

Expert Meeting on Empathy and Compassion

Leveraging Basic Research to Inform Intervention Development

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Acronym Definitions

AD	Alzheimer’s disease
ADRD	AD and related dementias
BBCSS	NASEM Board of Behavioral, Cognitive, and Sensory Sciences
BSR	NIA Division of Behavioral and Social Research
bvFTD	behavioral variant frontotemporal dementia
CBT	cognitive behavioral therapy
CM	compassion meditation
LKM	lovingkindness meditation
NASEM	National Academies of Science, Engineering, and Medicine
NIA	National Institute on Aging
RCT	randomized controlled trial
SOBC	Science of Behavior Change

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Executive Summary

Empathy and compassion on the part of the caregiver are important contributors to effective interaction between caregivers and care recipients, caregiver wellbeing, and the quality of care provided. Yet few caregiver interventions have incorporated cutting-edge, basic behavioral research on empathy. On September 16–17, 2019, at the request of the National Institute on Aging, the National Academies of Sciences, Engineering, and Medicine’s Board of Behavioral, Cognitive, and Sensory Sciences (BBCSS) convened an Expert Panel to explore advances in measuring and understanding (1) behavioral, affective, and cognitive processes underlying empathy and compassion; (2) interventions that modulate empathy and compassion; and (3) future research directions to incorporate basic science into development of interventions. Drs. Robert DeRubeis of the University of Pennsylvania and Sona Dimidjian of the University of Colorado, Boulder, served as Co-Chairs for the Expert Panel.

During the first day, Dr. Adrienne Stith Butler, Associate Director of BBCSS, provided opening remarks and Drs. Lis Nielsen and Lisa Onken of NIA provided background context. Then Expert Panel members delivered presentations on caregiver needs, basic research on empathy and compassion, and interventions to increase empathy and compassion. The second day was devoted to discussion. The Panel discussed methods, outcomes, and populations for measurement and study of empathy and compassion, then broke into two groups to discuss study design and implementation. Finally, the Panel convened for overall discussion and synthesis of themes.

Discussion Themes

- Caregiving contexts vary. Researchers should therefore consider how to tailor interventions for specific contexts, or to identify components that are generalizable across contexts. They should specify which target they want to measure and promote, as well as the nature and needs of the caregiving population they want to target.
- Consensus definitions of empathy and compassion are needed to guide efforts to measure and promote them.
- There was general agreement, as encouraged within the [NIH Stage Model](#), of the utility of incorporating understanding of mechanisms, including at the level of brain function, into broader formulations.
- Interventions for caregivers need to be practical and enjoyable. To increase the likelihood of intervention adoption, it may be useful for researchers to consider that caregivers often have limited spare time.
- Research on intervention development for caregivers may benefit from consideration of the experiences, symptoms, and capabilities of the care recipient.
- Interpersonal dynamics in the relationship or bond between caregiver and care recipient may be important considerations for intervention development research.
- Cultural differences, including differences in resources and perceptions of burden and suffering, are another consideration in intervention development research.

- The [NIH Stage Model](#) incorporates basic research at all Stages of intervention development and provides a conceptual framework for the development of principle-driven interventions targeting empathy and compassion in care providers.

Knowledge Gaps and Potential Research Questions

- What multilevel approaches are available for measuring empathy and compassion?
- How is empathy related to motivation to act? How is motivation to act related to compassion? Does motivation to act translate into action? How can this knowledge inform intervention development?
- What basic mechanisms explain reduced affective activity and empathy following overexposure to others' suffering, compared with the increased tenderness without increased empathic distress observed after compassion meditation? How can these findings relate to intervention development?
- What is the impact of lower cognitive empathy in the individual with ADRD? What is the impact of higher emotional empathy in the caregiver? How do these two states contribute to poor caregiver health?
- Who becomes a caregiver? What paths and processes determine who becomes a caregiver and who does not? How much of the process of becoming a caregiver is determined by empathy? Can this inform intervention development?
- Do individuals' responses to stressors in the caregiving context differ from their responses to other stressors? How do stressors impact empathy and compassion of caregivers, and how do the empathy and compassion of caregivers affect response to stress?
- What is the role of acceptance in compassion and self-compassion, for both the caregiver and the care recipient, and how is this knowledge relevant to intervention development?
- What is the role of touch in fostering empathy and compassion? Can targeted interventions be developed to harness the power of touch, and how might these interventions promote the wellbeing of the caregiver and care recipient?
- What impact does the caregiver's cognitive capacity have on their empathy, compassion, and caregiving, and how might this relate to intervention development?
- How is exploitation related to empathy and compassion? Can psychometrically sound measures of exploitation be developed, and can they help to identify who most needs support and advocacy?
- Can social media data be mined to develop interventions targeting empathy and compassion for caregivers?
- Given the relevance of empathy and compassion to caregiving, what kinds of interventions targeting empathy or compassion can help prepare individuals for caregiving? What is the best timing to administer such interventions and how can unintentional negative outcomes be monitored and avoided?
- Does compassion provide a means to alleviate, or respond to, emotions that arise from empathy? If compassion involves helping, when does helping provide a benefit? Is helping worthwhile only when the caregiver perceives that it led to an improvement?

- What aspects of compassion meditation should future research investigate? How might outcome measures be derived from past research on explicit attention to intention, affective elements that generate warmth, tenderness, and well-wishing, and perspective-taking?
- What is the social context (including cultural, interpersonal, and emotional factors) in which the caregiver provides care? How do levels and types of empathy and compassion relate to these factors? What interventions might be developed to prevent and address social isolation?
- How does culture influence empathy, compassion, altruism, and caregiving? What can be learned from group-centered cultures, and how can this knowledge be leveraged into new interventions? What functions might social expectations (e.g., communal motivation versus exchange motivation) play in empathy, compassion, and caregiving? How do these relate to development of effective interventions?
- How might interventions be developed to target empathy and compassion in contexts of dyad interactions (e.g., when a caregiver listens to a physician) to support and facilitate information processing?
- Can interventions targeting empathy and compassion be developed to help train clinicians and researchers to provide patients and caregivers with information about dementia in a sensitive way?

