

# Psychobiology of Health and Disease: Integrating Laboratory and Population Studies in Whitehall II

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# Pathways underlying psychosocial influences on health outcomes

## Lifestyle

- Smoking, food choice, physical exercise, alcohol consumption, healthy weight, adherence to treatment

## Biology

- Modifications in neuroendocrine, cardiovascular, inflammatory, immunological and other physiological responses

# Pathways underlying psychosocial influences on health outcomes

## Neuroendocrine

- cortisol, adrenaline, testosterone, noradrenaline

## Cardiovascular

- Blood pressure, heart rate, heart rate variability

## Immune

- Lymphocyte counts and activity, natural killer cells, immunoglobulins

## Inflammatory

- C-reactive protein, interleukin (IL) 6, fibrinogen

## Metabolic

- Lipids (cholesterol), glucose, insulin

# Psychobiological processes and health risk

## Levels of study

- Animal studies
- Psychophysiological stress testing
- Clinical studies
- Naturalistic monitoring
- Epidemiological studies

# Psychophysiological stress testing

- **Mentally challenging tasks:**  
Problem solving, emotional interviews, simulated public speaking
- **Measurement of:**  
Blood pressure, heart rate, hormones, cholesterol, blood clotting, inflammation, muscle tension
- **Comparison of:**  
Clinical groups  
People high or low on psychosocial characteristics relevant to health

# Psychophysiological stress testing

- Sophisticated biological measures
- Evaluation of dynamic responses
- Control of confounders
- Experimental manipulation of conditions
- Can establish causal links between stress-related factors and biology

# Why study these processes within the Whitehall II study?

- Well-characterised study sample
- Participant recruitment in relation to a documented indicator of cardiovascular risk (occupational status)
- Tracking of health outcomes allows stress-related biology to be linked to future health outcomes
- Investigations of associations with other processes (genetics, cognitive function, diet, arterial stiffness, etc)

# Psychobiology study

## Participants (2000-2001)

- 238 healthy members of the Whitehall II (prospective) cohort aged 47-59 years in full-time employment.

Sampled by grade of employment:

Higher	Men	49	Women	41	Total	90
Intermediate	Men	44	Women	37	Total	81
Lower	Men	36	Women	31	Total	67

## Conditions

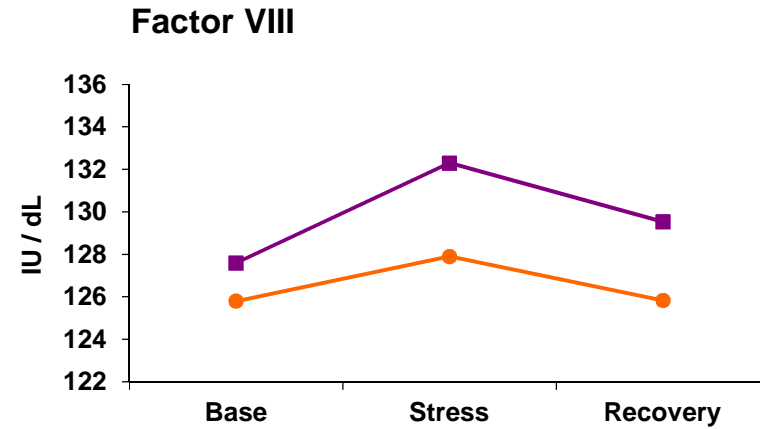
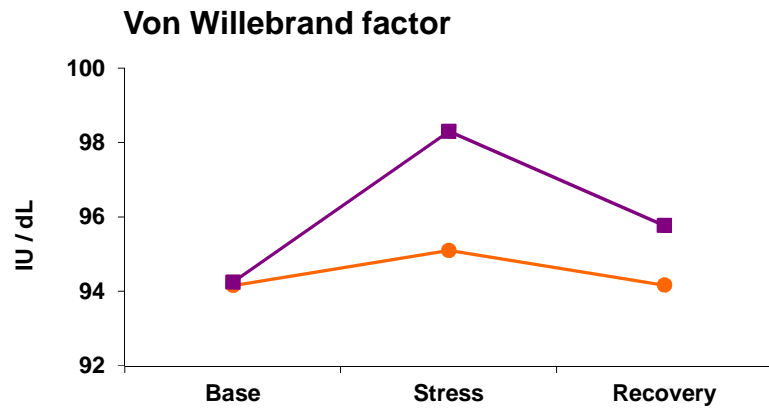
- Cardiovascular, neuroendocrine, cytokine and haemostatic responses to colour/word and mirror tracing tasks.
- Blood drawn at baseline, immediately post-task, and 45 minutes later.
- Salivary cortisol assessed 8 times over the day, along with momentary assessments of mood



