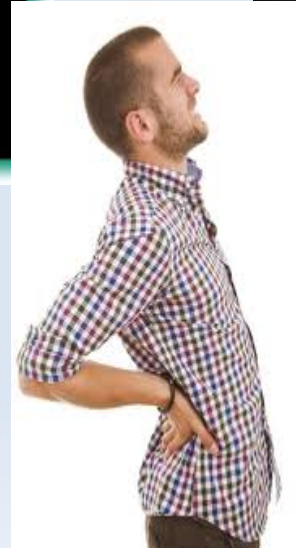
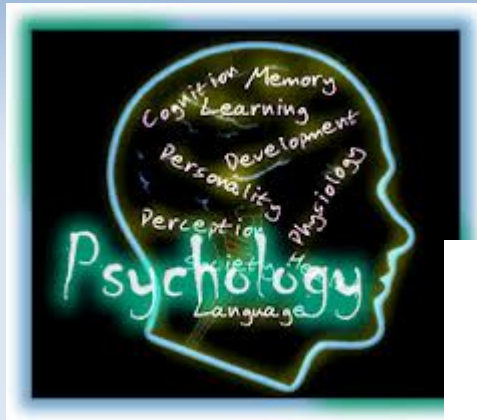


Toward a conceptual framework for linking biological mechanisms to symptom clusters in cancer

Donald L. Patrick, Mirjam A Sprangers,
and Madeleine King

ISOQOL, Miami, October 2013



DZ Twins

 Different DNA
 Same Environment

MZ Twins

 Same DNA
 Different Environment

If intelligence is the same it must be due to the environment.

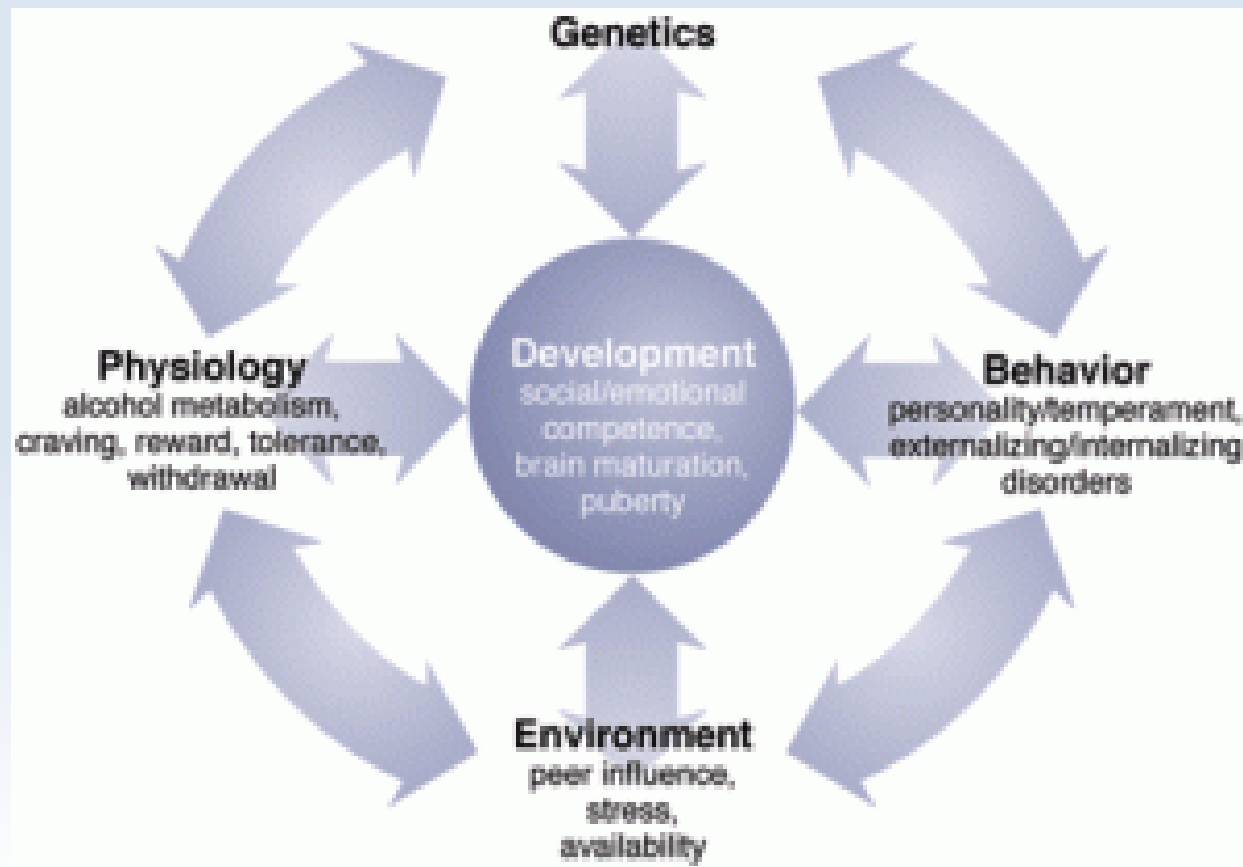
If intelligence is different it must be due to genetics.

