

**Research Network on Later Life Interventions to Reverse
Effects of Early Life Adversity**

MEETING SUMMARY

**Rockefeller University
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Meeting of The Research Network on Later Life Interventions to Reverse Effects of Early Life Adversity

Session 1: Introductions and Welcome from NIA and Network Team

The first session provided an overview of the Network's conceptual model and goals, as well as goals and potential topics of discussion for the first meeting. On behalf of the Network coordinators, Dr. Teresa Seeman described five perspectives on preventative intervention and the life course. The first perspective focused on life course programming; that the developing fetus is programmed by early exposures and the fetus's response is based on predictions of later environments. The second perspective emphasized multiple pathways leading from early adversities to intermediate and more distal health outcomes. The third perspective asked, what is the accumulation of health risk over the life course and how do those risks accumulate with differential exposures? The fourth perspective focused on interventions that open windows of plasticity. Specifically, how can windows of plasticity be opened using interventions to improve outcome? The final perspective examined the bidirectional role of environmental influence - how people are both influenced by their environments and are also influencing their environments.

Next, Dr. Keith Godfrey discussed life course programming and health risks. Without interventions, the risk of disease increases throughout life. Interventions early in life may increase an individual's functional capacity, as well as improve responses to stressful challenges, but early in development may not be the only time when interventions are successful. Adolescence may be a potential window of time when enhanced neural plasticity can be leveraged. Finally, later in adulthood may provide another opportunity for interventions to mitigate the effects of early life adversity or reset disease risk. Looking solely at early life environments, without understanding accumulation of health risk or corresponding later life outcomes, may hinder progress towards reducing disease risk. Early life cues can influence the development of a phenotype that is normally adapted to the environmental conditions of later life. However, when the predicted and actual environments differ, mismatch between the individual's phenotype and the conditions later experienced can have adverse consequences for reproductive fitness and health.

Dr. Christine Power and Dr. David Reiss provided a general overview of health trajectories and mediating pathways. Accumulations of health risk and health trajectories are in a state of constant flux relative to different influences at different points in time. The pathways trajectory is much simpler than the health accumulation model and recognizes that circumstances early in life can have an impact on health later in life by affecting other outcomes (e.g. behavioral, social) that in turn link to later health. Early life adversities take many forms (e.g., neglect, threat, deprivation, etc.) and a lot of these adversities co-occur. Risk can be transmitted inter-generationally; it may be that parent-child relationships are particularly promising for intervention strategies for multiple forms of risks.

Importantly, there are many pathways through which early life adversity can link to adult outcomes; not solely via neurocognitive function, the topic of this meeting. In addition to neurocognitive function, the network is interested also in physical health, growth and development, social identity, and emotional health. Further, it is important to take into

account different intergenerational effects in the environment, functional capacities a person acquires early in life, and secondary causal pathways (e.g., social identity, health behavior, epigenetic changes, micro biome, etc.) when linking early adversity to later life outcomes. Dr. Reiss presented a modification of the well known Scarr and McCartney model that illustrated how genetic factors may confound apparent environmental effects, including those of severe adversity and also of the very substantial impact of the developing person's impact on his or her environment.

Finally, Dr. Bruce McEwen discussed the social environment and links to health outcomes. He emphasized the important idea that the same mediators (e.g., cortisol) that help an individual adapt, can also cause serious damage when overused or dysregulated. It is well known that many stressors in life (e.g., traumas, major life events) do negatively impact health outcomes, but it is the daily grind and everyday stress that people experience, and their reaction to these daily stressful experiences (e.g., not sleeping enough, eating too much, drinking, not exercising), that creates the allostatic load and consequently our bodies' response to stress. With regards to interventions, the challenge is to find interventions to safely open windows of plasticity, without unintended negative consequences. Examples of possible interventions include changing sustained patterns of maladaptive behavior, regular physical activity, mindfulness-based stress reduction, and social support. However, although interventions can produce changes in cognitive decline, at the level of a population, it may be that better understanding of which individuals are sensitive or resistant to changes will improve outcomes from interventions further. Specifying pathways from adversity to aging –related decline may allow for better tailored interventions.