Meeting Summary

Overview

With the increasing research focus on Alzheimer's disease and related dementias (ADRD), more attention has been paid to those caring for individuals with ADRD. Growing evidence suggests that the health and wellbeing of caregivers contribute to the quality of care they provide and, ultimately, to the health of the individual in their care. Empathy and compassion on the part of the caregiver influence the interactions between caregivers and care recipients. The level of empathy also plays an important role: too much empathy can negatively affect the caregiver's wellbeing, whereas too little can disadvantage the individual under their care. More than 200 interventions for caregivers have been tested in randomized controlled trials (RCTs). However, results from most of the RCTs remain inaccessible. Moreover, few interventions have incorporated cutting-edge, basic behavioral research on empathy.

The National Institute on Aging (NIA) Division of Behavioral and Social Research (BSR) aims to explore and support the development of interventions to modulate the amount and type of empathy and compassion caregivers experience and express. On September 16–17, 2019, at the request of NIA, the National Academies of Science, Engineering, and Medicine's (NASEM) Board of Behavioral, Cognitive, and Sensory Sciences (BBCSS) convened an Expert Panel to explore advances in measuring and understanding (1) behavioral, affective, and cognitive processes underlying empathy and compassion; (2) interventions that modulate empathy and compassion; and (3) future research directions to incorporate basic science into development of interventions. Drs. Robert DeRubeis of the University of Pennsylvania and Sona Dimidjian of the University of Colorado, Boulder, served as Co-Chairs for the Expert Panel.

To begin the meeting, Dr. Adrienne Stith Butler, Associate Director of BBCSS, provided an overview of NASEM and BBCSS, after which Drs. Lis Nielsen and Lisa Onken, both of BSR, briefly introduced NIA and reviewed the NIH Stage Model for behavioral intervention development. Afterward, three sessions explored caregiver needs, basic research on empathy and compassion, and interventions to increase empathy and compassion. Each session included presentations by Panel members, followed by discussion. The second day focused on discussion. The Panel discussed methods, outcomes, and populations for measurement and study of empathy and compassion, then broke into two groups to discuss study design and implementation. Finally, the Panel convened for overall discussion and synthesis of themes.

Background and Context

Lis Nielsen, PhD, and Lisa Onken, PhD, Division of Behavioral and Social Research, National Institute on Aging

NIA has traditionally been a life course rather than a disease-focused institute, supporting research aimed at understanding the processes of aging as they unfold. Much of the work supported by BSR focuses on adaptive aging and wellbeing in later life. This includes many projects that integrate biosocial and biobehavioral research, including studies of loneliness,

social connection, emotional function, and interpersonal interactions. BSR, and NIA overall, are building an interventional portfolio that is grounded in basic science. NIA has been heavily involved in the NIH Science of Behavior Change (SOBC) program, which aims to dismantle the silos that separate basic science from clinical/interventional science, and focuses on the mechanisms underlying the effects of interventions, such that interventions are developed in line with basic science and are fit for real-world implementation. NIA has incorporated behavioral and social topics such as self-regulation and stress processing, as well as interpersonal and environmental processes, into SOBC-associated funding opportunity announcements.

Interpersonal processes that drive behavior constitute an area of increasing interest to many individuals as they age. With the dramatic increases in targeted funding to support ADRD research, NIA and BSR can continue longstanding investments in research on caregiving, with respect to both the care provided and the health and wellbeing of the caregiver and care recipient. This meeting provides NIA with an opportunity to explore interpersonal interactions relevant to dementia and to expand its portfolio of research on caregiving.

In its efforts to integrate basic and clinical/interventional science, NIA has relied on the [NIH Stage Model](#), which embraces the SOBC focus on mechanisms of behavior change and aims to develop principle-driven behavioral interventions, defined in the broadest sense, that can be delivered with the greatest possible efficacy, fidelity, and ease. “Principle-driven” means that interventions are defined by mechanisms of action or by major rules governing the intervention’s effects. Within the [NIH Stage Model](#), understanding the mechanism is akin to understanding the basic behavioral, social, affective, and even neurobiological processes underlying the effects of an intervention. Rather than having basic research as a precursor to inform intervention development only, basic research is integrated throughout, thereby enhancing the following aspects of an intervention:

- Potency: knowing how and why an intervention works to increase the chances of improving it.
- Personalization: knowing who is, and is not, likely to respond to an intervention, as well as to what extent and in what circumstances an intervention is generalizable.
- Potential for scalability: knowing how and why the intervention works to offer insight into how to streamline and simplify it, train others to conduct it, and ensure its fidelity.
- Pragmatics: knowing how to create interventions in their most potent, simplified, efficient, and scalable form.
- Parsimony: knowing which interventions operate under the same principles and which function by different principles.

Correspondingly, the NIH Stage Model is nonprescriptive, multidirectional (i.e., nonlinear), and iterative and recursive. It aims to create a cumulative intervention development science and to maximize intervention efficacy and scalability.

- Stage 0 focuses on basic research to inform intervention. However, a focus on basic science related to mechanisms of behavior change may be integrated into any Stage of intervention development.
- Stage I refers to any time an intervention is created, adapted, modified, or refined, and it includes pilot testing. It also includes the development and testing of materials to maximize real-world fidelity of the intervention, including training materials.
- Stage II refers to traditional efficacy testing in the most highly controlled conditions possible, with high internal validity, not in real-world conditions.
- Stage III refers to testing in the most highly controlled conditions possible in a community setting or among community providers, with high internal validity (although it is inherently not as high as during Stage 2, where the intervention may be delivered by someone on the research staff). This stage helps researchers understand whether an intervention will work under optimal real-world conditions, before proceeding to a Stage IV trial.
- Stage IV refers to real-world effectiveness trials with high external validity. Stage IV includes pragmatic trials.