If intelligence is the same it must be due to genetics.

If intelligence is different it must be due to the envirc

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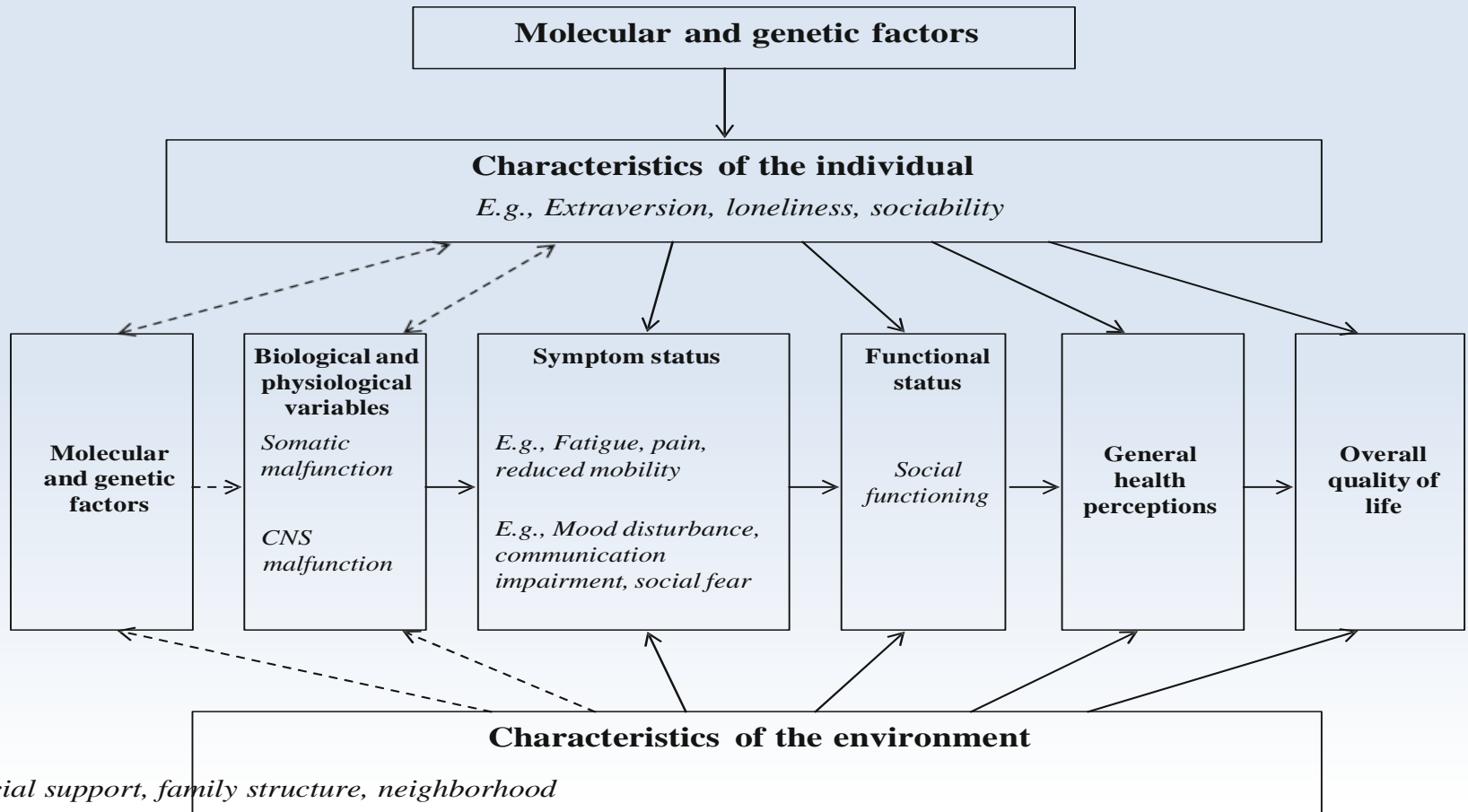