Session 2: Mechanisms that may account for the association of early life adversity with adult health outcomes

The second session, led by Dr. Power and Dr. Godfrey, emphasized the important findings in neurobiology and behavioral science relating to early life adversity and later life physiological or behavioral dysregulation and disease risk. The first presenter, Dr. Margaret Sheridan, discussed potential mechanisms linking adversity to neural structure and function. The current most common model of the impact of early life adversity on health risk is the Adverse Childhood Experiences (ACEs) cumulative risk model where the odds ratio for disorder onset increases as the number of childhood adversities increases. As a linear, cumulative risk model, ACEs does not account for the variety of pathways through which adversity might come to impact aging outcomes, which is a major problem and not addressed within the current literature. Further, the ACEs model, which emphasizes stress exposure as the primary mechanism through which adversity shapes health risk, ignores other impactful exposures (e.g., cognitive stimulation). Adding neurobiology as an intermediate step between the exposure and health outcome can provide more evidence for specific pathways and identifying pathways may lead to increasingly specific interventions, as urged in Session 1.

Dr. Sheridan presented a model: the “Deprivation and Threat” model (Sheridan & McLaughlin, 2014), which proposes two separable dimensions of adversity. One dimension, threat, is characterized by exposure to trauma and another, deprivation, is characterized by lack of exposure to cognitive stimulation. These dimensions cut across classically described

“exposures” such as maltreatment or poverty. Indeed, there are certain types of exposure, by their very nature, that suggest that an individual is exposed to a certain type of trauma. But some types of adversity (e.g., poverty) confer risk for certain types of exposures (e.g., deprivation), but this does not mean the individual will necessarily encounter that exposure. Finally, Dr. Sheridan noted that complex exposures are the norm and not the exception, but that within complex exposures, these dimensions could be separately measured. It was suggested by the group that this model could be enhanced by indicating the frequency or proportion of actual experiences to these exposures, severity, life course timing, role of cognitive appraisal, and by adding other important dimensions (e.g., prenatal experiences).

Dr. Sheridan then presented several findings demonstrating a neural basis for separating early adversity into different dimensions or pathways. Early brain development is characterized by proliferation and pruning of synaptic connections, and Dr. Sheridan suggested that this process may be affected by deprivation, yielding one mechanism through which adverse experiences could shape neural structure and function. For example, institutionalization early in life is associated with smaller cortical volume and decreased grey matter thickness. This decrease in cortical thickness mediates the link between exposure to institutionalization and inattention/hyperactivity. Similarly, parental education has been associated with differences in prefrontal cortex function, mediated by linguistic exposure in the home, and parental SES also predicts the persistence of ADHD symptoms from early to middle childhood, cortical thickness, and cortical surface area. Dr. Sheridan reported that a significant link between maltreatment and amygdala activation and cortisol response to stress in children persists even after controlling for SES – demonstrating that these two different types of exposures, although correlated, can be teased apart. These studies provide preliminary support for independent effects of deprivation and threat on neural structure and function.

The second presenter, Dr. Sara Jaffee, presented work on examining marriage as a turning point in reducing men’s antisocial behavior. Many studies have reported that married men engage in significantly less antisocial behavior than unmarried men, with researchers proposing that this outcome could be due to increased social bonds between partners or changes in daily routines or identity. Alternatively, it could also be that being married doesn’t necessarily make you less antisocial but that less antisocial men are more likely to be attractive mates. Dr. Jaffee presented different quasi-experimental and statistical methods (e.g., matching by design, propensity score matching) to examine this question of causal mechanisms. Using the nationally representative Adolescent Health (Add Health) Dataset, which followed adolescents from 1995 to 2008, a range of approaches were used to test the association between marriage and antisocial behavior. Accounting for selection bias (propensity score matching, within-individual change models, sibling models), all models demonstrated significantly less antisocial behavior by married men than unmarried men. Even adjusting for a range of potential confounders, marriage on average reduces the rate of men’s antisocial behavior by approximately 50%. These results extend to unmarried men who are cohabitating. Among married men, higher-quality marriages are more strongly associated with reductions in antisocial behavior than lower-quality marriages, but marital quality does not moderate the effect of cohabitation on reducing men’s antisocial behavior. These results tie to early life adversity as antisocial behavior is a frequent consequence of early life adversity and marriage may disrupt this

trajectory. In other studies, supportive marriages also interrupt the cycle between a mother's own early adversity and her later poor parenting. These results suggest that marriage (or quality cohabiting partnerships) may possibly serve as a protective or ameliorative factor. Although interventions to promote marriage may not be feasible, being unmarried may serve as a risk factor for intervention identification; establishing interventions focused on social bonds or positive communication may be similarly effective in reducing antisocial behavior in men.

