Psychosocial biomarkers in studies of ageing

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Department of Epidemiology and Public Health
University College London
What are biomarkers:

- Body shape: weight, height, waist, BMI
- Physiology: blood pressure, lung function
- Blood analytes: cholesterol, glucose, C-reactive protein, interleukin (IL)-6, fibrinogen
- Physical function: grip strength, walking speed, chair rises
- Saliva, cheek cells: cortisol, DNA
- Hearing and vision tests
Purpose of biomarkers

- Measures of clinical (or preclinical) conditions
  - blood pressure, fasting glucose, lung function measures, body mass
Undiagnosed high blood pressure

Pierce et al, 2006
ELSA wave 2 report
Diagnosed and undiagnosed diabetes

Pierce et al, 2009
Diabetic medicine
Purpose of biomarkers

• Measures of clinical (or preclinical) conditions
  - blood pressure, fasting glucose, lung function measures, body mass

• Markers of processes involved in disease and disability
  - Waist circumference, inflammatory markers, fibrinogen, grip strength
Purpose of biomarkers

• Measures of clinical (or preclinical) conditions
  ➢ blood pressure, fasting glucose, lung function measures, body mass

• Markers of processes involved in disease and disability
  ➢ Waist circumference, inflammatory markers, fibrinogen, grip strength

• Non-specific indices of adaptation and resistance to future illness
  ➢ Cortisol, IGF-1, DHEA sulfate, vitamin D
Psychosocial biomarker research

Measurement of physiological processes that reflect psychological, social and economic experience

• Life stress exposure
  Work stress, financial strain, caregiving, neighbourhood factors, family conflict, life events

• Social participation factors
  Social networks, social support, social isolation

• Psychological factors
  Depression, anxiety, hostility, optimism, loneliness, positive well-being
Psychosocial biomarker research

Measurement of physiological processes that reflect psychological, social and economic experience

- Mediation of psychosocial influences on disease risk
- Markers of optimal functioning and well-being
- Corroboration of self-report differences:
  - Individual
  - Population
Psychosocial biomarker research

Measurement of physiological processes that reflect psychological, social and economic experience

- Cortisol
Some effects of high cortisol

Potentially damaging effects
- Increased lipid (LDL-cholesterol) in the blood
- Suppression of immune function
- Decalcification of bone
- Deposition of abdominal fat
- Damage to the hippocampus
- Muscle wasting
- Impaired reproductive function
Cortisol profile over the day

Cortisol in nmol/l

- Waking value
- Cortisol area under the curve
- Cortisol slope
- Cortisol awakening response

Wake +30 min 8.00-8.30 10.00-10.30 12.00-12.30 14.00-14.30 16.00-16.30 18.00-18.30 20.00-20.30 22.00-22.30
Cortisol and job strain

Cortisol waking response

Work day  Weekend

Kunz-Ebrecht et al, PNEC, 2004
## Cortisol awakening response – meta analysis

<table>
<thead>
<tr>
<th>Factor</th>
<th>Correlation</th>
<th>95% C.I.</th>
<th>N studies</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Job stress</td>
<td>0.061</td>
<td>0.012 – 0.110</td>
<td>22</td>
<td>0.045</td>
</tr>
<tr>
<td>General life stress</td>
<td>0.065</td>
<td>0.007 – 0.123</td>
<td>35</td>
<td>0.029</td>
</tr>
<tr>
<td>Depression</td>
<td>-0.026</td>
<td>-0.084 – 0.033</td>
<td>17</td>
<td>0.13</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.040</td>
<td>-0.032 – 0.112</td>
<td>22</td>
<td>0.27</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-0.148</td>
<td>-0.255 - -0.037</td>
<td>6</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Chida and Steptoe  
2009, Biol Psychol
Salivary cortisol and positive affect

8 samples (08:00 – 22:30)
Adjusted for gender, age, occupational grade, smoking, bmi, and GHQ

Steptoe et al, 2005
PNAS
Cortisol and coping study

- 740 men and women from the Whitehall II epidemiological cohort (age 60.9 ± 5.5 years)
- Salivary cortisol sampled 6 times over the day
- Psychological coping inventory identifies three broad strategies:
  - Problem engagement
  - Seeking social support
  - Avoidant coping
Cortisol and coping study

- Lower cortisol associated with:
  - Greater problem engagement ($\beta = -0.135$, $p = 0.003$)
  - More support seeking ($\beta = -0.093$, $p = 0.034$)

Independently of age, gender, SES, smoking, depression, and self-rated health

O’Donnell et al, 2008, PNEC
Psychosocial biomarker research

Measurement of physiological processes that reflect psychological, social and economic experience