Again, this model is nonlinear. Some projects may proceed from Stage II to Stage I (e.g., if an intervention requires modification). Other projects, where an intervention is extremely simple and training and fidelity issues are not relevant, may sometimes proceed from Stage I to Stage IV. As it brainstormed directions for future research, the Expert Panel considered this model and discussed ways to incorporate basic research findings, principles, and concepts into research on development of interventions that optimize the amount—and type—of empathy and compassion caregivers experience and express.

Discussion Points

- Understanding the underlying features and principles of interventions and how these properties affect an individual's personal characteristics may help to personalize interventions, rather than relying on studies that group together people with a variety of characteristics and report average responses.
- Implementation research questions (e.g., to better understand why an intervention that works well in a research setting does not translate to the community setting) may at least partially be addressed within the [NIH Stage Model](#). If investigators hypothesize why an intervention does not translate, such an hypothesis could help guide modifications of the intervention at Stage I.
- Intervention development can benefit from collaborations among researchers and the wider care community to develop an infrastructure that supports the translation of interventions into real-world settings. Whenever appropriate, stakeholders should be involved as early as possible in the intervention development process. The newly reconceptualized Edward R. Roybal Centers for Translational Research in the Behavioral and Social Sciences of Aging are supported by NIA, structured in accordance with the [NIH Stage Model](#), and support the full range of efforts in behavioral intervention research.
- More education of the research community may be needed to address misconceptions about the NIH Stage Model. For example, it is not necessary to begin at Stage 0. One may

begin at any Stage, depending on how well-developed and tested an intervention is, and what is needed to maximize an intervention's potency and or scalability. Also, there is sometimes a misconception that the model is prescriptive and linear. It is neither.

Session I: The Caregiving Context: Problems and Needs

Challenges, Strengths, and Hurdles in the Interpersonal Relationship

Robert DeRubeis, PhD, University of Pennsylvania

The relationship between the caregiver and the individual receiving care is usually dyadic, longstanding, and often intimate. To define a potentially successful caregiving relationship, one can look at the literature on marital relationships. In this context, successful relationships depend on respect, affection, trust, cooperation, and generally manageable problems. If a relationship is strong in these factors, one can assume that problems associated with dementia will be more tractable, less disruptive, and less destructive to the relationship. Yet even within that constellation of factors, caregiving can present new challenges. More empathy is needed: on the part of the caregiver as the recipient's abilities diminish, and on the part of the recipient in recognition of the new challenges and adjustments faced by the caregiver. The partners also need more compassion, both for each other and for themselves.

Research by Dr. DeRubeis' collaborators in Europe has focused primarily on caregiver depression. Often, this depression is fueled by guilt the caregiver experiences, as illustrated by statements such as "I'm not doing enough," "I shouldn't be enjoying myself," and "I yelled at my partner when it's not their fault." Guilt in the caregiver can also be induced by the recipient's complaints, such as "You don't care about me" or "You were having fun when you were with your friends and now you're miserable being with me." These experiences are not necessarily antithetical to empathy and compassion. Instead, they present a different perspective. Thus, research on and interventions to promote empathy and compassion in the caregiving relationship can identify and address similarities in behavior and mechanisms underlying empathy, compassion, guilt, and depression.

Interpersonal Effects of Suffering and Compassion in Older Adult Caregiving

Joan K. Monin, PhD, Yale School of Public Health

A large body of literature has shown that being a caregiver has negative psychological and physical consequences, such as psychological distress, poor health habits, physiologic responses, and psychiatric and physical illness. There are also positive aspects of caregiving, such as providing meaning and purpose to caregivers, who may also view caregiving as an expression of love. Still, much of the available evidence suggests that caregiving is harmful to one's health. Many caregiving health stress models emphasize disease-related stressors such as impaired physical function, cognitive impairment, and disruptive behaviors such as agitation. Others focus on caregiving-related stressors such as the type and amount of assistance given, time spent, and vigilance demands.

An expanded model of caregiving health stress includes the disease- and caregiving-related stressors highlighted in traditional models, but it also incorporates the interpersonal effects of care recipient suffering based on physical, psychological, and existential or spiritual appraisals. In this model, caregivers experience emotions through empathy, but they also experience emotions through mimicry (i.e., displaying the patterns they observe in the recipient) or through complementary processes (i.e., wanting to alleviate the recipient's suffering). All of these emotion theories and relational processes lead to physical and psychological morbidity in the caregiver. This model is supported by studies showing that the perception of a loved one's suffering has more impact on the caregiver's health than do other behaviors (e.g., severity of the care recipient's disease). Care recipients' suffering predicts depression in caregivers. Exposure to the recipient's suffering leads to physiologic reactivity associated with adverse health effects in the caregiver. Treatment of depression in the care recipient alleviates caregiver distress without affecting the recipient's function in other domains. Studies also have shown mood convergence in older, married couples, such that depression in one spouse leads to depression in the other. Evidence suggests the unique impact of perceived suffering on caregivers' health as shown by improved caregiver outcomes following the death of a care recipient but not for the placement of the recipient in a care facility.

Dr. Monin and colleagues have explored the process of communication between the caregiver and the care recipient. Care recipients experience and report on their suffering—which they may minimize or exaggerate—and caregivers perceive and respond to that suffering, leading to distress in the caregiver. Caregivers' perceptions and responses depend on individual differences in empathy, closeness, intimacy, and attachment styles. For example, in one study, Dr. Monin and colleagues found that spousal caregivers high in attachment anxiety experienced a high level of distress when watching their partners perform pain-eliciting tasks, whereas those with avoidant attachment experienced less distress, even though both attachment types showed greater perceptions of their partners' pain. In another study, feeling satisfied in one's marriage actually made caregiving more difficult. The level of distress experienced by women with high marital satisfaction depended on the level of suffering they saw in their partners. Among men high in marital satisfaction, however, there was no such relief; their distress remained high regardless of the level of their partner's suffering. Thus, the more an individual loves his or her spouse and relies on the spouse for interpersonal coping and physiologic regulation, the more difficult it is to adapt to the partner's decline. Other studies suggest that attachment style influences caregiver distress for various relationship types, including that between parents and children.

