jam, line at the grocery store, etc.
 - **Major Negative Events:** personal, negative events
 - Divorce, death of a loved one, serious illness, etc.
 - **Catastrophic Events:** tend to occur unexpectedly and affect large numbers of people e.g. Hurricane Katrina

Stressful Life Events (Holmes & Rahe 1967)

- Holmes and Rahe examined the medical records of 5000 patients that had recently suffered illnesses. They then asked the patients whether they had experienced any life events preceding the illness.
- They put the common events into a list and asked a panel of judges to rate the relative stressfulness of each.


Sources of Stress

TABLE 3.1 MEASURING LIFE CHANGES

Social Readjustment Rating Scale

Life Events	Life Change Units	Life Events	Life Change Units
Death of spouse	100	Spouse or daughter leaving home	29
Divorce	73	Trouble with in-laws	29
Marital separation	65	Outstanding personal achievement	28
Jail term	63	Spouse begins or stops work	28
Death of a close family member	63	Begin or end school	26
Personal injury or illness	53	Change in living conditions	25
Marriage	50	Revisions of personal habits	24
Fired or laid off	47	Trouble with boss	23
Marital reconciliation	45	Change in work hours or conditions	20
Retirement	45	Change in residence	20
Change in health of family member	44	Change in school	20
Pregnancy	40	Change in recreation	19
Sex difficulties	39	Change in church activities	19
Gain of a new family member	39	Change in social activities	18
Business readjustment	39	Mortgage or loan for house purchase	18
Change in financial state	38	(See major appliances)	17
Death of a close friend	37	Change in sleeping habits	16
Change in different line of work	36	Change in number of family get-togethers	15
Change in number of arguments with spouse	35	Change in eating habits	15
Mortgage or loan for major purchase	31	Vacation	13
Fore-close on mortgage or loan	30	Christmas	12
Change in responsibilities at work	29	Minor violations of the law	11

Source: Reprinted from Journal of Psychosomatic Research, No. 10, Holmes and Rahe, "The Social Readjustment Rating Scale," 213-218, 1967; permission from Elsevier.

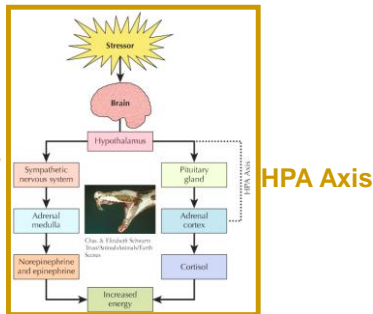


What is Stress?

- Stress can be a *response*
- Physiological response to stress e.g. 'Fight-Flight' response
- Also, the presence of negative emotions including feeling tense, difficulty concentrating and losing your temper easily

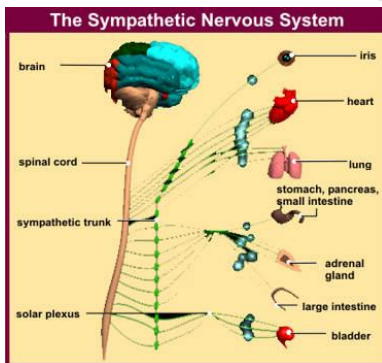
Effects of Stress

Sympathetic Nervous System

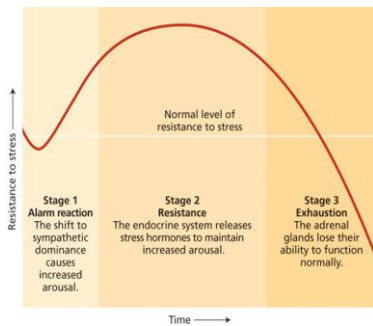


HPA Axis

Sympathetic Adrenal Medulla System



General Adaptation Syndrome (Selye, 1956)



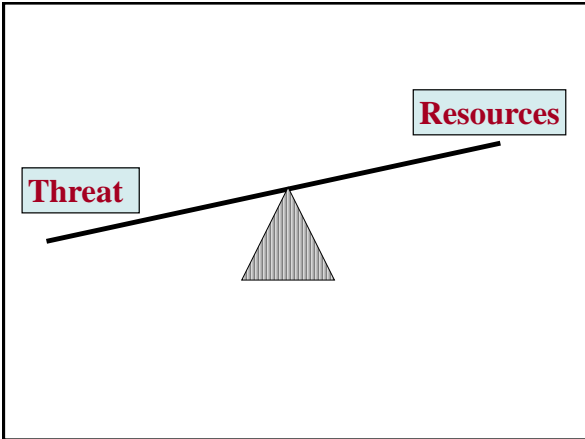
What is Stress?

