Neurobiological pathways linking SES and cardiovascular health

Pete Gianaros
Department of Psychiatry
University of Pittsburgh
Context for research

Recent findings

Next steps
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Next steps
Acute / Chronic Stress (Brain) vs Coronary Heart Disease (Body)
Functional MRI studies of neural regulation of cardiovascular stress reactions implicated in CHD risk

Structural MRI studies of brain morphology patterns associated with chronic psychosocial stress and other CHD risk factors
Cardiovascular reactivity & CHD risk

- Individual differences in reactivity are reliable, & associated with psychosocial risk factors for CHD (e.g., SES)\(^1\)
- Suspected role in CHD etiology\(^2-5\)
  - Hypertension
  - Ventricular hypertrophy
  - Atherosclerosis\(^5\)

\(^1\)Strike, Steptoe 2004 Prog Cardiovasc Dis 46: 337-47
\(^2\)Manuck et al 1983 Psychosom Med 45: 95-108
\(^3\)Chida, Steptoe 2010 Hypertension 55: 1026-32
\(^4\)Treiber et al 2003 Psychosom Med 65: 46-62
\(^5\)Jennings et al 2004 Circulation 110: 2198-2203

Mean carotid IMT (top) and 7-y progression (bottom) plotted by quartile of SBP reactivity\(^5\)
Psychosocial stressors and CHD risk factors
Paralimbic brain systems & cardiovascular stress reactivity

- Dual role in (i) processing stressful or emotional information and (ii) regulating peripheral physiology\(^1\)-\(^5\)

- Key regions
  - Cingulate
  - **Amygdala**
  - Orbital / Medial Prefrontal Areas
  - Insula

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\(^1\) Ulrich-Lai, Herman 2009 Nat Rev Neurosci 10: 397-409
\(^2\) Critchley 2005 J Comp Neurol 493: 154-66
\(^3\) McEwen, Gianaros (in press) Annu Rev Med

\(^4\) Gianaros, Sheu 2000 NeuroImage 47: 922-36

* Brodmann 1909 figure from Mesulam 2000
Amygdala & stress reactivity\textsuperscript{1-4}

- Cell complex important for assigning emotional and behavioral salience to sensory events\textsuperscript{1-2}

- Central nucleus regulates cardiovascular stress reactivity via reciprocal prefrontal and brainstem pathways\textsuperscript{3-4}

\textsuperscript{1}Sah 2003 Physiol Rev 83: 803-34
\textsuperscript{2}LeDoux 2000 Annu Rev Neurosci 23: 155-84
\textsuperscript{3}Saha 2005 Clin Exp Pharm Physiol 32: 450-6
\textsuperscript{4}Dampney 1994 Physiol Rev 74: 323-64
Amygdala activation to acute stressor predicts blood pressure reactivity

1Gianaros, Sheu, Matthews, Jennings, Manuck, Hariri 2008 J Neurosci 28: 990-99
Amygdala activation to emotional faces predicts preclinical atherosclerosis

1Gianaros, Hariri, Sheu, Muldoon, Sutton-Tyrrell, Manuck 2009
Biol Psychiatry 65: 943-50
Interim summary

SES?

mediation

Sunday, October 10, 2010
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SES is a multilevel & multidimensional construct that relates to CHD risk by multiple neurobiological pathways across life\textsuperscript{1-5}

\textsuperscript{1}Adler, Rehkopf 2008 Annu Rev Public Health 29:235-52
\textsuperscript{2}Braveman 2006 Annu Rev Public Health 27:167-94
\textsuperscript{3}Braveman et al 2005 JAMA 294:2879-88
\textsuperscript{4}Chen et al 2002 Psychol Bull 128: 295-329
\textsuperscript{5}Matthews, Gallo (in press) Annu Rev Psychol

*Figure from Gianaros, Manuck 2010 Psychosom Med 72: 450-61
Subjective socioeconomic status (sSES)\textsuperscript{1-5}

- Refers to perceived standing in a social hierarchy\textsuperscript{1}
- Typically anchored to educational, occupational, & monetary indicators at individual or parental level
- Lower sSES associated with:
  - poorer self-reported health\textsuperscript{1,2}
  - non-habituating cortisol reaction to stress\textsuperscript{1}
  - exaggerated rise in AM cortisol\textsuperscript{3}
  - metabolic syndrome\textsuperscript{4}
  - common cold susceptibility\textsuperscript{5}

\textsuperscript{1}Adler et al 2000 Health Psychol 19:586-92
\textsuperscript{2}Singh-Manoux et al 2005 Psychosom Med 67:855-61
\textsuperscript{3}Wright, Steptoe 2005 Psychoneuroendocrinol 30:582-90
\textsuperscript{4}Manuck et al 2010 Psychosom Med 72: 35-45
\textsuperscript{5}Cohen et al 2008 Health Psychol 27:268-74
'Think of this ladder as representing where people stand in the United States. At the top of the ladder are the people who have the most money, most education, and most respected jobs. At the bottom are the people who have the least money, least education, and least respected jobs or no job. The higher up you are on this ladder, the closer you are to the people at the very top, and the lower you are, the closer you are to the people at the very bottom. Where would you place yourself on this ladder? Please, place an “X” on the rung where you think you stand at this time in your life, relative to other people in the United States.'

1Adler et al 2000 Health Psychol 19: 586-92
Question: Is subjective childhood SES associated with amygdala reactivity to threatening or ambiguous emotional facial expressions?