Sprangers et. al

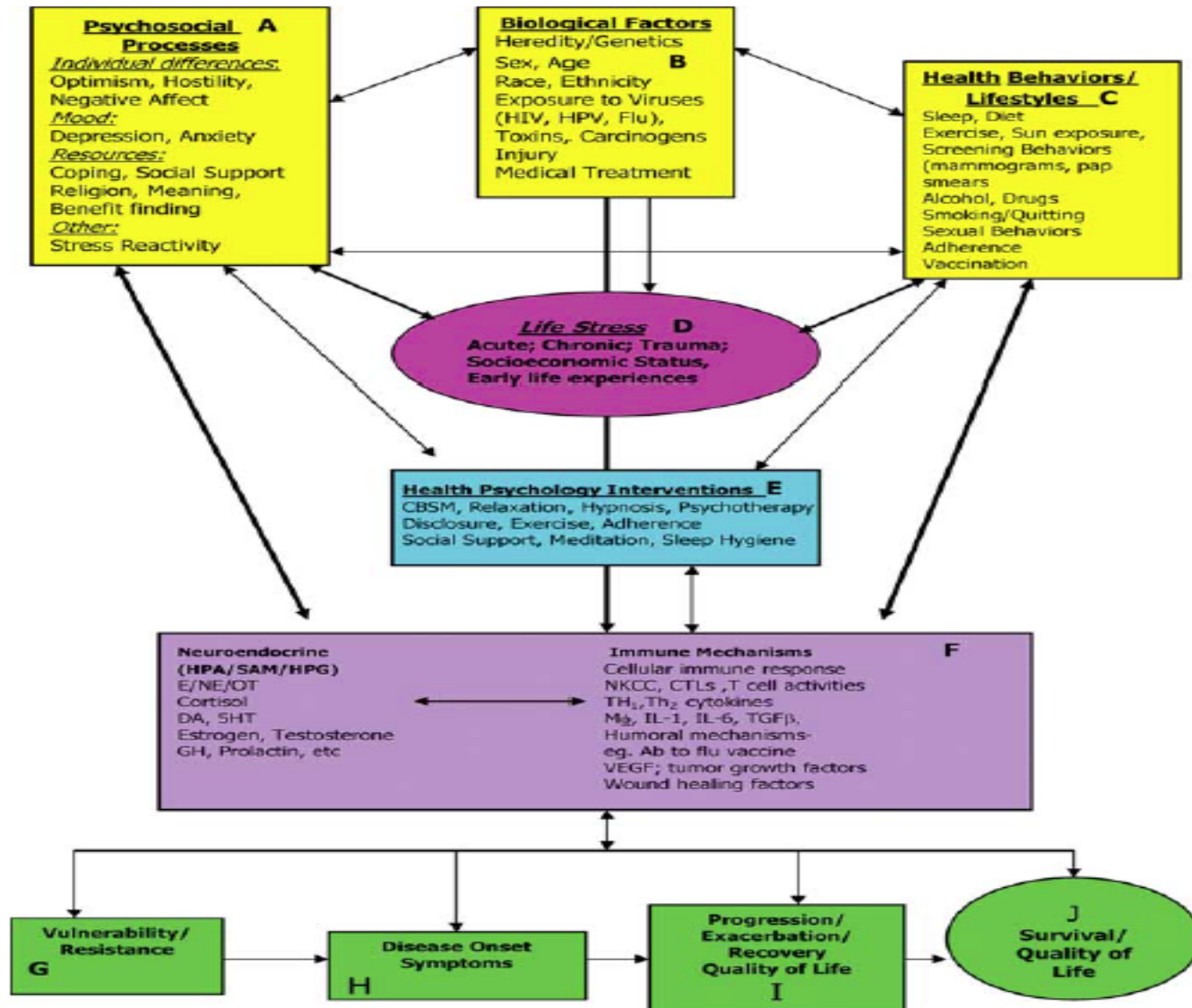
Qual Life Res (2010) 19:1395–1403

Encyclopedia of Quality of Life (Forthcoming)