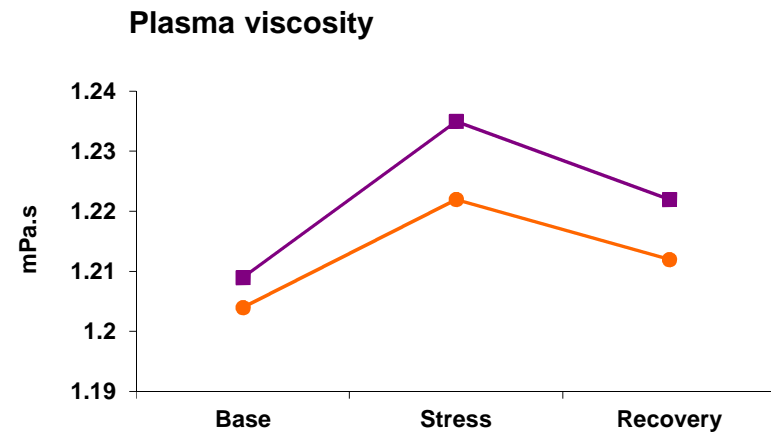
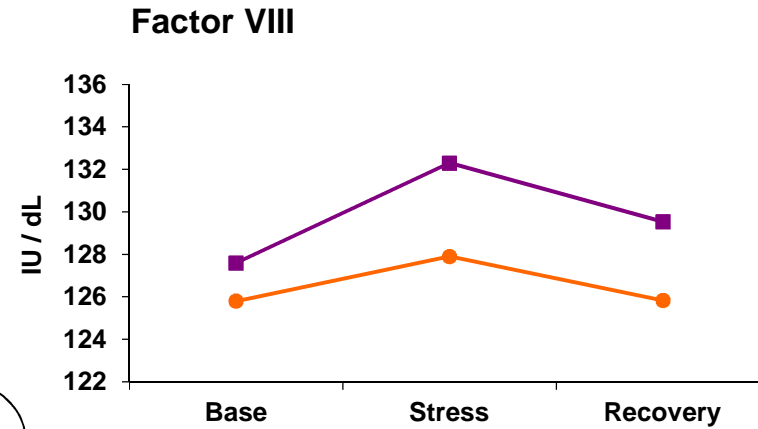
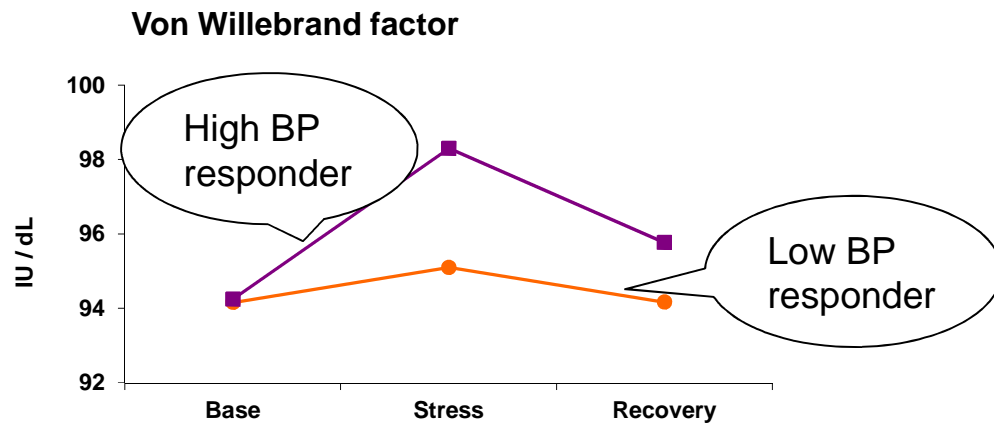
# Findings

- Psychosocial factors are associated with a broad range of health-related dynamic biological responses to mental challenge