- Combination of stimulus and response as a *person-situation interaction*
- Stress can be defined as a pattern of cognitive appraisals, physiological responses and behavioural tendencies that occur in response to a perceived imbalance between situational demands (**primary appraisal**) and the resources needed to cope with them (**secondary appraisal**).

Transactional definition of stress

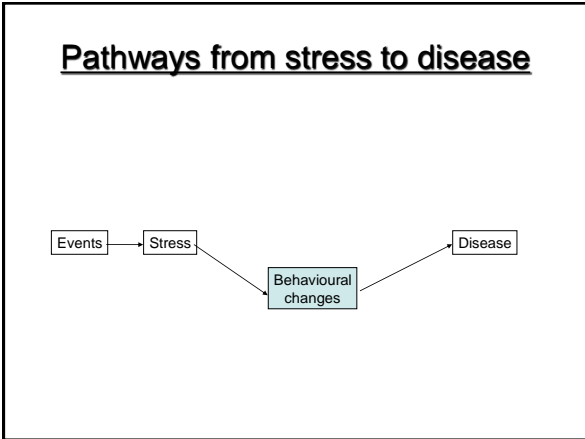
- Stress is a condition that results when the person / environment transactions lead the individual to perceive a discrepancy between the demands of the situation and the coping resources available.

Lazarus & Folkman 1984



Cognitive Appraisal

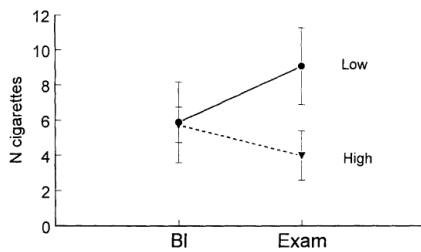
- For example, when considering an exam you will evaluate how hard it will be and how much it counts (*primary appraisal*) and how your current knowledge equips you to pass (*secondary appraisal*)
- You will also take into account *potential consequences* of failing with regards to their likelihood and seriousness
- Finally, the *psychological meaning of the consequences* may be related to your beliefs about yourself or the world, e.g. "I am a total failure if I don't do well in all my exams"



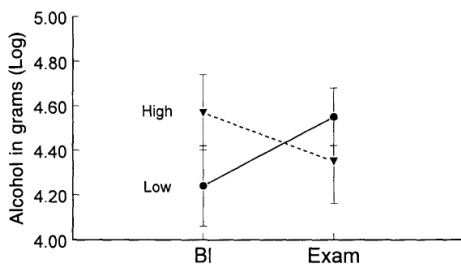
Health Behaviour and Stress Step toe et al (1996)

- 115 students assessed for amount of cigarette smoking and alcohol use in week.
- Assessed 2-3 months before exam and then 2 weeks before exam.
- Perceived social support also measured.

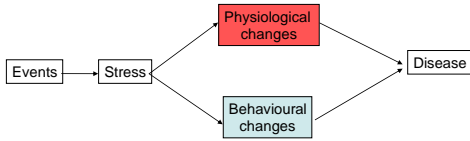
Step toe et al (1996) - Smoking



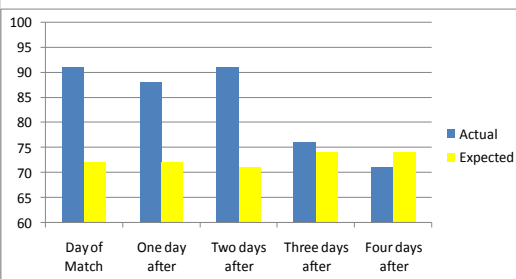
Step toe et al (1996) – Alcohol consumption



Pathways from stress to disease



MI and World Cup 1998 (Carroll et al., 2002)

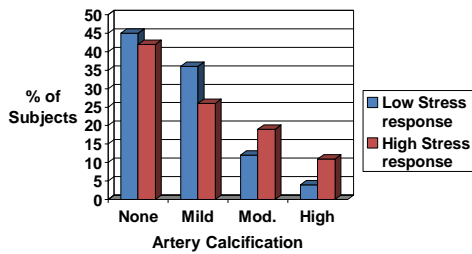


Psychosocial stress and coronary heart disease

- 514 healthy men and women without history or objective signs of CHD
- Cortisol was measured in response to mental stressors (cognitive task)
- Measured the degree of coronary artery calcification
- Conclusion: heightened cortisol reactivity is associated with a greater extent of CAC.