The third presenter, Dr. Godfrey, discussed some findings pertaining to epigenetic mechanisms and the microbiome. At various time points during early development (conception, fetal life, infancy, childhood), nutritional and other environmental variations (within the normal range) alter development with lasting effects on later health and chronic disease risk. Studies have consistently shown that maternal under-nutrition, obesity, GDM, and stress are major drivers for epigenetic changes. Dr. Godfrey's team is now using novel epigenetic biomarkers to find parallels between drivers of change and outcomes of interest. One study found associations between large thalami and higher verbal IQ in children ages 4-7, with associations between basal ganglia injury and lower verbal IQ at 4 years. Examining HES1 function (important transcription factor in neural development) higher percent methylation of CpG2, 5, & 7 at birth was associated with higher WPPSI IQ at age 4. Similarly, higher percent methylation of CpG5 & 7 at birth was associated with higher working memory capacity at age 6. Finally, higher percent methylation of CpG7 at birth was associated with lower externalizing behavior (ITSEA) at 12-months of age. Aspects of maternal nutrition were associated with some of these findings and other similar factors like stress will need to be examined in conjunction. Finally, some work in Singapore examining the microbiome early in development was discussed. Findings indicate that even as early as day 3, some infants have very advanced (anaerobic) types of microbiome, whereas other infants have slower progressing bacteria; rate of development of a more anaerobic microbiome was found to predict later adiposity. Overall, societal interventions may be more important but personalized interventions using the microbiome may become more useful over time and it may be possible to engineer different bacteria with different functionalities. A limitation to this work is that although there are persisting patterns of microbiome across time, there are a variety of factors (diet, medications, microstructure of the bowel) that may alter the trajectory or functionality of the gut bacteria.

Finally, Dr. Andrea Danese presented his work on longitudinal studies of cognitive impairment in victimized children. The goal of this research is to add a methodological layer on top of the association between child victimization and cognitive deficits. Past studies have reported associations between early life stress and brain function, but the interpretation and implications have been disputed across many scientific fields. There are three main aspects to this debate. First, it is hard to establish causality. Some outcomes are stable over time and cross-sectional group differences in victimized vs. non-victimized individuals may not reflect the causal role of child victimization, but rather a pre-existing condition. Victimization happens in the context of many other adversities and experiences and utilizing longitudinal data could potentially tease apart confounding variables. Second, studies may not be representative or reproducible. Many studies use convenience or extreme samples and the results may not apply to the general population. Finally, not all methods may have the same predictive value or clinical significance. Brain imaging

studies are extremely important to understand the fine-grained biological associations with victimization, but these types of studies may not be informative to predict everyday functioning.

Dr. Danese presented two studies, one longitudinal birth cohort (UK E-Risk Longitudinal Twin Study) and one retrospective (NZ Dunedin Multidisciplinary Health and Development Study), to try and examine the associations between child victimization and cognition. Both cohort studies assessed IQ early in life (age 5 in E-Risk Study and age 3 in Dunedin Study), had an observational period for poly-victimization during childhood, and assessed cognitive functioning and IQ later in life (age 18 in E-Risk Study and age 38 in Dunedin Study). When examining unadjusted values, poly-victimized children demonstrated lower IQ and cognitive functioning in later life than non-victimized children. However, when adjusting for measures of cognition assessed prior to the observational period for victimization - IQ at age 5 (E-Risk Study) or IQ at age 3 and Maternal IQ (Dunedin Study) - the effect sizes for the association between victimization and IQ/cognitive scores are markedly reduced. Dr. Danese argued that these results strengthen the evidence for cognitive deficits in individuals with a history of childhood victimization, but also strongly challenge the conventional causal interpretations since differences between victimized and non-victimized children were markedly attenuated when considering pre-existing cognitive vulnerabilities. These results are not consistent with the animal literature for several potential reasons (i.e., differences in life histories and brain development timing across species, individual differences in human studies, universal interventions in human studies), but do emphasize the need to adopt a more circumspect approach to causal inference in human studies.