Dr. Monin and her colleagues are also exploring ways to maximize the positive aspects of caregiving. In one study of caregivers and spouses in the early stages of dementia, caregivers who felt more compassionate love for their partners reported less caregiving burden and more positivity, compared with caregivers who felt less compassionate love, suggesting that mutual compassion between spouses could be protective against caregiver distress. In collaboration with Dr. Stephanie Brown, another Expert Panel member, Dr. Monin found that caregivers caring for spouses with AD or chronic pain experienced more positive affect when they were providing high levels of care to the care recipient but believed their partner appreciated and

was happy because of their efforts. Now, in a pilot study, Dr. Monin and her colleagues are teaching spouses to use the Wish Outcome Obstacle Plan to accomplish self-care and personalized goals to reduce stress and increase relationship satisfaction and positive emotions in both partners. Forty couples have enrolled thus far. Dr. Monin is also conducting a study of mutual attachment behaviors, such as support-seeking and caregiving behaviors, in 200 pairs of adult children and their older adult parents with dementia.

Empathy, Compassion, and Caregiver Health: Implications for Treatment Development

Robert Levenson, PhD, University of California, Berkeley

Empathy is not a monolithic construct but rather exists in multiple forms including (1) cognitive empathy (i.e., knowing what another person is feeling); (2) affective or emotional empathy (i.e., feeling what another person is feeling); and (3) sympathy, compassion, or prosocial behavior (i.e., concern for and helping of a person in need). Although many studies in the research literature measure empathy using self-report inventories (e.g., “I typically cry at sad movies”), performance-based measures are used increasingly often. Thus, cognitive empathy can be measured using empathic accuracy tests in which judgments about what another person is feeling are evaluated against an independent standard. Because real-world judgments about others’ emotions are typically dynamic (emotions can change rapidly), involve integration of multiple sources of information (e.g., visual, auditory, contextual), and occur in interpersonal contexts, investigators have typically assessed empathic accuracy using a dynamic tracking test, in which a person watches another person engaged in an interpersonal activity and uses a rating dial to provide moment-to-moment ratings of how that person is feeling. These ratings are then compared to an independent standard such as similar ratings obtained from the other person or from a panel of expert raters.

Performance-based measures of emotional empathy are increasingly common. Dr. Levenson and colleagues performed studies on participants who watch films of other people experiencing strong emotions (i.e., distress) and measured their physiological responses, expressive emotional behavior, and self-reported emotional experience. Performance-based measures of sympathy, compassion, or prosocial behavior typically create situations in which participants are exposed to another person in distress and provided with an opportunity to help that person. For example, researchers have used a donation task in which participants receive an amount money and are told that they can donate none, some, or all to a charity that helps the distressed people they have seen.

Dr. Levenson and his colleagues have used these kinds of performance-based measures of different kinds of empathy to study care recipients and their caregivers with a particular interest in identifying factors that contribute to individual differences in the adverse health effects of caring for a person with dementia. In these studies, the dynamic tracking task has proved to be particularly useful. In a study of 43 persons with behavioral-variant frontotemporal dementia (bvFTD), 43 patients with AD, and 26 controls, results from the dynamic tracking test show that both dementia groups showed deficits in cognitive empathy, compared to controls. However, the deficits were more profound in the bvFTD group than in

the AD group. Structural magnetic resonance imaging further showed that neurodegeneration in right temporal areas of the brain were most strongly associated with deficits in empathic accuracy. In a study of 63 individuals with dementia and their caregivers, the individuals with dementia completed tasks whereby they identified a single emotion portrayed in photos and films and also changing emotions using the dynamic tracking test. Caregiver depression was assessed by standard questionnaires. The only significant predictor of caregiver depression in this study was the care recipient's poor performance on the dynamic tracking test of cognitive empathy. Another study of 80 individuals with dementia and their caregivers assessed both the cognitive and emotional empathy of caregivers. Caregivers' emotional empathy predicted greater caregiver depression, whereas caregiver's cognitive empathy did not. Although investigators usually think of empathy as highly desirable, these results indicate greater complexity. Caregivers who have very strong emotional reactions to the distress of others may be most likely to experience negative health effects when engaged in dementia caregiving.

The adverse health effects of caregiving have important public health implications, in part because so many caregivers experience mental and physical health problems, and because of the impact of these health problems on care recipients. For example, in a study of 176 individuals with dementia and their familial caregivers, Dr. Levenson and colleagues found that recipients cared for by caregivers with poor mental health were significantly more likely to die within a 9-year period. In addition, life expectancy among individuals with dementia receiving care from a person in relatively poor mental health was 14 months shorter than for those receiving care from caregivers in relatively good mental health.

This work suggests important pathways among particular types of empathy (measured in particular ways), caregiver health, and care recipient mortality. These pathways have implications both for assessing risk and for planning interventions. Although many aspects of these relationships will require additional study, including critical longitudinal assessments to help determine directional relationships, they do raise some cautionary notes. Interventions that attempt to target empathy should carefully consider the type of empathy, how empathy is assessed, and whether more or less of that type of empathy is associated with better outcomes for caregivers and care recipients. Although interventions that seek to reduce emotional empathy might at first seem cruel, they may help caregivers to achieve a more optimal position between indifference and overinvolvement.