Hamer, O'Donnell, Lahiri & Steptoe (2010) *Eur. Heart Jnl.* 424-429

Stress and CHD



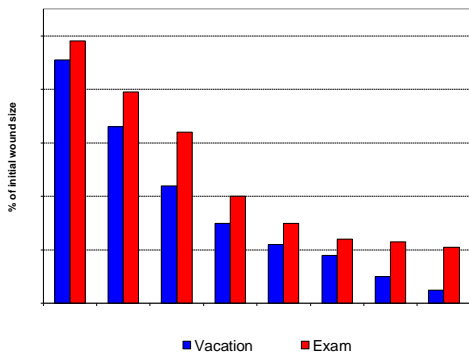
Effects of Stress

- **Stress and the Immune System**
- **Psychoneuroimmunology:** interdisciplinary field that studies the effect of psychological factors on the immune system

Mucosal wound healing and exam stress (Marucha et al 1998)

- **Method:** 11 Dental students were each administered two punch biopsy wounds on the hard palate. One during the summer vacation and one before a major exam.
- **Measures:** daily photographs of wounds

Marucha et al (1998)



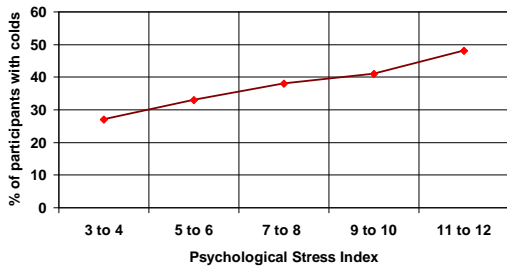
Marucha et al (1996)

- The wounds took an average of 40% (3 days) longer to heal during the examinations.
- All students had slower healing during exams
- Mechanism? Production of Interleukin-1 declined by 68% during the exam.

Immunosuppression

- Cohen, Tyrrell and Smith (1991) exposed 400 volunteers to a nasal wash containing a cold virus
- Participants were assigned a stress index from 3 (lowest stress) to 12 (highest stress) based on the number of stressful life events in the past year, the degree to which they felt able to cope with the demands of daily living and the frequency with which they experienced negative emotions such as anger or depression
- They were examined daily for cold symptoms

Stress and Colds

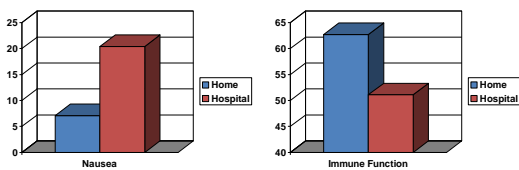


Cohen, Tyrrell and Smith (1991)

Stress and Immune Function (Bovbjerg et al., 1990)

- Cancer patients who received regular chemotherapy at hospital – known to cause nausea and immune suppression
- Took blood samples of patients at home and at hospital *prior* to chemotherapy
- Patients rated their feelings of nausea and their NK Cell activity was measured in response to mitogens

Stress and Immunity



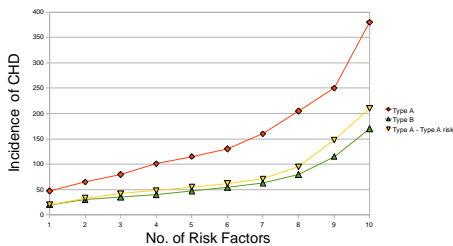
Personality and Illness

- Type A behaviour
- Experiment: Place your head on the desk and close your eyes. Raise your hand after you think a minute has passed. I will tell you when we start and when a minute is up.

Type A Behaviour

- Time urgency
- Free-floating hostility
- Hyper-aggressiveness
- Focus on accomplishment
- Competitive and goal-driven
- VIDEO EXAMPLE

Type A and CHD



Personality and CHD

- Western Collaborative Group Study followed >3000 males for 8.5 yrs. TABP doubled the risk of developing CHD in healthy males (aged 39 - 59) when cardiac risk factors controlled for (Rosenman et al. 1975)
- When compared to Type B, characterised by patience, serenity and lack of time urgency, Type A behaviour alone accounted for 31% increase in risk (Brand et al. 1976)

Personality and CHD

- Later studies highlighted central role of anger and hostility
- Recent studies of 'Type D behaviour', characterised by social inhibition and negative affect, showed a relationship with CHD possibly due to under-reporting of symptoms (Schiffer et al., 2007)



"Being happy is the key to living longer"
(Feb. 18, 2010)

Study followed 1739 adults over a 10 year period conducting a Type A behaviour interview and measuring positive affect.