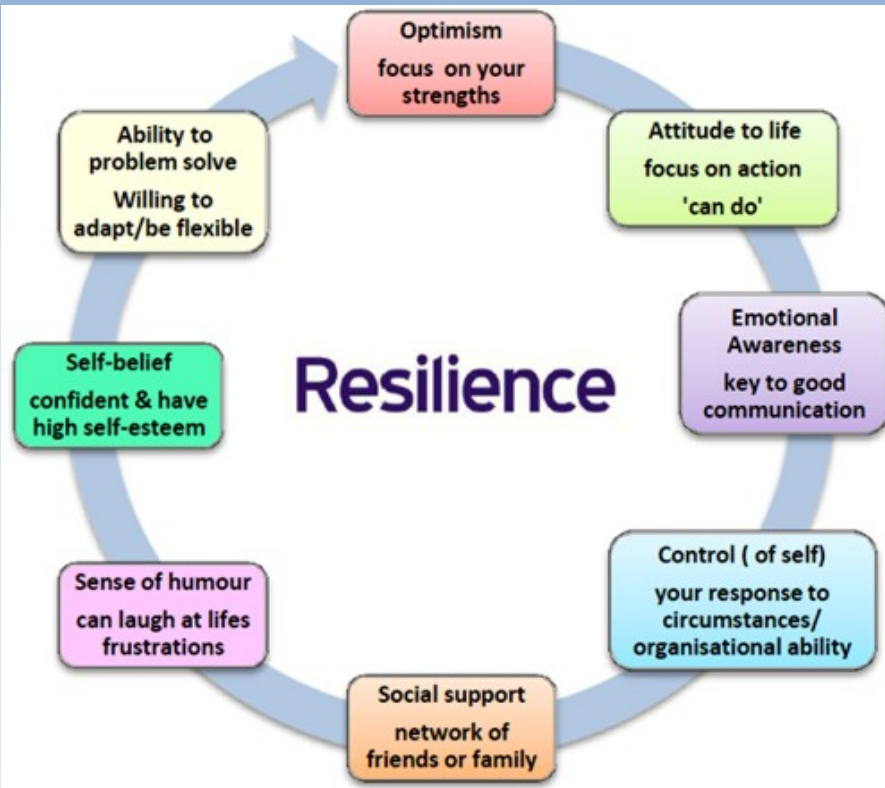
Based on Wilson and Cleary (1995)