Moreover, it is important to consider empathy in both the caregiver and the care recipient. Dr. Levenson and colleagues' work has found that low levels of cognitive empathy among care recipients (especially when measured using a dynamic tracking task) are associated with poor caregiver health. Given the progressive nature of dementia and other neurodegenerative diseases, interventions aimed at increasing cognitive empathy in individuals with dementia may not be a feasible long-term strategy. Thus, there may be benefits from interventions aimed at helping caregivers become less vulnerable to the devastating effects of loss of empathy in the person in their care. Dr. Levenson and colleagues expect that interventionists and other researchers who consider these results, and similar results from other laboratories, will develop several innovative approaches. As with all interventions designed for dementia caregivers,

adherence will be a challenge, especially as the care recipient's disease progresses and the caregiver's time and energy resources become increasingly drained. Thus, devising focused, compact, and minimally burdensome interventions will be critical. Consistent with the NIH Stage Model and SOBC experimental medicine guidelines, intervention development should assess whether the intervention engages its target (e.g., emotional empathy) and whether that engagement affects the distal outcome of reducing declines in caregiver mental health. A main goal for the future will be the ability to monitor these mechanisms to identify caregivers at heightened risk and provide early, effective preventive interventions.

Discussion

Multiple emotional pathways affect the caregiving relationship. Fear, sadness, and depression are often highlighted, but other emotions are also involved. Caregivers can experience anger toward themselves ("I'm not doing enough"), the recipient ("I'm doing too much" or "You're not trying hard enough"), and the situation ("This is unfair"). Embarrassment also plays a role; caregivers and recipients become secretive about the recipient's changes in abilities. Disgust is another emotional pathway; factors associated with the illness and the recipient's loss in abilities can be highly unpleasant. Caregivers face an emotional smorgasbord, but not all of them experience the same pathways. This is one reason why interventions should be personalized. There may be a list of emotion- and empathy-centric questions that health care providers can ask caregivers, but few providers are trained to ask these questions and often focus almost exclusively on the care recipient and not on the caregiver.

In Dr. Monin's study of attachment styles and caregiver distress, the investigators asked spousal caregivers to talk about their partner's suffering, then transcribed these conversations and performed linguistic analyses. The caregivers who were most distressed or showed higher levels of depression talked the most about negative emotions in their partners, whereas the ones who showed more cognitive processing did not. These findings were consistent with what Dr. Levenson and his colleagues have observed. Caregivers often focus on the loss of function in the recipient, and clinicians often compound this by asking about degenerative symptomology.

Interventions could therefore encourage caregivers to change their appraisal of the situation, for example by having them focus more on abilities that remain intact or by increasing the sense that caregiving benefits both the recipient and the caregiver. In a study of 20 individuals caring for individuals with AD, four showed lightheartedness and appeared to derive meaning from the caregiving experience. These caregivers differed from the others in how much they touched the recipients and reported that if they held the recipient, they felt that the recipient was intact. Likewise, caregivers often hesitate to transition their recipients to formalized care facilities because conjugal visits are not allowed. More research is needed to determine whether an individual who sustains the ability to share joy has a better experience with caregiving, or whether negative affect in care recipients can elicit positive affect in their caregivers.

Another mechanism to explore involves the role of self-care. It is possible that individuals who are too empathetic toward the care recipient have less attention resources for themselves.

Evidence suggests that a sense of social connectedness is greater in caregivers who practice self-care than in those who focus entirely on the care recipient. Likewise, a common theme throughout the history of psychotherapy research is that individuals fare better when they believe they have been heard and understood. Caregivers who participate in support groups often report benefits from that participation, most likely because these support groups help to replace some of what caregivers feel they have lost.

Session II: Basic Research on Empathy and Compassion

Understanding the Relationship between Empathy and Care

Abigail Marsh, PhD, MA, Georgetown University

Empathy is difficult to study in the laboratory. Because it is a socially desirable phenomenon, self-reported empathy might be biased or inaccurate due to participants' awareness that their empathy is being measured and their desire to attain social approval. Another barrier to progress in this field is the lack of a consensus definition of "empathy." Although there are inconsistencies among how empathy is defined and measured, most definitions characterize empathy as the ability to share, correctly interpret, or experience what someone else is feeling.

Social neuroscience appears to support this general definition. Early single-unit recording studies in macaques (which are not particularly prosocial) suggest that individual neurons can translate between a cognitive state in a monkey (e.g., intending to grasp an object) and that same state in another monkey or human, an early form of evidence that self-mapping at the neural level is possible and may support empathic processes that are not inevitably linked to prosociality and compassion. Work in humans has demonstrated mirror-like properties in neurons throughout the brain, such as the dorsal anterior cingulate cortex, a region which has been clearly shown to mirror affective and motivational features of pain. Individual neurons in this region have been shown to activate both when someone feels pain and when they watch someone else experience pain. These studies and others support an emerging consensus that individuals leverage neural networks to translate other people's affect. Although neuroimaging studies cannot directly identify mirror neurons and other cells with mirror neuron-like properties; data from neuroimaging studies generally support the findings of single-unit recording studies.

It is important to distinguish between empathy (i.e., translating the contents of another's mind) and care (i.e., caring if the other is distressed); however, the two processes are related. One study by Dr. Marsh and colleagues has linked extraordinary acts of compassion to increased empathy when watching others experience distress. In this study, half of participants were typical adults, among whom multivoxel patterns associated with experiencing and observing pain showed similarities but little overlap. The other half of participants were altruistic kidney donors (i.e., each had given a kidney to a stranger). These individuals showed more empathy at the neural level, and a stronger multivoxel pattern when experiencing anticipatory fear and pain and when observing these states in others. Alternatively, highly callous individuals do not empathize with others' distress well. For example, they fail to respond to other people's fear,

and they show weaker empathic responses. Thus, the strongest predictor of caring in Dr. Marsh's laboratory was sensitivity to others' fear. Stable inter-individual caring traits likely fall on a caring continuum that is associated with empathic sensitivity to others' fear and not to other states such as anger.