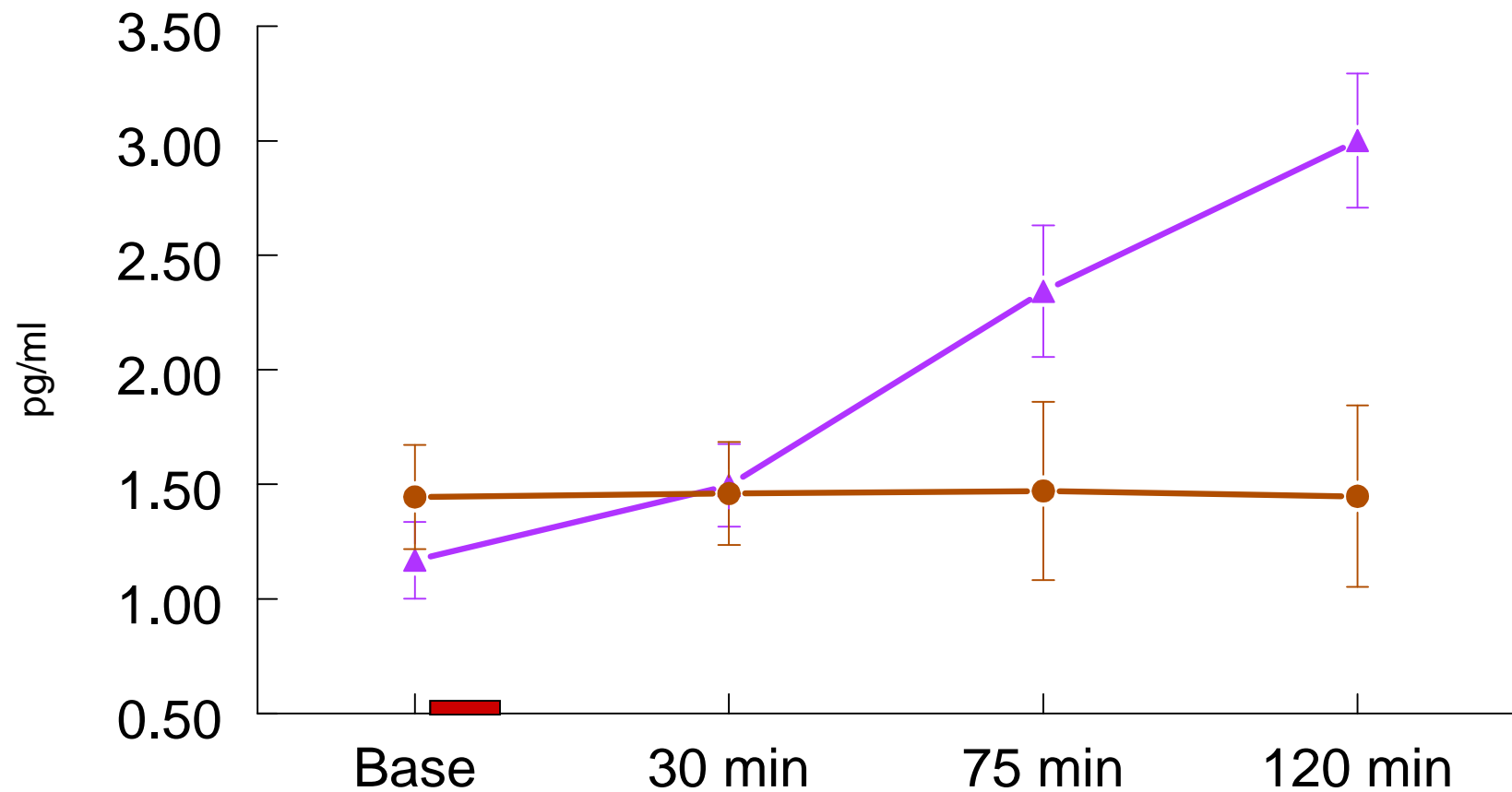
# Stress, endothelial and haemostatic responses



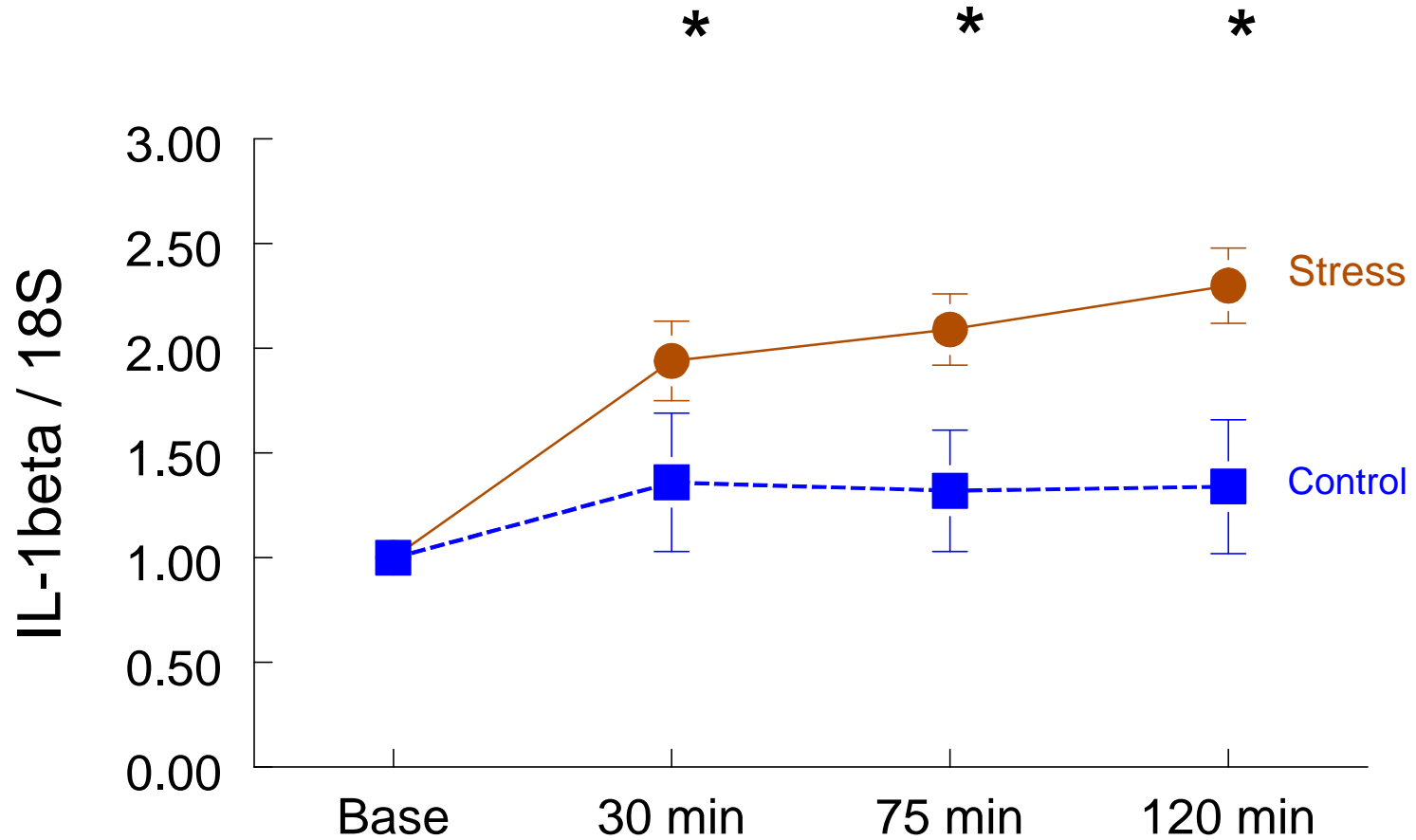
# Stress, endothelial and haemostatic responses