S.K. Lutgendorf, E.S. Costanzo / Brain, Behavior, and Immunity 17 (2003) 225–232



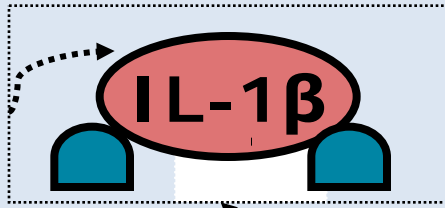
Resilience



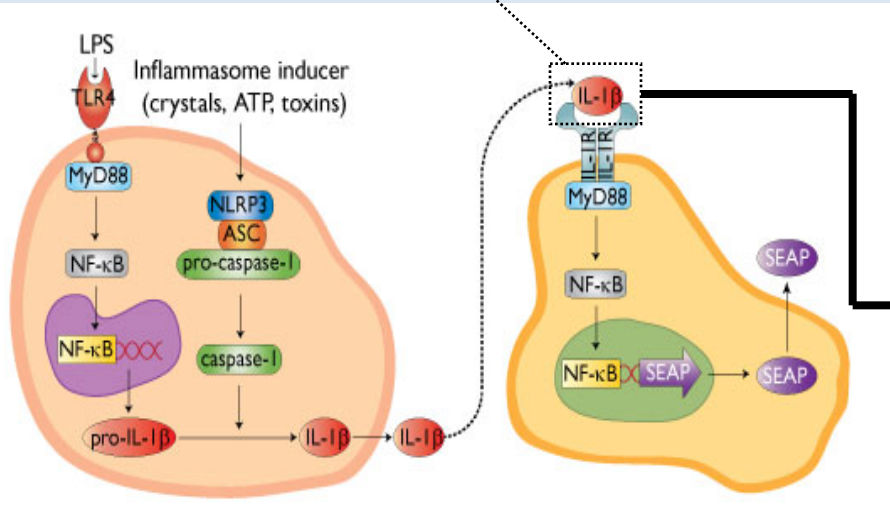
Genetics, Epigenetics and Pain

- Why do some people experience pain differently from other people?
 - Emerging data offer convergent evidence for the importance of ion channels in both pain sensitivity in normal populations and pathological pain states
 - Research suggests a SNP within the *SCN9A* gene that encodes the α subunit of the voltage gated sodium channel $Na_v1.7$ may play a role in determining risk for chronic pain conditions as well as variation in pain responding within normal populations.^[91] In a mixed cohort of sciatica, osteoarthritis, pancreatitis
- Why do some people get pain relief from a treatment and others do not?