Empathy is a multidimensional construct (i.e., "empathies"). A paper by Dr. Conway and colleagues states that the way an individual represents others' faces and minds is akin to a series of vectors in a multidimensional psychological space. Just as individuals can identify stable and transient features of other people's faces, they can also identify stable and transient features of other people's minds, for example whether they are planning something or know something. Different clinical groups have encountered different challenges in representing various vectors and have thus found different patterns of empathic deficits. Different types of empathic representation are served by different neural networks. Thus, people can converge on one conclusion—that someone is frightened—using a variety of networks and routes to reach that conclusion.

The suggestion that activating neural fear networks, which usually motivate avoidance and escape, is associated with care may appear counterintuitive. How that empathic representation translates into caring about another person's feelings is poorly understood. However, the capacity to care may have evolved from brain systems that support parental care, as suggested by research on rodent parental care. In these studies, female rats are trained to fear an odor, in response to which they freeze. However, female rats with pups do not freeze; instead, they act to protect the pups. However, when the rats are administered an oxytocin antagonist, they lose their courage, suggesting changes in signaling between the amygdala and the midbrain. This is consistent with imaging of altruistic kidney donors, who show stronger structural and functional connections between the amygdala and the midbrain. Thus, understanding primitive mammalian parental care systems may help to shed light on interpersonal caring.

Empathy and Compassion: A Social Affective Neuroscience Framework

Greg J. Siegle, PhD, University of Pittsburgh School of Medicine

In identifying ways to encourage and support sustained caregiving, neuroscience may help by explaining positive empathy—when individuals access their positive affect in response to someone else's pain—and compassion, which involves approach motivation (i.e., positive empathy combined with the motivation to act). The processes underlying positive affect and social information processing involve most of the brain in combined systems, some of which may be more social when a person perceives another person. Thus, intervention development targeting functional empathy (i.e., an empathic emotion that, in addition to being consistent with an emotion of the person being cared for, has a useful function) may require consideration of not only which neural systems are active, but also how they are used.

There are complexities associated with creating functional empathy with positive affect. First, provoking a positive emotion can differ greatly from maintaining it, particularly in the presence of negative affect. In one study in which participants were asked to return in their minds to the best times of their lives, healthy participants remained positive for 7 minutes, whereas those

who were depressed could not maintain their positivity. In participants who successfully maintained the positive emotion, medialfrontal areas of the brain associated with cognitive control and downregulation of emotions were inactivated, suggesting that maintaining positive emotion does not rely on increasing control, but on decreasing the control of ruminative processes. A second complexity is that brain activity and behavior do not always align; thus, changing mechanisms of empathy and emotion will not necessarily lead to behavioral change in compassionate action. For example, one study found that being kind to others made participants feel happier. However, focusing on themselves activated brain networks associated with emotion more than focusing on others, suggesting that the ability to care for others involves the ability to get out of one's own head. A third complexity is that emotional blunting and having extremes of negative affect may be normative in people undergoing stress and intervening on these features may not make people more "normal." For example, when individuals face stress, a wide variety of brain networks associated with cognition and emotion shut down; the individuals stop regulating emotion, and the effects of a single social stressor on mood proxies remain apparent in animal models after 4 weeks. Individuals may be likely to disengage in response to emotional stress due to integration between behavior guidance systems and emotional processing (i.e., emotional recognition) mechanisms. Thus, any system guiding activity should not be treated in isolation, and positive empathy is likely to contribute to motivational salience.

With these cautions in mind, researchers could leverage several naturally occurring states when developing interventions to facilitate functional empathy. For example, trust activates neural reward circuitry and decreases activity in fear circuits, including activity in the amygdala, especially in the presence of high oxytocin levels, and synchronizes emotion-regulatory brain function across individuals. As a second example, flow states are associated with positive affect and vitality and arise when strenuous activity meets a person's needs; in contrast, frustrative non-reward leads to need-thwarting, burnout, depression, arousal, and aggression. Compassion meditation is associated with increased activity in social and reward brain regions, yielding positive affect. Thus, interventions that promote trust and flow states, which counter frustrative non-reward and capitalize on compassion meditation, could all potentially facilitate functional empathy through well-characterized neural mechanisms.

These and other approaches center on affecting brain mechanisms through psychological means. Indeed, emotion states are identified with observable changes throughout the body, and an increasingly large literature suggests that addressing features felt throughout the body can affect emotional functioning, from temperature to vibration. For example, Dr. Siegle and colleagues have shown that providing individuals with posttraumatic stress disorder with a wrist-worn device that provides various frequencies of vibroacoustic stimulation allowed them to better sustain focus, regulate emotions, sleep when desired, and return from a "shut down" psychological state. Investigators are currently examining the extent to which linking these patterns to specific semantic messages associated with functional empathy can increase empathic behaviors. Supporting the feasibility of these approaches, Dr. Siegle and his colleagues have previously shown that caregivers of people with dementia will indeed use technology-based mobile solutions with minimal training/prompting.

A final consideration is that functional empathy may be especially useful to address in specific populations but may also take tailored interventions. For example, depressed individuals are notoriously characterized by self-relevant negative thinking and a lack of other-relevant positive thinking. Moving toward more positive and more social thinking in this group may be particularly useful. Individual differences in the neurobiology of depression may make change in either positive affect or social functioning a higher priority.

A take-home message is that neural substrates of empathy and compassion, including brain networks underlying social, affective, and approach motivation processing, are detectable, dissociable, interactive, and likely malleable. Interventions to increase compassionate action on behalf of the elderly may benefit from developing innovative ways to engage these systems.

Putting Empathy and Compassion into Context: Implications for Neuroscience, Resilience, Wellbeing, and Health

Stephanie Brown, PhD, Stony Brook University

Current approaches to understanding the influence of social behavior on health assume that rational self-interest, psychological hedonism, and other selfish pleasures and benefits drive social behavior. Even studies of empathy, compassion, and prosocial behavior assume self-interest. One paradigm suggests that an individual's empathy and positive emotions arise to relieve that individual's negative state, whereas another paradigm suggests that empathy is ultimately other-focused behavior that is crushed under the weight of self-interest. As a result, a long-time assumption is that individuals who receive more support and resources from others will be happier and healthier, and will live longer, than caregivers who experience burnout and associated health problems. However, a meta-analysis published in 1994 demonstrated that social support was associated with satisfaction but not with physical health outcomes. Another meta-analysis found that individuals who helped other caregivers lived longer, suggesting that giving is not itself harmful. The discovery that helping behavior is associated with reduced mortality risk has been replicated repeatedly and has implications for the development of interventions for caregivers. Thus, by adopting a different set of assumptions (e.g., that social behavior involves interest in both the self and others), behavioral and social researchers might learn more or generate new questions.