Session 3: Gene expression mechanisms linking early adversity with adult health – programming or reversible predisposition?

The third session was the keynote presentation by Dr. Michael Meaney. The presentation reviewed epigenetic studies that demonstrated possible evidence of markers of early adversity and reversibility in both rodent and human studies. Many past studies have reported differences in biological mechanisms of offspring as a function of maternal behavior. Dr. Meaney argued that there is good evidence that both prenatal and postnatal negative effects can be reversed with enrichment (enrichment being a total package of enhanced stimuli, complexity of the environment, increased physical activity, and increased social interaction). It is possible that the enrichment effect is masking for some pre-existing effect (predictive adaptive response), rather than necessarily reversing it. For example, a group in Spain examined the effects of enrichment in animals that were genetically disposed to certain outcomes; genetic characteristics moderated the effect of enrichment in this study. Dr. Meaney stressed throughout the presentation that information on the mechanism by which enrichment may or may not influence outcomes is limited, but there is very compelling data at the level of function. The lack of mechanistic understanding may also be in part due to the nature of recovery. Enrichment may not be reversing the effects, per se, but could be an active compensatory mechanism.

Next, epigenetics and its role in downstream effects were discussed. Epigenetics is the mechanism in which variation or multiple functional genomes from a common DNA

template are produced. Past work has demonstrated that maternal caregiving behaviors, such as licking and grooming, lead to intercellular changes in hippocampal neurons; these effects appear to sustain long-term differences in gene transcription and may account for how these early experiences are embedded within the organism across the lifespan. Examining human studies, there are significant associations between glucocorticoid receptor expression and suicide, where glucocorticoid receptors are influenced by history of reported abuse as well as degree of methylation. Additionally, amongst US combat veterans, measures of methylation are significantly associated with clinical symptomology. Therefore, it is possible that the human epigenome could reflect variations in the quality of the early social environment. Using a small sample from the Nurse Family Partnership study, blood samples from the 27-year-old offspring of mothers from the intervention study were examined and significant associations between DNA methylation and abuse were found. Looking at another cohort study in Singapore, the variation in neonatal epigenomes was best, but not uniquely, explained by gene by environment (GxE) interactions. In on-going and future studies, the question is if the researcher can take the epigenetic information and interrogate the biology, it may be possible to see if specific SNPs associated with the outcome of interest (e.g., depression) predict or moderate the variation in brain structure or function. Similar pathway models could be examined using the epigenome in order to fully understand the effects of early gene by environment interactions on later outcomes and potential for recovery.

Session 4: Day 1 Afternoon Discussion

Extending from the presentation by Dr. Meaney, the group first discussed the biological mechanisms that may link early adversity to later outcomes. Dr. Godfrey emphasized the complex interaction between regions of the transcriptome that are fixed from conception to death with regions that are open to modification and change by the environment. Cells, which at first glance may not seem to be directly linked to the negative adversity (i.e., early abuse and buccal cells), may be the result of pervasive effects like inflammation and endocrine dysregulation. Dr. Meaney emphasized that genetics and epigenetics studies often alter one gene and attribute a change in outcome to the modification of that specific gene, when in reality, the modification of that one gene influences an entire network of changes. These studies shouldn't be interpreted as demonstration of a candidate gene, but more so that one gene can have downstream effects through network differences. Individual variability in experience plays an important role in understanding the effects of gene by environment interactions. Even when using genetically identical rodents (homogenous population), their non-shared experience predicts later outcomes. Environment is not the same as experience and may produce different epigenetic consequences. An important point by Dr. Seeman was raised in that due to the myriad of environments and experiences that an individual may encounter, these networks may not have enough stability to predict longer-term outcomes and that this dynamic nature may hamper a study's ability to show how early conditions in life relate to later outcomes due to the ongoing evolution of the underlying biology.