# Stress and plasma IL-6 response



# Stress and IL-1 $\beta$ gene expression

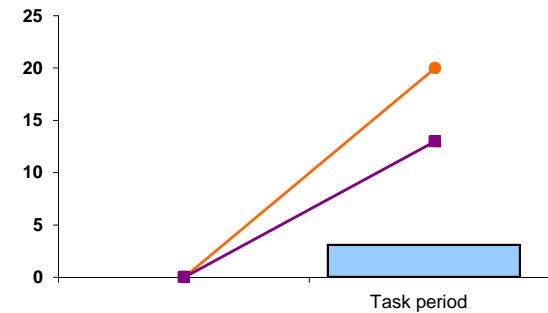


# Findings

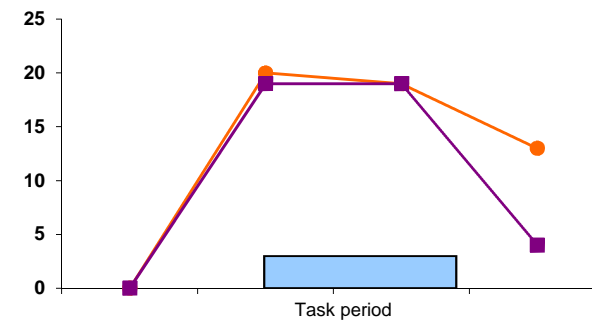
- Psychosocial factors are associated with a broad range of health-related dynamic biological responses to mental challenge
- Impaired post-stress recovery characterises higher risk groups