Selective investment theory posits that interpersonal bonds were designed by evolution to unlock other-focused motivation and the associated physiology, such that individuals suppressed their self-interest when necessary. Although the neural circuitry involved in other-focused motivation may have its evolutionary origin in activating parenting behavior, it can be activated in anyone by a variety of circumstances. In this context, empathy and compassion arise from the activation of other-focused neural circuitry, which can also include values and a sense of meaning, belonging, and purpose. This neurohormonal circuitry, which has been identified as the basis of mammalian parenting behavior, also activates mechanisms that promote physiologic homeostasis in the body.

The physiology underlying other-focused motivation and helping is regulated by the medial preoptic area of the hypothalamus. It inhibits the fight-or-flight response pathway and possibly the reward motivation pathway, and it activates helping behaviors through inhibitory influences in the nucleus accumbens, which normally serves as a brake that prevents exploitation. Cells in the medial orbitofrontal cortex, amygdala, and anterior cingulate cortex activate this neural circuitry in response to cues associated with social bonding, interdependence, and the perception of vulnerability in another person. The circuitry is connected to physiologic homeostasis through release of serotonin and activation of oxytocin (which promote progesterone release and immune system changes) and through inhibitory binding of dopamine in the nucleus accumbens.

With respect to interventions, the physiology underlying other-focused motivation can be mediated by situational, interpersonal, and personal information. However, this system is also a dangerous one to manipulate, as doing so could cause individuals to repeatedly suppress their self-interest. It will be important to create true interdependence, as opposed to the perception of it. As is always the case, intervention development should involve both science and ethics.

Discussion

Investigators studying empathy and compassion need a common language and vocabulary. Empathy has several conflicting definitions and sometimes has been used to describe sympathy.

The extent to which empathy and compassion are evolutionarily conserved is unclear. Certainly, other mammals display behaviors that intuitively resemble the types of “caring” described by Dr. Marsh. Although studies of empathy and compassion have been conducted in humans, primates, and rats, researchers should be careful not to anthropomorphize the behaviors observed in animals. For example, the circuitry associated with threat perception has been identified, but it is unclear whether rodents can experience fear as humans do. Whether emotional experiences are uniquely human is a subject of ongoing debate.

In a caregiving context, where an interpersonal bond is deteriorating, the neural circuitry underlying other-focused motivations may be inhibited, potentially resulting in a feeling of obligation. In identifying ways to circumvent that deterioration, it may be useful to study parental and alloparental care behaviors as models across species to identify common mechanisms underlying caregiving for individuals with dementia.

It is unclear, based on the first two sets of talks, whether increasing empathy is a reasonable goal. It is also an open question whether decreasing empathy is possible and beneficial. However, increasing positive affect toward others and compassionate action were largely agreed on as goals, with less of an emphasis on empathy, writ large, as being useful.

Session III: Interventions to Increase Empathy and Compassion and Support Caregiver Wellbeing

Compassion and Loving-Kindness Meditation as Treatment Approaches

Stefan Hofmann, PhD, Boston University

Frederickson's "broaden and build" model posits that positive emotions enhance experiences through a positive feedback loop. This loop broadens thoughts, activities, and relationships, which in turn build the individual's resources, leading to further experience enhancements. In a related model, emotional disorders arise not only from dysregulation of negative affect, but also from deficiencies of positive affect. Thus, interventions should focus decreasing anxiety or depression and on increasing positive affect. These models are supported by one study showing that an intervention focused on positive factors such as mindfulness, life purpose, and support increased personal resources among healthy adults. Another study has shown that 12 weeks of lovingkindness meditation (LKM) lessens telomere shortening, which is associated with aging. The implications of this finding, with respect to accelerated aging, are under debate.

Both LKM and compassion meditation (CM) focus on all beings, including oneself; CM focuses on compassion for the suffering of all beings, whereas LKM focuses on the happiness of all beings. Both meditation practices rely on interactional and interpersonal engagement, and both target anger, depression, hostility, and anxiety. Although the literature is not substantive, it shows several promising implications associated with these practices. For example, neuroimaging studies have shown that LKM and CM activate the insula and other brain regions associated with emotional processing and empathy.

Dr. Hofmann and his colleagues are exploring LKM as an intervention for several indications, including depression, anxiety, marital conflict, and issues with long-term caregiving. In one laboratory study of individuals with depression, Dr. Hofmann and colleagues presented a task that induced a depressive state, then asked participants to accept their experiences, and either to reappraise them or to use self-compassion in response. Reappraisal was most effective among individuals with low mood, whereas self-compassion was most effective among those with high mood. Self-compassion operated independently of negative thinking styles such as poor self-esteem and negative, automatic thoughts. In other studies, Dr. Hofmann found that a 12-week intervention that gradually introduced LKM substantially reduced self-reported depression symptoms and increased positive affect, compared with a cognitive behavioral therapy (CBT) intervention, among dysthymic individuals or those with treatment-refractory depression. These results were consistent with those of a study by Craske and colleagues, who found that 4-week positive affect training was more effective than negative affect training in increasing positive affect and reducing depression, anxiety, stress, or suicidal ideation. In Dr. Hofmann's study, participants reported increased awareness and acceptance, increased generosity, increased empathy and tolerance, and a new relationship with negative thoughts and emotions as benefits of LKM training.