After controlling for known risk factors, for each point on a five point scale there was a 22% drop in risk in developing CHD.

Davidson, Mostofsky, and Whang. *European Heart Journal* (2010)

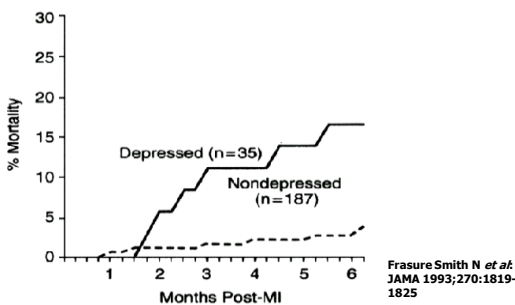
Depression

- Literature supports both an etiologic and prognostic role for depression in coronary heart disease *Frasure-Smith and Lesperance (2006)*.
- Etiologic studies suggest relative risk of depression leading to onset of CHD is 1.64 to 1.90 times higher

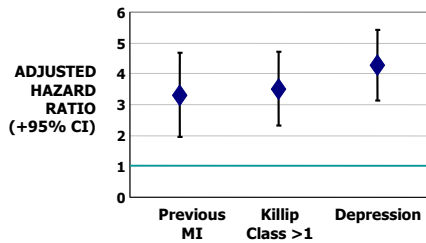
Depression

- Prognostic studies conclude that CHD pts with depression have 2.0 to 2.5 times higher risk of mortality in first two years
- Explanations vary from physiological changes (e.g. platelet activity) to behavioural changes (e.g. levels of physical activity)

6-MONTH MORTALITY AFTER MI

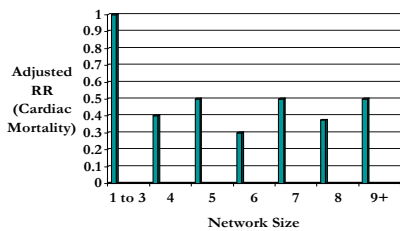


BASELINE PREDICTORS OF 6-MONTH MORTALITY AFTER MI



Frasure Smith N *et al*:JAMA 1993;270:1819-1825

The Social Network



Network Size associated with risk of cardiac death (Brummett et al., 2001)

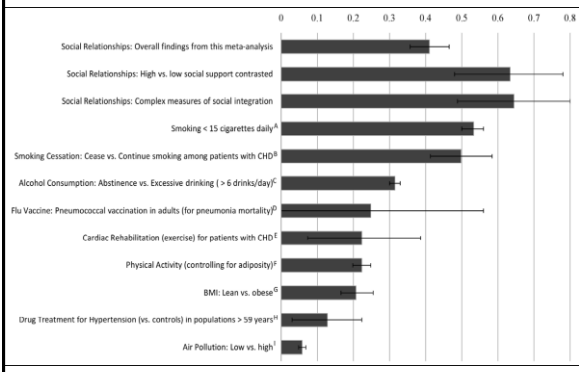
Social Support

- Brummett et al (2001) found that the most socially isolated cardiac pts scored higher on a hostility measure, had lower incomes, and were more likely to be smokers.
- Although when these variables were adjusted for, social isolation remained robust predictor of cardiac mortality

Holt-Lunstad et al (2010)

- Conducted a meta-analysis of the literature investigating the association between social relationships and mortality
- 148 studies (308,849 participants), suggested a 50% increased likelihood of survival for participants with stronger social relationships
- *“The magnitude of this effect is comparable with quitting smoking and it exceeds many well-known risk factors for mortality”*

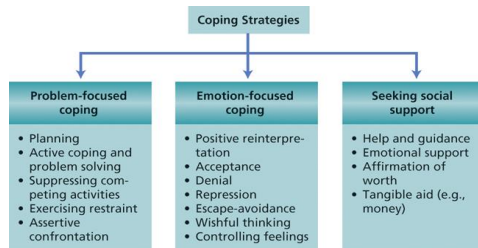
Risk Factors and Mortality



Social Support

- Lack of social support linked to suppressed immune function (Berkman, 1995). Proposed mechanisms include physiological pathways and non-adherence
- Perceived social support may buffer the effect of depression (Frasure-Smith et al., 2000)

Coping With Stress



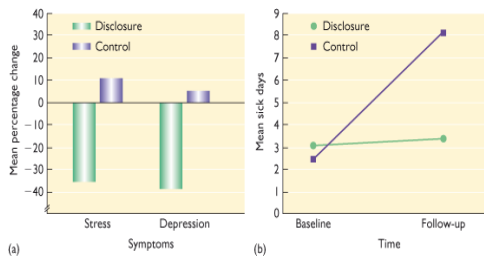
Problem Focused Coping

- In disease may involve finding out information on the disease, learning new skills to manage their disease and rearranging their lives around the disease.
- For exams may involve reviewing the learning objectives, organising notes and forming a study group.