# Acute biological responses to mental stress

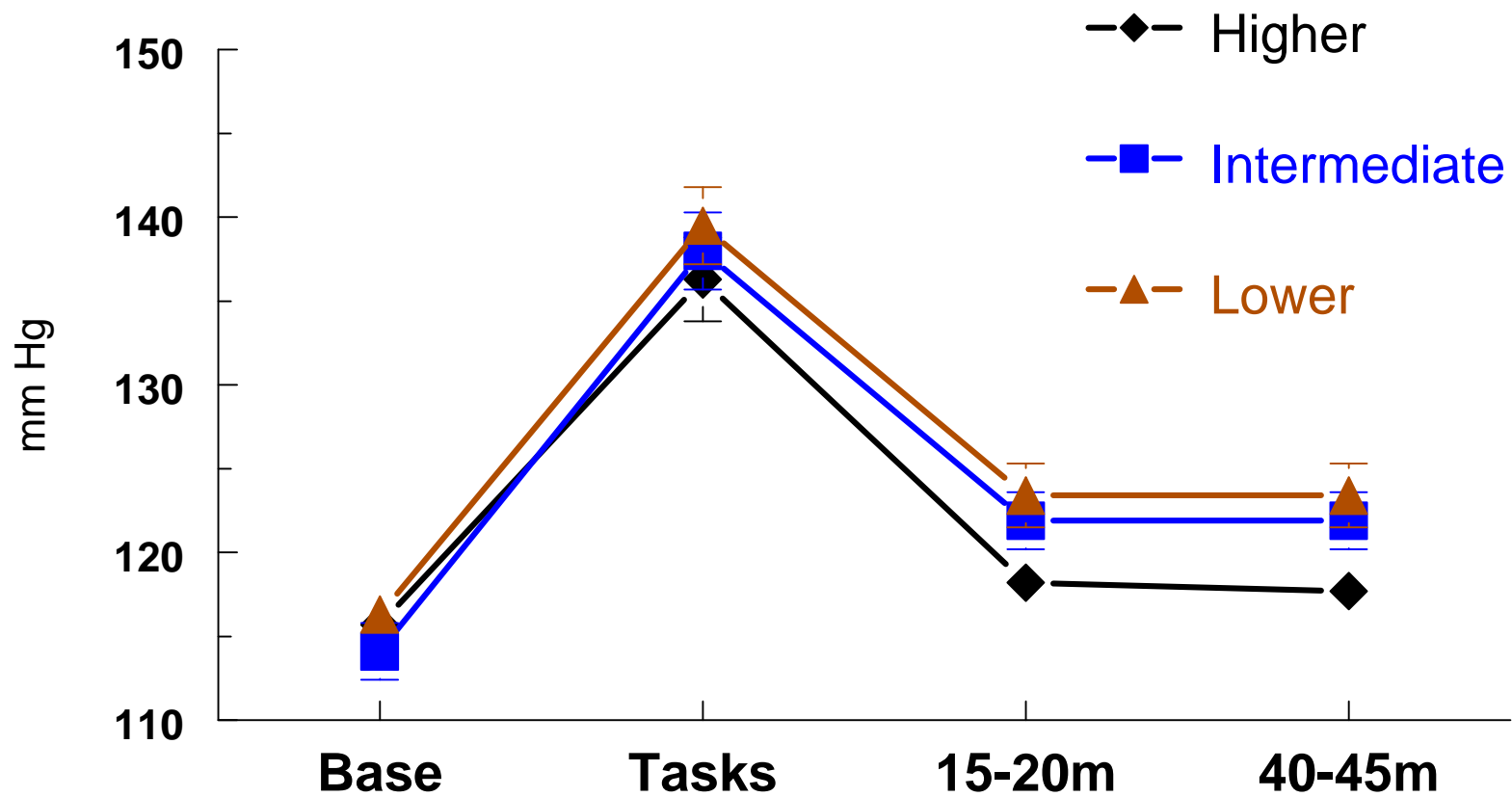
- Size of the response



- Rate of recovery

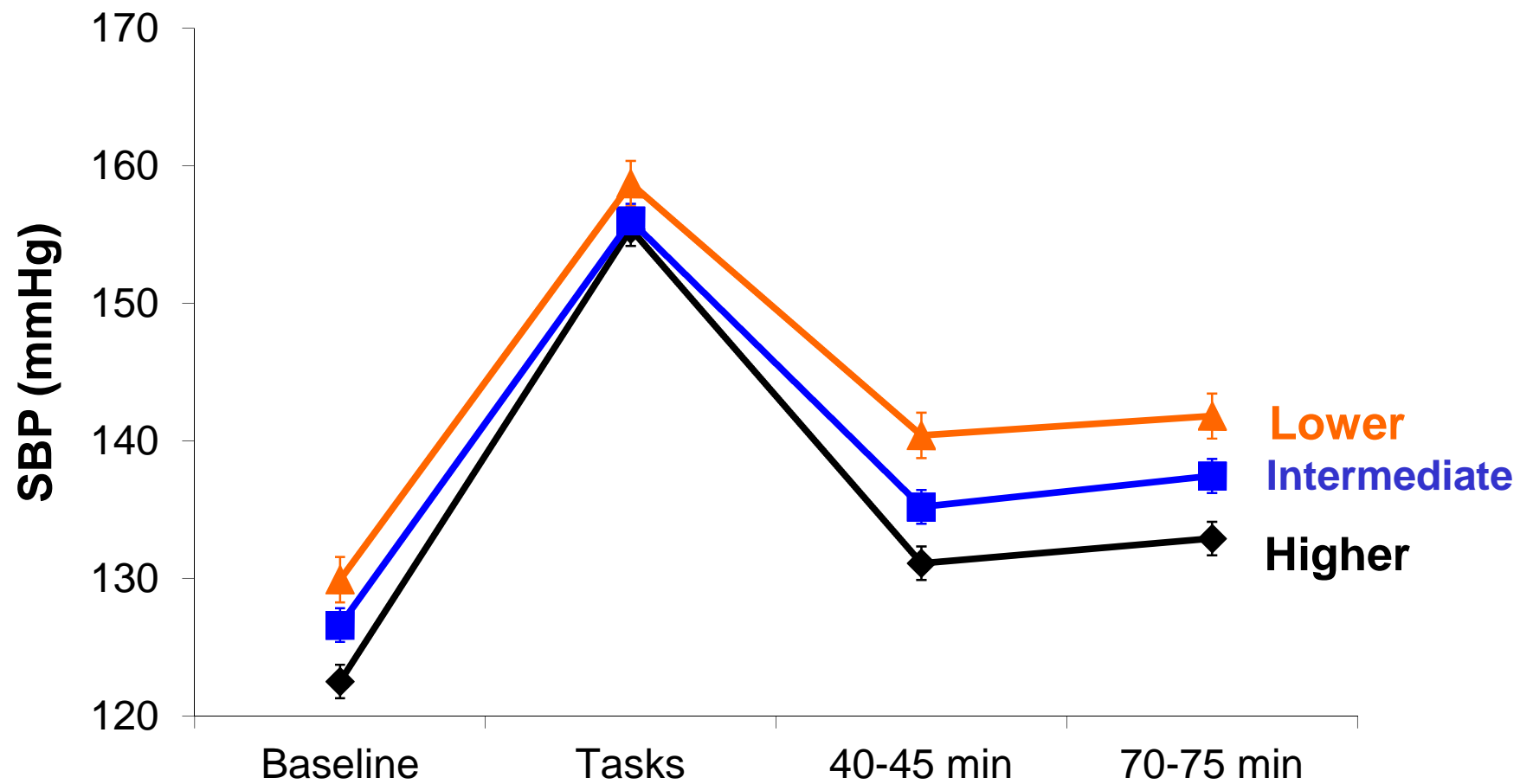


# Systolic BP by grade of employment

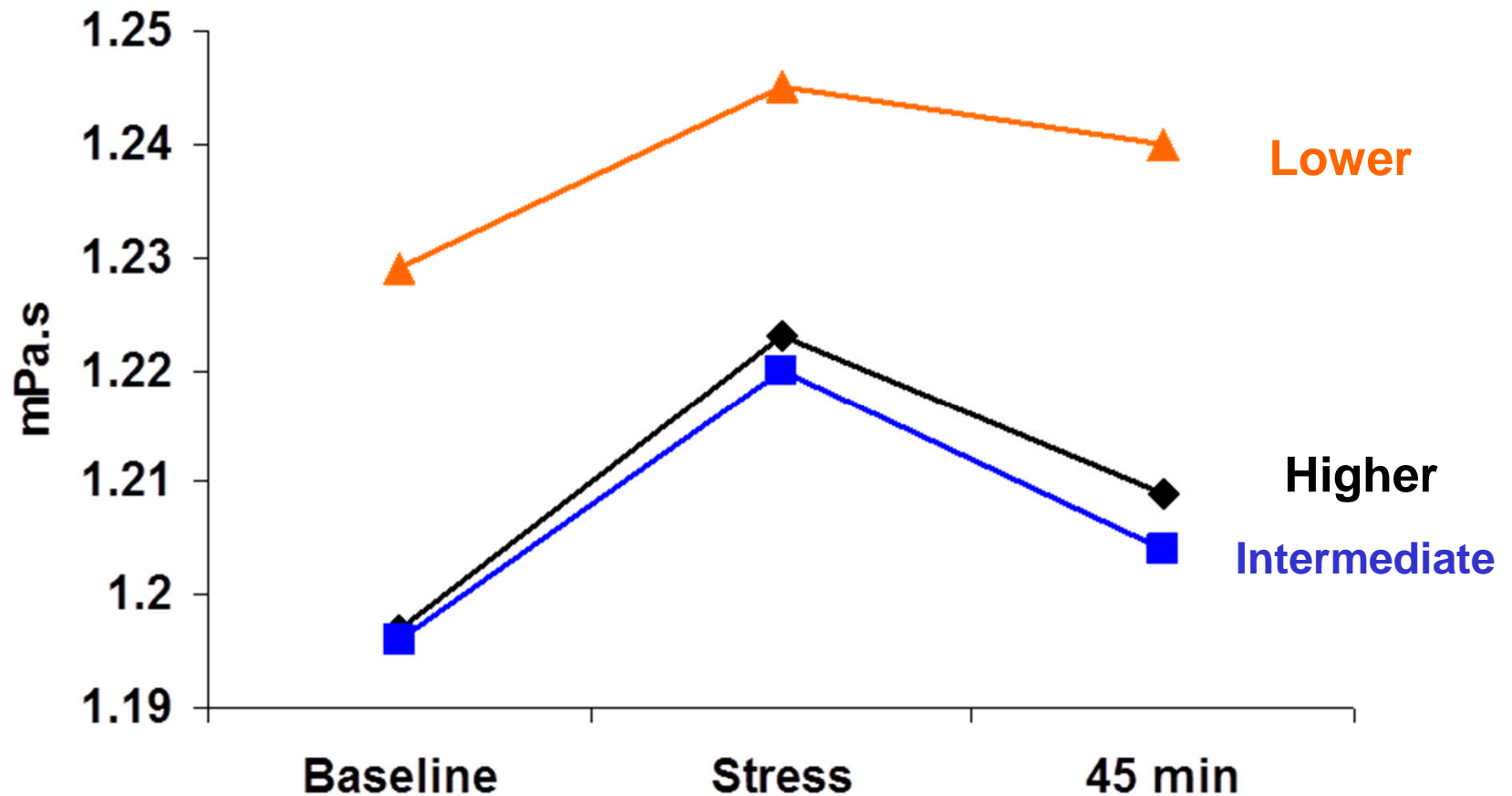




# Systolic BP by grade – heart scan study



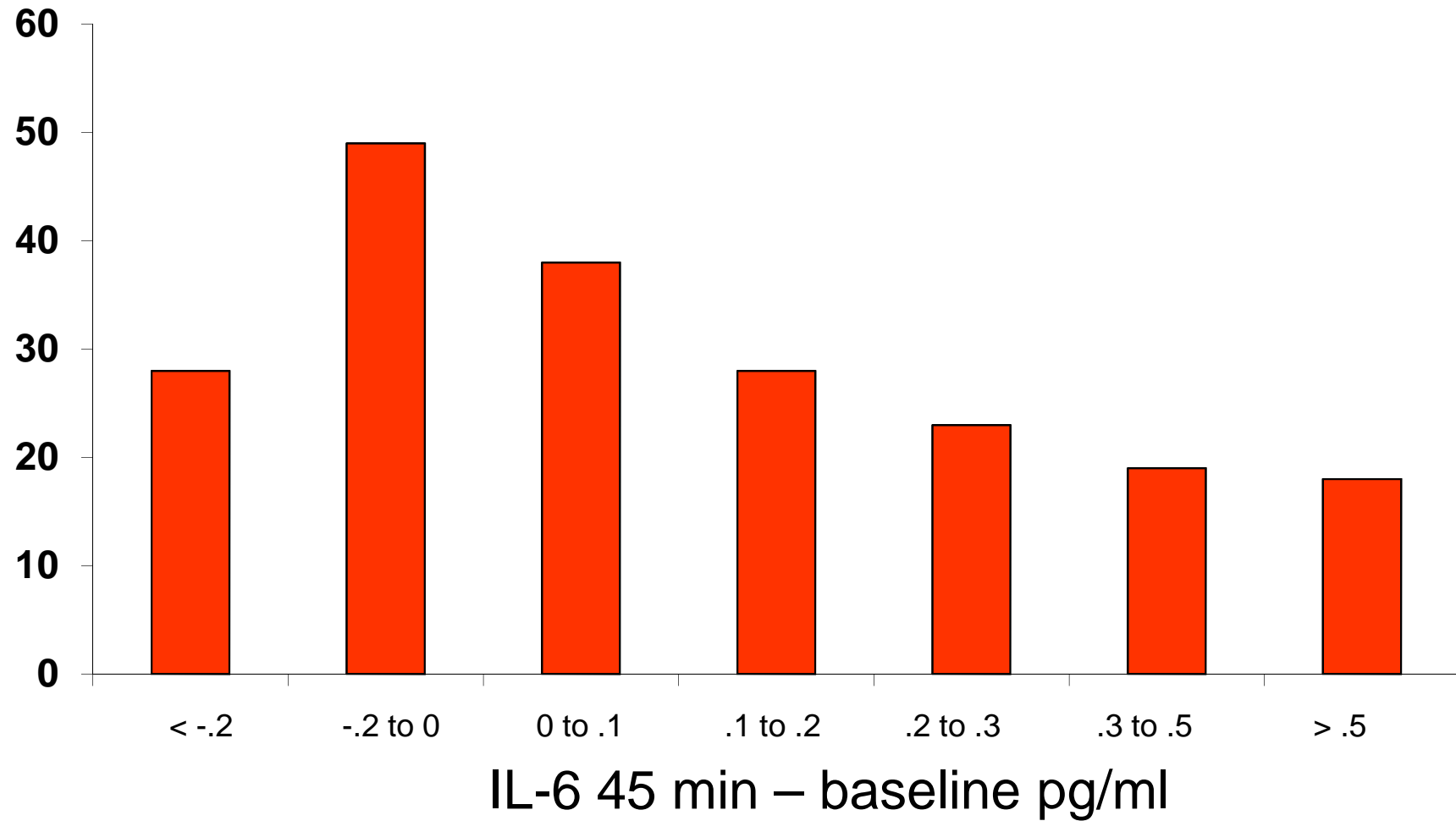
# Plasma viscosity by grade



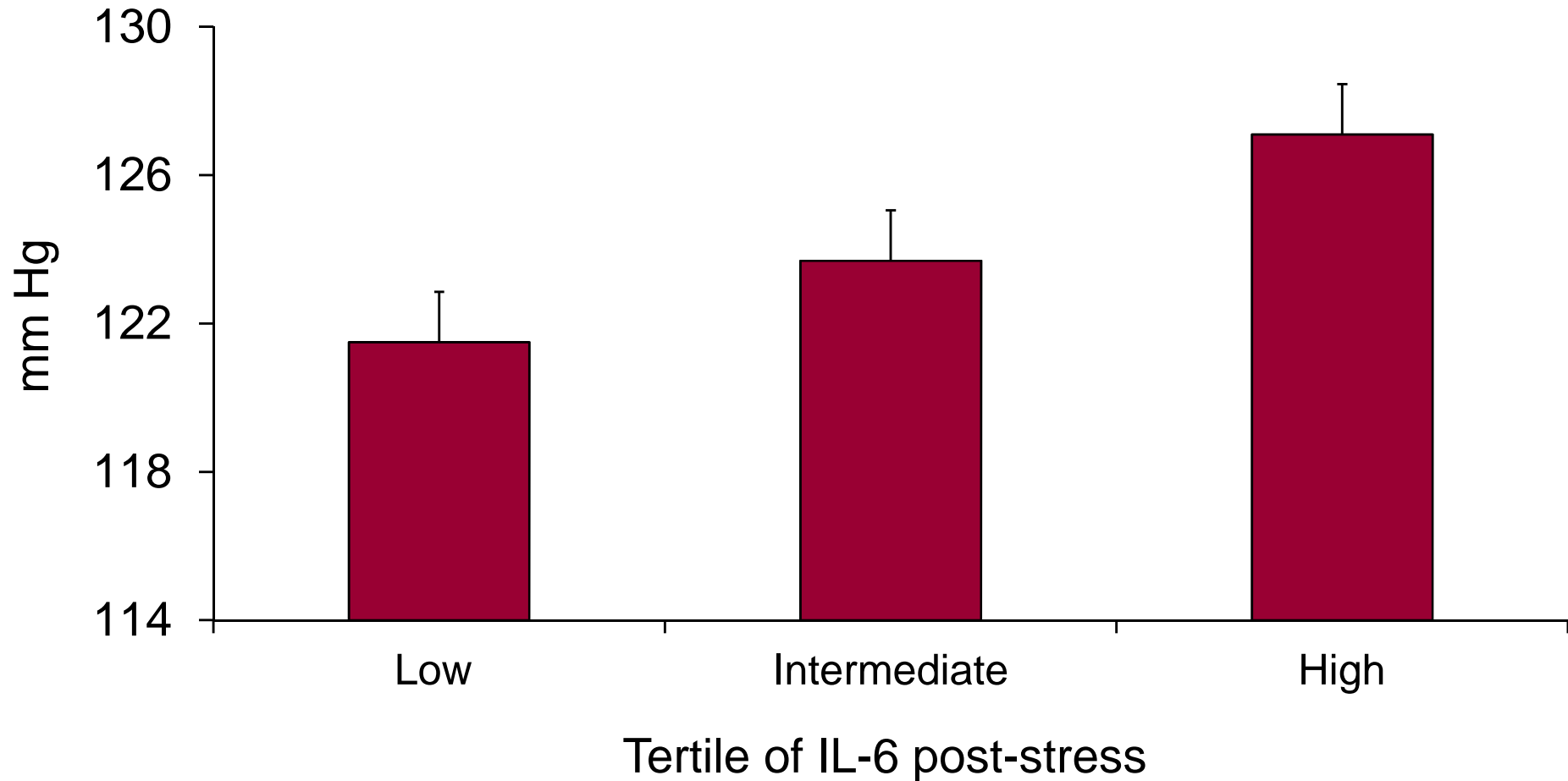
# Findings

- Psychosocial factors are associated with a broad range of health-related dynamic biological responses to mental challenge
- Impaired post-stress recovery characterises higher risk groups
- Individual differences in biological responses predict disease development

# IL-6 stress responses



## 3 year ambulatory systolic BP



Adjusted for T1 ambulatory BP, age, gender, grade of employment, medication, BMI, smoking, baseline IL-6, and SBP responsivity/recovery