Pro-inflammatory Pathway

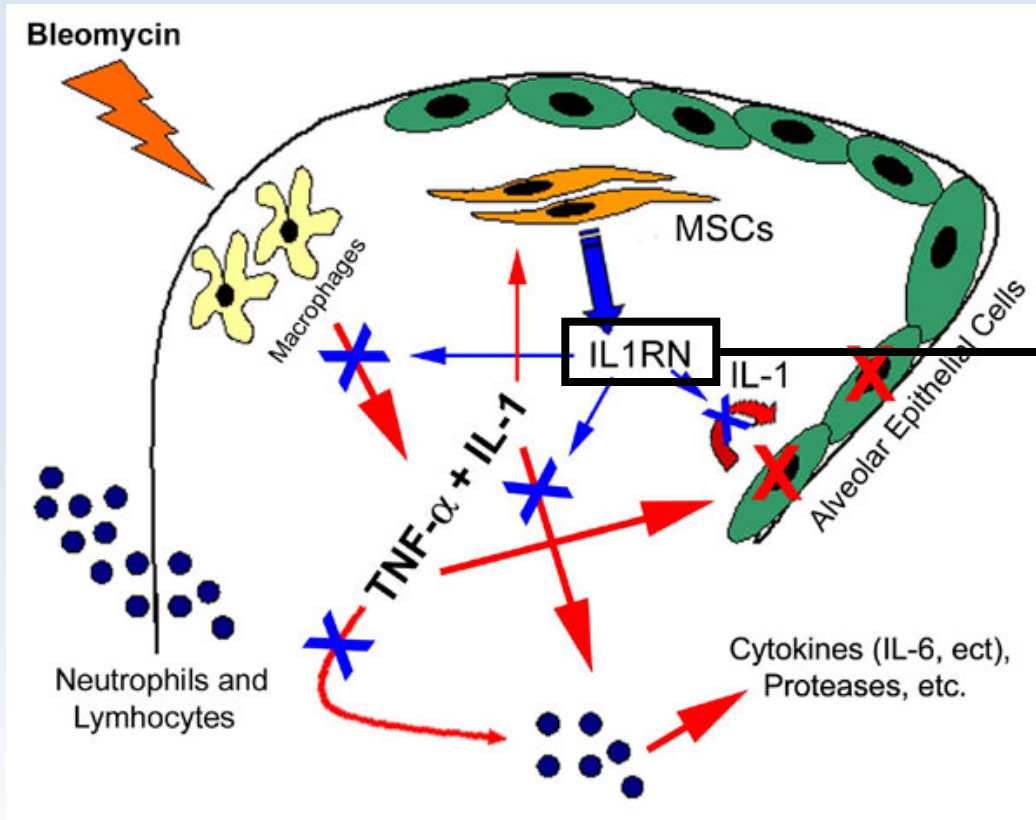


x5



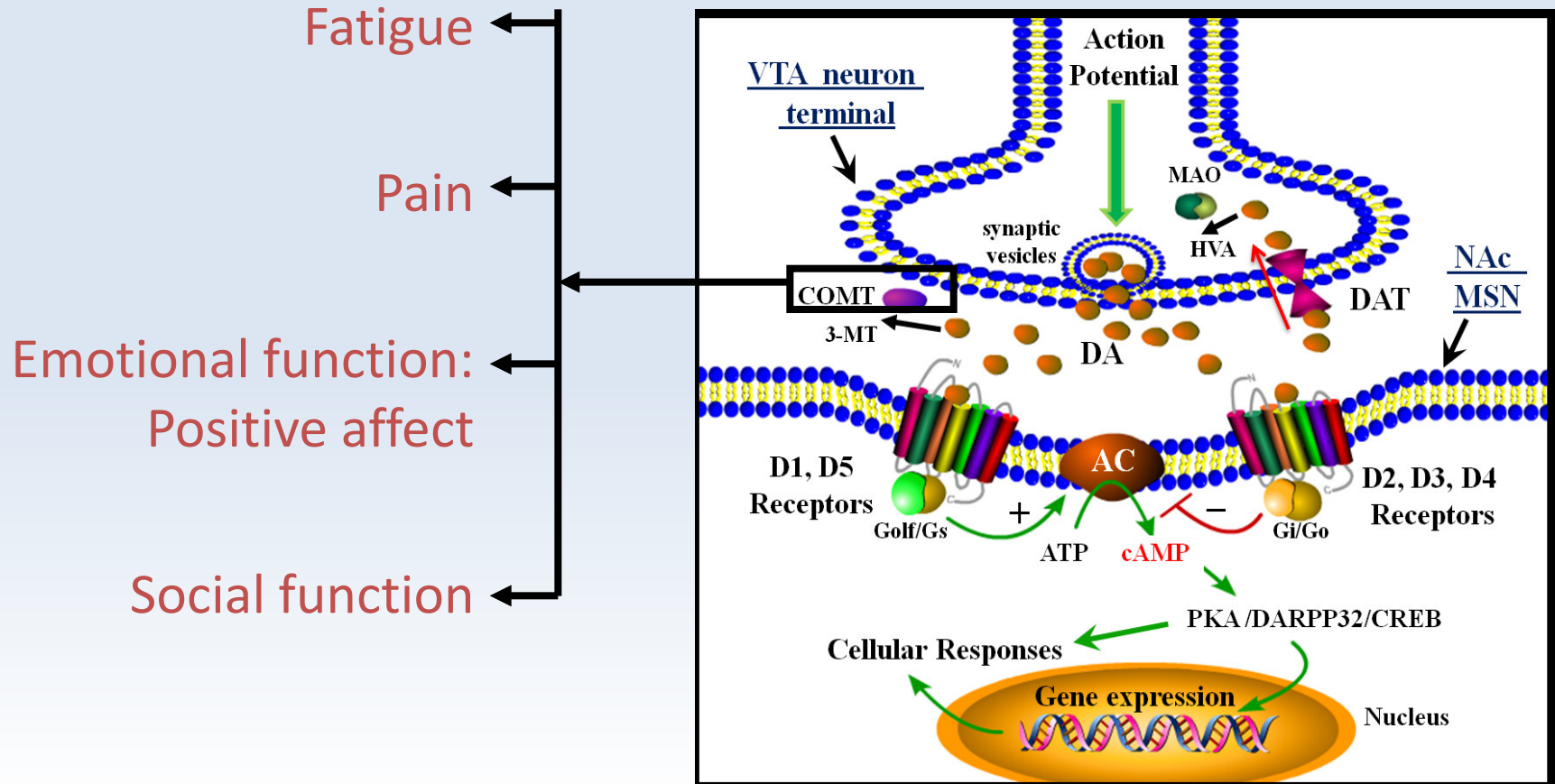
- Fatigue
- Pain
- Depression
- Anti-depressant response
- General health
- Physical function