- Cortisol
- Blood pressure
Stress and Hypertension

Sparrenberger et al 2009
J Hum Hypertension

<table>
<thead>
<tr>
<th>Study (n)</th>
<th>OR</th>
<th>CI 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case-control</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Acute</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radi 2005 8</td>
<td>0.37</td>
<td>(0.20-0.67)</td>
</tr>
<tr>
<td>Radi 2005 8</td>
<td>0.32</td>
<td>(0.12-0.89)</td>
</tr>
<tr>
<td><strong>Chronic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schnall 1990 18</td>
<td>3.09</td>
<td>(1.30-7.30)</td>
</tr>
<tr>
<td>Radi 2005 8</td>
<td>2.60</td>
<td>(1.15-5.85)</td>
</tr>
<tr>
<td>Radi 2005 8</td>
<td>3.20</td>
<td>(0.92-11.12)</td>
</tr>
<tr>
<td><strong>Affective response</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perez 2001 11</td>
<td>5.02</td>
<td>(2.25-11.19)</td>
</tr>
<tr>
<td>El-Shafei 2002 22</td>
<td>10.10</td>
<td>(3.03-33.72)</td>
</tr>
<tr>
<td><strong>Cohort</strong></td>
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<tr>
<td><strong>Acute</strong></td>
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<tr>
<td>Perini 1991 15</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Dorn 2007 16</td>
<td>1.48</td>
<td>(1.09-2.02)</td>
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<tr>
<td><strong>Chronic</strong></td>
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<td></td>
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<tr>
<td>Kahn 1972 20</td>
<td>1.62</td>
<td></td>
</tr>
<tr>
<td>Levenstein 2001 12</td>
<td>1.30</td>
<td>(1.00-1.60)</td>
</tr>
<tr>
<td>Nakanishi 2001 16</td>
<td>0.48</td>
<td>(0.31-0.74)</td>
</tr>
<tr>
<td>Feuvel 2003 17</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>Manzolo 2004 14</td>
<td>2.06</td>
<td>(1.01-4.26)</td>
</tr>
<tr>
<td><strong>Affective response</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sparrow 1982 13</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Everson 2000 21</td>
<td>3.22</td>
<td>(1.56-6.67)</td>
</tr>
<tr>
<td>Cozler 2006 9</td>
<td>1.20</td>
<td>(1.00-1.30)</td>
</tr>
</tbody>
</table>
Ambulatory and clinical BP

5 year risk of death in relation to ambulatory and clinic BP in 1114 older patients (65+ years)
From Burr et al, 2008
# Job stress and blood pressure

<table>
<thead>
<tr>
<th>Clinical/casual BP</th>
<th>Positive Associations</th>
<th>Null effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesana, 96; Kawakami, 98; Pieper, 89</td>
<td>Albright 92; Alterman, 94; Carrere, 91; Emdad, 97; Tarumi, 93; Greenlund, 95; Netterstrom, 91; Kivimäki, 07</td>
<td></td>
</tr>
<tr>
<td>Ambulatory BP</td>
<td>Cesana, 96; Harenstom, 88; Light, 92; Schnall, 94; Theorell, 91; van Egeren, 92; Steptoe 04</td>
<td>Knox 85; Steptoe 99</td>
</tr>
</tbody>
</table>
Ambulatory systolic pressure: working day

Adjusted for gender, age, occupational grade, smoking, bmi, and physical activity

J. Hypertension, 2004
Systolic BP and happiness – 3 year

Adjusted for gender, age, occupational grade, work at follow-up, smoking, bmi, GHQ. N = 160

P = .030
The Inverse Correlation Between Hypertension and Life Satisfaction: 16 European nations Aggregated into Quartiles

Blanchflower & Oswald
J Health Econ, 2008
Psychosocial biomarker research

Measurement of physiological processes that reflect psychological, social and economic experience

- Cortisol
- Blood pressure
- Inflammatory markers (C-reactive protein, fibrinogen, IL-6)
Interleukin 6

An ‘endocrine’ cytokine associated with
- Coronary heart disease
- Type 2 diabetes, insulin resistance
- Depression
- Disability

- Sensitive to acute and chronic psychosocial factors
Caregiver stress and plasma interleukin-6

Kiecolt-Glaser et al
*PNAS*, 2003
IL-6 and depressed mood

3024 men & women aged 70-79
Adjusted for gender, age, body mass, chronic illness, smoking, alcohol, medication

Penninx et al, *Biol Psychiat* 2005
IL-6 and cognitive impairment

4 year follow-up of 2632 men and women aged 70-79 years
Cognitive impairment, adjusting for baseline cognitive score, age, education, race, depression, alcohol, stroke and statins
• High inflammation RR: 1.66 (1.19 – 2.18)
• Low inflammation RR: 1.08 (0.89 – 1.30)

Yaffe et al
JAMA 2004
IL-6 and happiness

Adjusted for age, income, ethnicity, BMI, smoking, waist/hip ratio, employment, CES-D

Steptoe et al, 2008
Am J Epidemiol
Psychosocial biomarker research

Measurement of physiological processes that reflect psychological, social and economic experience

- Cortisol
- Blood pressure
- Inflammatory markers (C-reactive protein, fibrinogen, IL-6)
- Heart rate variability
Heart rate variability

Neural regulation of homeostasis

Sympathetic nervous system accelerates
Parasympathetic nervous system slows

Heart rate
Low heart rate variability

• Higher risk of death or recurrent events in patients with coronary heart disease (Atrami study, 1998)

• Incident CHD in apparently healthy cohorts (Liao, 1997)

• Future hypertension (Schroeder, 2003)

• Post-stroke mortality (Makikillio, 2004)
Low heart rate variability

- Poorer cognitive executive function (Hansen et al 2003)
- Less effective impulse control in children (Allen et al 2000)
- Reduced sleep efficiency (Hall et al 2004)
- Social isolation (Horsten 1999)
- Work stress (Vrijkotte 2000; Hemingway 2005)
- Depression (Rottenberg 2007)
Positive affect and HF-HRV

Adjusted for age, gender and β-blockers
Bhattacharyya et al, 2008; Psychosom Med
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