Brydon & Steptoe  
2005, J Hypertension

# Heart scan study

## Phase 1 (2006-2008)

- 543 men and women from Whitehall II cohort
- No history of CHD and no diabetes or hypertension
- Measurement of psychobiological responses to colour/word and mirror tracing tasks
- Salivary cortisol assessment over a single day
- Assessment of coronary artery calcification using electron beam computed tomography

## Phase 2 (2009-2011)

- Repeat assessment of coronary artery calcification
- Accelerometry for 7 days

## Heart Scan Study

Coronary artery calcification (CAC) measured using electron beam computed tomography (EBCT)



**No CAC**



**High CAC**

# Predictors of progression in subclinical coronary artery disease

Factor	Odds ratio	95% C.I.
Age	1.05	1.01 – 1.10
Male sex	2.11	1.23 – 3.63
Systolic BP	1.25	1.01 – 1.56
Fibrinogen	1.47	1.20 – 1.81
Smoking	2.50	1.06 – 5.89
<b>Cortisol stress response</b>	<b>1.27</b>	<b>1.02 – 1.60</b>



# Combining studies to assess clinical health outcomes

- Do individual differences in stress-related responses predict incident cardiovascular outcomes?
- Combination of Psychobiology and Heart Scan studies
- 736 (94.4%) assessed in Phase 11
- Exclusion of participants with high resting BP during stress testing – 636 analysed
- Hypertension defined as BP  $\geq$  140/90 or medication

# Stress responses and incident hypertension

Exposure variable	Category	Incident hypertension (%)	Adjusted odds ratio	P
Systolic BP task reactivity	Low	16.5%	1	0.28
	Medium	22.3%	1.35 (0.78 – 2.32)	
	High	29.3%	2.02 (1.17 – 3.48)	
Systolic BP recovery	Low	19.4%	1	0.037
	Medium	25.1%	1.74 (1.03 – 2.94)	
	High	23.7%	2.06 (1.19 – 3.57)	
Fibrinogen task reactivity (women)	Low	21.9%	1	0.12
	Medium	18.5%	1.99 (0.83 – 4.98)	
	High	26.2%	2.64 (1.11 – 6.30)	

# Other investigations

- **Biological processes**

Endothelial function, vascular stiffness, telomeres, heat shock proteins, pericardial fat, infectious disease burden, corticosteroid receptor sensitivity, troponin, lipid metabolism

- **Psychosocial factors**

Work stress, financial strain, neighbourhood factors, early life adversity, marital roles, social isolation, self-esteem, depression, loneliness, attachment, positive wellbeing, optimism

- **Health and behavioural outcomes**

Diabetes, objective physical activity, metabolic syndrome

# Acknowledgements

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