Anti-inflammatory Pathway

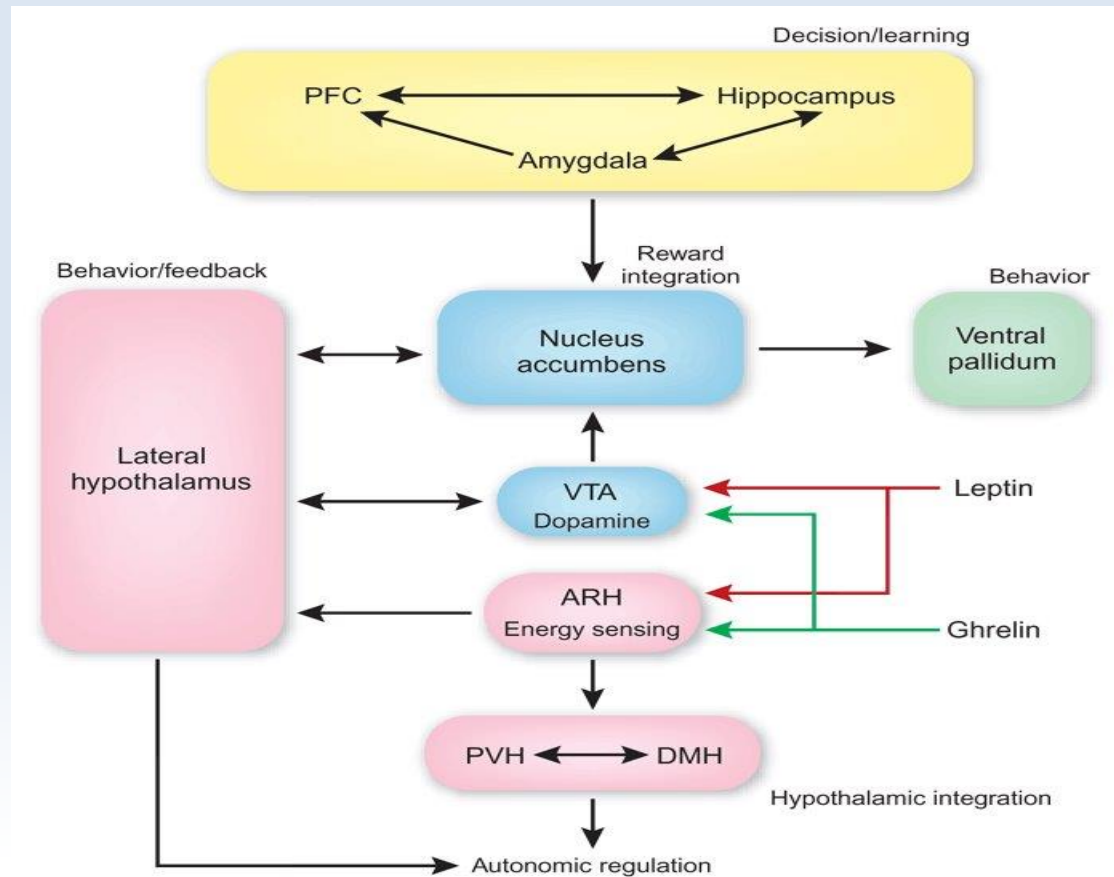


- Fatigue
- Pain
- Depression
- Social function
- General health
- Physical function

Dopaminergic Synapse



Amygdala and Neural Pathway



So what might help us put it together?

- Make advances helped by blurring research boundaries and using multi and trans disciplinary perspectives
- Examine pathways by placing questions on a theoretical model such as Sprangers et al expansion of Wilson and Cleary or Lutgendorf ***as starting point***
- Include important modifiers or confounders such as resilience and personality
- Add each subjective domain as a correlate individually or together in clusters, i.e., pain, depression, fatigue

PRO Measurement in the Pathways

- Use symptom and sign measures with clear concept and dimensionality
- Consider measures of personality and resilience (assessed with PROS or ?)
 - --Strengths and Difficulties Questionnaire for Infants and Youth
 - --Measures of Coping
 - --Optimism Pessimism
 - --Cognitive Reserve
- Measures of impact more distal but related
 - --Functional status
 - --Perceived quality of life

Cautionary Thoughts

- Missing heritability
 - Even when dozens of genes linked to a trait or behavior, cumulative effects disappointingly small
 - No surprise it isn't one gene, one phenotype but more complex
 - Possibly 1000s of variants
 - GWAS and SNPS – to sequencing whole genomes
- Brain “plasticity” --brain changes with experience
- We can move along with basic science

Other challenges

- Difficulties of causal inference even with personalized risk profiles using genetics
- Findings “need” to be placed within structural determinants of population and individual health—the social patterning of health and illness
- Need for use of innovative research designs such regression discontinuity design, pretest post-test with thresholds