

Developmental Origins of Health and Disease (DOHaD) Preconference:

Fundamental concepts in DOHaD and emerging research on later-life interventions to remediate and redirect unhealthy lifecourse trajectories induced by early life adversities

The systematic study of early life influences on adult mental and physical health gained momentum a half century ago, with a focus on the biological and behavioral consequences of a range of adverse pre-natal and early life exposures. Early life adversities (ELAs) come in many forms, including poverty, life in depriving orphanages, nutritional deficiency in utero and beyond, deficiencies in parental nurturing, various forms of maltreatment, and loss of a parent or other attachment figure. Human and animal research on the Developmental Origins of Health and Disease (DOHaD) has established that ELAs engender a liability for ill health. The DOHaD field promotes scientific exploration of early human development in relation to chronic disease in later life, the search for causal mechanisms that account for these links, and seeks to promote the development and application of public health strategies to prevent chronic disease.

While there are interventions for children that offset some of this risk, there are fewer interventions to counter this liability in adults. A coordinated effort to develop interventions for adults is urgent. The Reversibility Network is a *research network on later-life interventions to reverse effects of early life adversity (ELA)*, focusing on identifying opportunities for later-life reversibility/remediation of phenotypes associated with ELA. Established with funding from the US National Institute on Aging and the UK Economic and Social Research Council/Biotechnology and Biological Sciences Research Council, the network brings together senior and junior scientists to foster and facilitate the *interdisciplinary* research needed to stimulate rapid advances in this field. Overall goals are to (a) promote needed increases in scientific knowledge regarding the array of processes and pathways through which different ELAs (e.g., low socio-economic status [SES]; stressful experiences, including social isolation, poor parent-child relationships [e.g. child neglect/abuse] or other violence; poor maternal diet, body composition and lifestyle) may similarly or differentially impact later life health and well-being, and (b) leverage evidence from this body of research to promote development and evaluation of novel later-life interventions to remediate/redirect risk trajectories and processes related to ELAs.

Through meetings, pilot funding, and scientific outreach, the Reversibility Network is advancing research addressing three major challenges, hoping to ready the field to explore the potential for interventions in mid-later life to address the health risk associated with early life adversity (ELA). First, we examine the relative strengths and limitations of prospective vs. retrospective measures of ELA and consider efforts to improve upon retrospective measures and to use those measures to distinguish subgroups for whom tailored interventions might be appropriate. Second, we examine pathways (immune, epigenetic, metabolic, neural,

microbiome) through which ELAs become biologically and psychologically embedded and consider whether distinct dimensions of ELA exert differential impacts on physiological and neurobiological systems. Third, we examine how emerging research on neural and behavioral plasticity – particularly in mid-later life -- might be leveraged to design interventions to reverse or compensate for the persistent risk associated with ELA.

Objectives of the preconference: This preconference will introduce participants to the foundations of the DOHaD field, summarizing evidence underscoring the importance of ELA in adult health. Building on work in the Reversibility Network, new approaches to conceptualizing and measuring ELA will be presented, along with the relative advantages and disadvantages of retrospective and prospective ascertainment of ELA. Additional presentations will illustrate research seeking to elucidate causal pathways linking ELA and later life health, as well as potential strategies for targeting and ameliorating risk mechanisms along these pathways. Finally, participants will be introduced to research resources for DOHaD and reversibility research relevant to psychosomatic medicine.

Participants can expect to gain knowledge of:

- key principles of DOHaD and its relevance to psychosomatic medicine
- fundamental challenges in the field related to measurement, causal pathways, and the design of interventions
- available resources for advancing the field

APS DOHAD/REVERSIBILITY PRECONFERENCE AGENDA

March 6, 2019

8:30 am – 4:45 pm

Chair(s): Gerry Giesbrecht (University of Calgary) & Lis Nielsen (National Institute on Aging)

8:30 am – Introduction to Workshop – 10 min – Lis Nielsen

8:40 am – SESSION 1: Introduction to DOHaD and the Reversibility Network

- 8:40 - *History of DOHaD and introducing a Lifecourse Model*
– Keith Godfrey (University of Southampton) – 15 minutes
- 8:55 - *DOHaD: a psychosomatic medicine perspective*
– Gerry Giesbrecht – 15 minutes
- 9:10 - *The NIA/ESRC/BBSRC Network on Reversibility of Early Life Adversity Effects on Later Life Health* – Teresa Seeman (UCLA) - Orientation to network goals and how talks relate to the developmental model/conceptual model – 15 minutes

9:25 am – SESSION 2: Measuring Early Life Adversity

- 9:25 - *Prospective vs. Retrospective Assessments of Early Life Adversity: Links to Adult Health Outcomes*
– Jessie Baldwin (Kings College London) – 20 minutes
- 9:45 - *Dimensions of Early Life Adversity: Neural and Psychological Assessments*
– Margaret Sheridan (UNC Chapel Hill) – 20 minutes
- 10:05 – **DISCUSSION** – 20 minutes

10:25 – BREAK – 20 minutes

10:45 – SESSION 3: Pathways Linking Early Adversity to Later Life Health

- 10:45 - *Mental and Physical Health Consequences of Childhood Adversity – Neural, Psychological and Inflammatory Pathways*
– Keely Muscatell (UNC Chapel Hill) – 20 minutes
- 11:05 - *Epigenetic and Microbiome Related Pathways*
– Keith Godfrey – 20 minutes
- 11:25 - *Biological pathways: Leveraging Cohort Studies*
– Teresa Seeman – 20 minutes
- 11:45 - *Sleep Disruption: Insights from Human Studies*
– Andrew Fuligni (UCLA) – 20 minutes
- 12:05 - *Sleep Disruption: Insights from Animal Studies*
– Yuichi Makino (Harvard) – 20 minutes
- 12:25 - **DISCUSSION** – 20 minutes

12:45 – LUNCH BREAK – 1 hour

1:45 – SESSION 4: Reversibility – New Approaches to Intervention in Later Life

- 1:45 – *Reversibility Interventions – Principles, Outcomes, Examples from Exercise Research*
– Kirk Erickson (U Pittsburgh) – 20 minutes
- 2:05 - *Nutritional and Exercise Interventions and Later Life Cognition*
- Terrence Forrester (University of the West Indies) – 20 minutes
- 2:25 - *Mindfulness Interventions: Differential Outcomes as a Function of Early Adversity*
– Eric Loucks (Brown) – 20 minutes
- 2:45 – **DISCUSSION** – 20 minutes

3:05 – Introduction to Breakout Groups – 5 minutes

3:10 – BREAK – 20 minutes

3:30 – SESSION 5: BREAKOUT SESSIONS – 1 hour

- *Mining existing datasets to understand pathways and identify targets for reversibility intervention*
– Teresa Seeman, Keith Godfrey, Andrew Fuligni, Keely Muscatell
- *Measures of ELA and recommendations for their use*
– Margaret Sheridan, Jessie Baldwin
- *Intervention design: a focus on plasticity and mechanisms of change*
– Eric Loucks, Kirk Erickson, Terrence Forrester, Yuichi Makino

4:30 – Wrap-up, Next Steps

4:45 – END