Emotion Focused Coping

- Disclosing trauma can enhance immune system functioning, lower stress, reduce depression, and help the individual cope with stress more effectively
- Sloan and Marx (2004) asked college students who had reported experiencing a traumatic event to write about it or assigned them to control condition
- All students completed measures of stress, depression and number of days sick in past month – there were no group differences at baseline

Trauma Disclosure



Which is more effective?



PRICE: £1.95

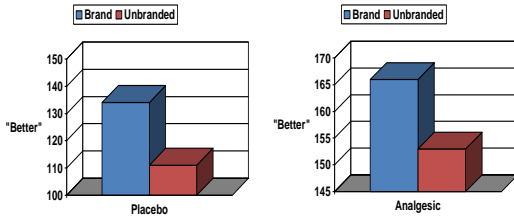


PRICE: £0.16

Branding and treatment of headaches

Branded Analgesic n=205	Branded Placebo n=206
Non-brand Analgesic n=215	Non-brand Placebo n=209

Branding helps!



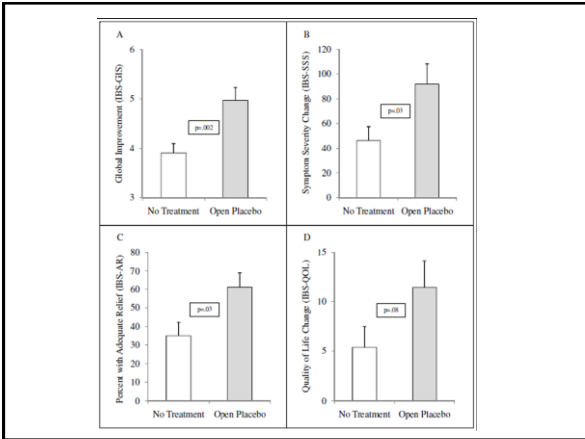
Placebo Effect

- The phenomenon in which a placebo - an inactive substance like sugar, distilled water, or saline solution - can sometimes improve a patient's condition simply because the person has the expectation that it will be helpful.

Placebo without deception

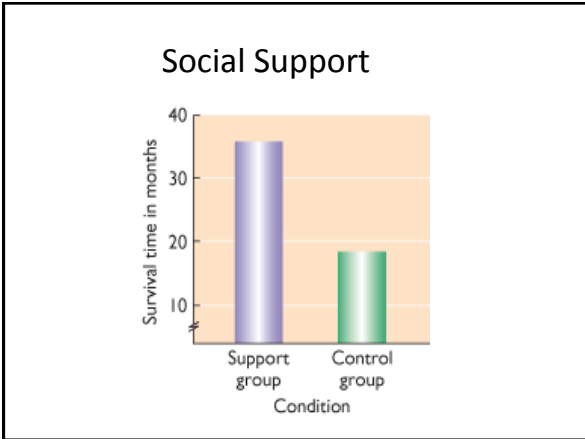
- 80 pts diagnosed with IBS were randomly assigned to 'open placebo' or treatment as usual
- Pts informed treatment was "placebo pills, made of an inert substance, like sugar pills"
- Symptoms of IBS and QoL were measured as outcome

Kapchuk et al., 2010, PLoS ONE 5(12)



Social support

- 86 women with breast cancer were randomly assigned to a support group or control – i.e. normal medical care
- Aim was to improve quality of life
- **BUT**, 48 months later all the women in the control had died whereas a third of the women from the support group were still alive (Spiegel et al. 1989)



Recurrent Coronary Prevention Project

- Trial of counselling to alter Type A behaviour
- 1013 post-MI pts randomised to cardiac counselling (n=270) Type A counselling (n=592) or simply follow-up (n=151)
- No differences btw groups on sociodemographic or CHD risk factors
- Study ran for 4.5 years with a total of 60 groups for the Type A counselling condition

RCPP Results