The discussion continued with a recap of the presentations from the morning and some information on other networks where there are potential opportunities for

collaboration. A discussion on how existing datasets may be leveraged to examine the timing of early adversity effects on later health outcomes and possibly underlying mechanisms. It was determined that how one operationalizes some of the adversities of interest (e.g., neglect or abuse) may influence the biological markers of interest or results. Dr. Cathy Widom emphasized that it is important to understand the different experiences and be careful in distinguishing between different concepts pertaining to adversity. Dr. Steve Suomi suggested that in the non-human primate literature, differentiation occurred at the level of the behavior and that this may be a way to identify different experiences. One of the challenges that Dr. Widom stressed is how to obtain information about experiences retrospectively. The stability of the individual's response changes over time, perhaps reflecting new experiences, and it is difficult to assess validity and reliability of their previous experiences. A discussion on whether the research emphasis (and funding) should be placed on understanding the pathways vs. treating the outcome was debated. There may be multiple pathways to the outcome; therefore, understanding the pathway may not lead research any closer to understanding how to reverse the effects at the population level. On the other hand, if the treatment is to be effective and sustaining, the mechanistic pathway may be essential. Dr. Reiss asked if the knowledge of the actual exposure (e.g., actual deprivation or unpredicted trauma) helps one to look for distinctive biological signatures. These different signatures (gene expression) may help to inform midlife interventions.

The afternoon discussion ended with an overview of other research networks with overlapping interests. The Canadian Research Network was initiated 20 years ago (formerly the Human Development Network) with the aim of examining all aspects of development across SES and culture. The underlying theme of the network was to understand health disparities in relation to income disparities. The Child and Brain Development Network has similar goals, but limits examinations of biological mechanisms to pre-pubertal development. The Hope for Depression Network is a privately funded organization with a focus on treatment for depression and involves both animal model and early life stress models. The JPB Research Network on Toxic Stress (headed by Dr. Jack Shonkoff) aims to bring biological sciences into prevention programs. Thinking about these different but overlapping research networks, the conversation ended with a discussion on how epigenetics and neural circuits could be informative and where to implement prevention/intervention efforts that could possibly target both individuals at mid-life and childhood (parent-child dyads).

Session 5: Behavioral and brain plasticity in child and adult development – critical and sensitive periods and responses to intervention

The fifth session, led by Dr. McEwen and Dr. Suomi, focused on the evidence for brain and behavioral plasticity that enhance opportunities to remediate or compensate for early life adversity effects. The first three presentations provided an overview of the biology of sensitive and critical periods. Dr. Takao Hensch first reviewed studies on initial attempts to understand the basic biology of critical periods, with the goals of re-opening windows of plasticity. Most of the work presented focused on the visual system model, as the timing of the critical period for vision is well mapped. Studies of gene manipulation in

mice have allowed researchers to identify triggers, which open windows of plasticity and the results suggest that this involves the maturation of inhibitory neurons. Two key results have emerged from this literature. First, when a critical period is triggered, closure of this window of plasticity follows after a certain time. This suggests that prolonged opening of a critical period may not be advantageous and there may be “molecular brakes” in place to keep the brain stable. Second, critical periods themselves are plastic, so that different interventions could trigger to open or close windows of plasticity. Early events can also shift critical periods and examining the molecular level can help to identify the mechanism.