Gianaros, Horenstein, Hariri, Manuck, Matthews, Cohen 2008
Potential neural embedding of parental social standing.
Rationale

• Lower childhood SES may increase sensitivity to social threats and bias interpretation of ambiguous information as threatening\textsuperscript{1-3}

• Increased threat sensitivity may relate to stress responses that raise risk for ill health\textsuperscript{4-5}

• If lower childhood SES increases sensitivity to direct or ambiguous threats, then lower childhood SES may predict increased amygdala reactivity to threatening and / or ambiguous social stimuli

• Amygdala expresses developmental plasticity, is sensitive to emotionally salient & ambiguous information, & regulates stress reactivity\textsuperscript{6-8}

\textsuperscript{1}Chen, Matthews 2001 Ann Behav Med 23:101-11
\textsuperscript{2}Chen et al 2002 Psychol Bull 128:295-329
\textsuperscript{3}Taylor et al 2004 J Pers 72:1376-93
\textsuperscript{4}Hertzman 1999 Ann NY Acad Sci 896:85-95
\textsuperscript{5}McEwen, Gianaros 2010 Ann NY Acad Sci
\textsuperscript{6}McEwen 2007 Physiol Rev 87:873-904
\textsuperscript{7}Pollak 2005 Dev Psychopathol 17:735-52
\textsuperscript{8}Whalen 1998 Curr Dir Psychol Sci 7:177-88
Protocol (n = 33 healthy undergraduates)
Lower childhood sSES predicted greater amygdala reactivity to threatening faces*

*Persisted after control for sex, ethnicity, self-mastery, optimism, neuroticism, extraversion, agreeableness, depressive symptoms, parental education, & participants’ perceptions of their own sSES (L amyg $\Delta R^2=0.204$, $F[1,21]=10.9$, $p=0.003$; R amyg $\Delta R^2=0.152$, $F[1,21]=7.4$, $p=0.01$.

Question: Is ‘objective’ childhood SES associated with corticostriatal activation or functional connectivity evoked by processing rewarding stimuli?

Rationale

• Socioeconomic disadvantage experienced in early development predicts ill health in adulthood\(^1\)-\(^2\)

• Lower parental education in particular predicts health-impairing adult behaviors, including tobacco & alcohol dependencies\(^3\)-\(^6\)

• These behaviors depend on corticostriatal brain systems that (i) show developmental plasticity & early vulnerability, (ii) process reward-related information, & (iii) regulate impulsive decisions and actions\(^7\)-\(^10\)

• Corticostriatal functionality in adulthood may thus covary directly with parental education

\(^1\) Power, Hypponen et al. 2005 Int J Epidemiol 34: 335-44
\(^3\) Galobardes et al. 2006 Ann Epidemiol 16: 91-104
\(^5\) Fergusson et al. 2007 Addiction 102: 475-82
\(^6\) Melchior et al. 2007 Am J Epidemiol 166: 966-74
\(^7\) Haber, Knutson 2010 Neuropsychopharmacology 35: 4-26
\(^8\) Chambers et al. 2003 Am J Psychiatry 160: 1041-52
\(^9\) Ernst, Fudge 2009 Neurosci Biobehav Rev 33: 367-82
Protocol (n = 75 healthy adults, aged 31-51)

Higher parental education predicted greater activation of the perigenual anterior cingulate cortex (pACC; Brodmann Area [BA] 32) and lateral prefrontal cortex (LPFC; BA45) to stimuli signaling monetary gains compared with monetary losses (Panel A), along with greater activation of the dorsomedial prefrontal cortex (dMPFC; BA10) and inferior parietal cortex (IPC; BA39) to stimuli signaling monetary gains compared with a control condition (Panel C). Results were attained at a whole-brain corrected statistical thresholds implemented in mixed-effects parametric analyses with covariate control for adult educational attainment. Participants in the higher parental education group had a biological mother or father who attained a post-secondary or higher degree. Participants in the lower parental education group did not have a biological mother or father who attained a post-secondary or higher degree.
Higher parental education predicted a comparatively stronger directional (effective) connectivity from the dorsomedial prefrontal cortex (dMPFC, BA10) to the ventral striatum, as modulated by positive feedback stimuli signaling monetary gains. Variables used for covariate adjustment by multiple regression were participants’ own (adult) educational attainment, age, sex, family income, community-level socioeconomic position, alcohol use, depressive symptoms, and dispositional reward responsiveness.
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• Are neural correlates of childhood and adult SES relevant for predicting mental or physical health outcomes, particularly through stress-related or other pathways? If so, can or should we develop brain-based targets for intervention?

• Would longitudinal data help determine the temporal ordering of SES variables and structural or functional brain phenotypes that may relate to health across the lifespan?

• What is subjective socioeconomic status (sSES), and why does it vary with health-related outcomes ‘over-and-above’ conventional (‘objective’) SES indicators?
Socioeconomic status and the developing brain

Daniel A. Hackman and Martha J. Farah

Center for Cognitive Neuroscience, Department of Psychology, University of Pennsylvania, 3720 Walnut Street, Room B51, Philadelphia, PA 19104-6241, USA

Effects of socioeconomic status on brain development, and how cognitive neuroscience may contribute to levelling the playing field

Rajeev D.S. Raizada* and Mark M. Kishiyama

1. Naumkin Institute for Computational Science, Dartmouth College, Hanover, NH, USA
2. Helen Wills Neuroscience Institute, University of California at Berkeley, CA, USA

Socioeconomic status and the brain: mechanistic insights from human and animal research

Daniel A. Hackman, Martha J. Farah and Michael J. Meaney
Thank you!

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