One strategy undertaken by Dr. Hensch and his colleagues is to identify if there is a clock that determines when the critical period should happen – as critical periods tend to occur at different times in different brain regions. These studies have examined circadian oscillations and found that circadian rhythmicity in cortical neurons is developmentally regulated and emerges just as the critical period is starting. Manipulating inhibitory cells that are expressing clock can modify the timing of plasticity. This leads to the question of, if inhibitory neuron maturation determines normal critical period, could you open a second critical period by transplanting inhibitory neurons in the brain? Studies are now starting to answer this question using a variety of models. Circadian rhythm disruption may also be contributing to shifts in the timing of certain critical periods, which may be influencing the emergence of mental illness during development. Similarly, a previous study reported shifts in the critical period for perceptual narrowing during infancy in infants who were exposed to SRIs in utero. The prenatal exposure to antidepressants was directly associated with the early closure of the critical period of consonant discrimination. Thus, both the timing of the opening of the critical period, as well as the closure, seem to play an important role in plasticity and neuro-protection. Dr. Reiss brought up an important point that these results suggest that stress may also prolong a period of plasticity and negatively affect a cascade of developments and that part of the effect of sustained early stress may be the failure of neuro-protection. Dr. Hensch ended his presentation with some evidence that early life experiences during certain critical periods do influence behavior later in life. In these studies mice were exposed to music early in life during a critical period and were tested as an adult. Mice who developed a preference for music were more likely to exhibit less anxious behavior than mice that were not exposed to music, but this effect was contextual and only in the presence of the cued music. Next steps in Dr. Hensch’s work will examine attention and social-emotional processes in relation to plasticity and associations between critical periods and early adversity.

The second presentation, by Dr. Nim Tottenham, continued the discussion of multiple and overlapping sensitive periods – not only across domains but also within. Childhood is an important time to examine how the environment is molding this circuitry to open and close critical periods. Stimuli that are learned early in life, during certain sensitive periods, may possibly be leveraged in adulthood. For example, Dr. Tottenham reported that listening to music from one’s childhood gives anxiolytic effects while stressed. This result was associated with decreases in heart rate and recruitment of the mPFC, further supported by a negative correlation between the mPFC signal and anxiety ratings. Similarly, an important cue during childhood is the presence of caregivers; the absence of caregivers has been associated with altered timing of developmental trajectories, including accelerated development of fear related systems. It may be that animals are designed to adapt based on cues received from the environment or experience,

and that this adaptation (more mature responses to fear) may be beneficial in certain circumstances. The trade-off is that an earlier shift in the timing of the critical period truncates this window of plasticity and may help to explain negative outcomes (rigidity in emotional regulation) in adolescence and adulthood.

Dr. BJ Casey's presentation focused primarily on the biological state of the developing brain during adolescence. The peak of most mental illness occurs during adolescence, and this developmental stage may provide insights into alterations of trajectories of brain development. In mice and humans, adolescents behave differently than children or adults. Both adolescent mice and humans show less fear extinction than younger or older peers. This information is important to know for clinicians using Cognitive Behavior Therapy (CBT) in children and adolescents. In addition to an age effect, there is individual variability in fear regulation where altered fear extinction is dependent on BDNF Val66Met genotype. This suggests that there is a genetic composition to predict how well an individual responds to therapy and that one way to optimize therapies is to attempt to bypass prefrontally mediated fear regulation by changing the timing of CBT.

The next three presentations emphasized planned interventions that illustrated the plasticity of brain and behavioral processes in adulthood. Dr. Kirk Erickson presented work on physical activity and its relation to neuroplasticity in adults. By age 50, the hippocampus declines from 1 to 2 percent per year and there is a large amount of individual variability in this decline. Although some of this variation could possibly be due to methodological variations, individual differences in environment, experience, or behavior could also account for these differences. Past studies have demonstrated a significant association between physical activity and reduced risk of cognitive impairment; associations between increased fitness and larger hippocampal volume persisted even after controlling for age, sex, and education in cross-sectional datasets. In meta-analyses of randomized control trial interventions of exercise, the largest effects were seen in the domain of executive function with moderate sized effects. Significant effects of an exercise intervention were found in the hippocampus, with changes in hippocampal volume correlating with changes in fitness over the intervention period. Demonstrating specificity, there were no differences in the volume of the caudate nucleus or thalamus and the effects were found only in the brisk walking group and not the tone/stretch group. Dr. Erickson ended his presentation with remaining questions that needed to be investigated to fully understand the association between physical activity and neuroplasticity including: dose of physical activity, type of activity, participant population, specificity of cognitive domains, individual differences, and mapping out mechanisms of change.

Next, Dr. Sara Lazar presented her data on meditation and neuroplasticity. Meditation primarily focuses on breath, bodily sensations, and sensory stimuli and has been shown to be useful in treating many different ailments. A past study found that meditation prevented depression relapse in a group of participants with major depressive disorder; participants with more early life adversity responded better to meditation than people with low early life adversity. The mechanism supporting the link between meditation and cognitive function is not fully clear; it is hypothesized that meditation may facilitate in the preservation of cortical thickness (decline of white matter). Studies have also found widespread effects of meditation on the posterior cingulate, temporoparietal junction, cerebellum, hippocampus, and the amygdala. Dr. Lazar stressed that although it is difficult to assess the quality of meditation and that these changes are modest, meditation

may be an incredibly useful intervention during adulthood in that it impacts both emotion and cognition and the biggest gains are in participants who have experienced high early life adversity.

The final presentation by Dr. Brent Roberts provided an overview of the interventions to change personality traits in adults. There is a significant association between personality traits and poorer functioning or negative outcomes in adulthood. Personality traits predict a host of risk factors including educational attainment, occupational attainment, relationship outcomes, health behaviors, physical health, Alzheimer's and longevity. Personality traits may be poor candidates for reversibility in that they are highly heritable, but studies have demonstrated that personality traits do change and are not perfectly stable over the lifecourse. These changes in personality traits are correlated with many different types of life experiences (e.g., being committed and invested in your work, marital stability, refraining from drugs) and stress. In a 3-year longitudinal study (ages 18-75), increases in stress (perceived stress scale) led to decreased conscientiousness over time. Additionally, in a meta-analysis (193 studies, N = 19,199) of the effect of clinical interventions (therapy) on personality trait, therapy was reported to have sustained effects on changes in personality traits. Many common factors did not seem to affect the results, including type of therapy, type of presenting problem, duration of treatment, gender, or age. Therefore, Dr. Roberts concludes that personality traits may be potential intervening mechanisms between early life adversities and health and should be considered as a mechanism for reversibility.

Session 6: Valid assessment of early adversity in adults

The final session examined the evidence on associations between prospective vs. retrospective data on early life adversities and adult outcomes. As studies rely on the retrospective reporting of early life adversities in order to predict later health outcomes, it is important to better understand the relative strengths and weaknesses of various approaches to retrospective collection of early life adversity information from adults. Dr. Widom gave a brief overview on studies examining the difference between retrospective and prospective results in relation to childhood abuse and later health outcomes. Dr. Widom stressed that accurate measurement of childhood adversities is quite difficult in that good trauma assessments are lengthy and sometimes impose a burden on the participant. In one study, children were followed up during adulthood and, despite the fact that these individuals met the criteria for post-traumatic stress disorder, only a third of participants who had a documented case of childhood abuse or neglect reported having a traumatic event during childhood. Additionally, in other analyses with this same sample, there were inconsistencies in self-reports of childhood victimization over time, and this variability in reporting may be related to psychopathology or current life situations. The main point of the presentation was that there were differences between retrospective and prospective results in terms of the reporting of early adversity (i.e., childhood abuse) and later outcomes (i.e., drug abuse during adulthood), which may complicate the identification of participants for specific interventions. Other complicating factors include sleeper effects (saying no in the first interview could prime the individual to change their answers later) and individual differences in the cognitive experience of early adversity.

Dr. Danese's presentation continued this discussion of retrospective and prospective measures of adverse childhood experiences by examining reporting agreement, validity, and source bias within large datasets using the Adverse Childhood Experience (ACEs) Scale. Distributions for both the retrospective and prospective measures were slightly skewed, with more participants reporting none or few early life adversities. There are little differences in ACEs scores between the retrospective and prospective measures in the Dunedin Study, but very low agreement when examining within-subject differences across retrospective and prospective ACEs scores. Overall, prospective measures outperform retrospective measures on both construct and predictive validity, with personality traits and psychopathology possibly triggering source bias within the retrospective data. As such, prospective measures are more valid and may be better measures of disease risk; prospective measures of early life adversity must be considered when planning interventions targeting adults. However, prospective measures likely underestimate the real prevalence of adversity. Retrospective measures might be used pragmatically to predict risk, particularly with regard to mental illness.