Thus, LKM and CM, although not well studied, might be effective interventions for emotional disorders. Additional research is needed to determine their efficacy, the mechanism(s) of behavior change, and who is most likely to respond to these interventions.

Designing Interventions to Target Specific Cognitive-Affective Processes

Arielle Baskin-Sommers, PhD, Yale University

Despite substantial progress in the development of strong interventions, the effectiveness of these interventions is limited for some individuals. Moreover, high dropout rates, particularly among individuals with dependents, have raised questions about motivation and readiness for change. Research among caregivers, particularly those caring for individuals with dementia or cancer, has shown small effect sizes in interventions, but they have also shown the strongest effects when interventions are individualized and implemented earlier. A large amount of research is under way to specify, define, and measure psychological constructs and to determine how best to match these constructs with individuals and their needs.

Creation of an intervention development should include a clear definition of the target users. Because caregivers form a heterogeneous group, researchers should identify the type of caregiving they are targeting; define the specific cognitive-affective processes on which to focus; and select exercises that address those processes and align with the target users, not only to design an intervention that might benefit the user, but also to avoid the pitfalls of providing a potentially problematic intervention. Finally, researchers designing an intervention must determine whether enhancing an existing intervention is warranted or whether creating a new one is scientifically justifiable.

Dr. Baskin-Sommers and her colleagues are conducting a randomized study among individuals with substance use disorders at outpatient clinics in New Haven, Connecticut. At baseline, most of the individuals in the study have shown trait externalizing behavior, including impulsivity and aggression. On the basis of previous research, Dr. Baskin-Sommers and her colleagues have designed a computerized training intervention that trains individuals to inhibit in the presence of a reward, engage working memory in the presence of distress, and make decisions in the presence of ambiguity, thereby addressing interrelated cognitive-affective processes that show abnormalities in individuals with substance use disorders. Preliminary results suggest that participants receiving the cognitive remediation training display substantial changes in distress tolerance abilities and improvements in working memory, compared with the group receiving a computerized control unrelated to specific cognitive-affective processes. In addition, these same individuals still exhibit such changes 1 month after their training ends. Participants have commented that the intervention is fun and exercises the brain. Others have identified what the intervention is asking them to practice, and others have identified how these games help them to address issues underlying their substance use.

This model of intervention development aligns with the SOBC method of “identify, measure (broaden and hone), and influence.” It is possible that this work could translate to CBT interventions that ask questions in a specific way or circumvent individuals’ limitations. In addition, computerized approaches offer a portable way to engage users and match tasks with

the user, process, and target behavior. Researchers designing interventions for caregivers will need to define the caregivers they want to target (e.g., the age group and what they do), the target behaviors (e.g., better care or less burnout for the caregiver), the target processes and their complexities (e.g., empathy and compassion), and efficient and effective ways to target these processes (e.g., considering the time commitment of caregiving).

Study of Compassion Meditation as an Intervention

Sona Dimidjian, University of Colorado, Boulder

In a study at the University of Colorado, Boulder, Dr. Dimidjian and colleagues explored the potential effects of a CM intervention on compassionate behavior. Study participants were randomized to a 4-week, CM-based intervention, an “oxytocin control” group that received a nasal spray and was told that using it would make them more compassionate, or a “repeated exposure and familiarity” group that looked at photos and heard stories about the suffering of others. At baseline and at study end, study participants heard 24 true stories and received \$100, which they could keep or distribute to charities. They rated their feelings, attributions, and sense of similarities with the people in the stories and the photos, and they underwent neuroimaging after the 4-week training. The CM group showed significant increases in their subjective experiences of compassion and their response to others’ suffering compared with the repeated exposure group, who showed less subjective compassion and response, and the oxytocin placebo group, who showed no change. However, the CM group showed no significant changes in donations, and the repeated exposure and familiar group showed significant declines.

These findings suggest that CM-based practices may have specific efficacy in increasing compassion. However, simply believing one is more compassionate does not necessarily translate into more compassionate behaviors. It is important to distinguish among the different types of contemplative practices. For example, mindfulness meditation focuses attention on the present moment and is neutral with respect to relationships with other people, whereas CM begins with lovingkindness to create goodwill, then builds onto that compassion, joy, and equanimity. In addition, the idea that individuals can practice compassion for close others in their lives, but that the most evolved and developed sense of compassion is non-referential, for example as observed in altruistic parenting, has broad implications for caregiving. Future work should focus on the components of CM training: explicit attention to one’s intention; affective components that generate warmth, tenderness, and wishing others well; and perspective-taking. The incorporation of stakeholder views and subjective experiences is also important.

Discussion

Empathy and compassion appear to be different but linked phenomena. Empathic processes are unavoidable in social situations, and they ebb and flow based on the type of interaction. For example, individuals are more likely to be empathetic if their bond with the other person is closer. As presentations earlier in the day suggest, it is possible to have too much or too little empathy. Compassion may provide a means to alleviate or respond to the emotions brought

about by empathy, allowing individuals a mechanism to regulate their own suffering. For example, in a study by Dr. Monin and colleagues, individuals' distress decreased as they described what they had done to relieve someone else's suffering. Another example may be found in a mother caring for a child, someone with whom she does not have a peer-to-peer interaction.

Evolutionarily, there is reason to believe that the systems associated with empathy, compassion, and giving arose to increase fitness within an ingroup. When one's fate is tied to the fate of another who can influence evolutionary fitness, the situation that arises prevents the exploitation of helping behavior. However, the systems arising in ancestral times, in the context of interacting with an ingroup, can be generalized outside of the traditional cues associated with similarity, proximity, and familiarity. With increased understanding of the behavioral, cognitive, and affective processes and the neuronal systems that can be activated to promote empathy and compassion, interventions such as LKM practices could be designed to promote helping behaviors.

Although the meditation studies described in this session show promising results, these studies have not focused on the effects of such interventions in the context of caregiving, and they may not be practical in that context. For example, caregivers are unlikely to have a free hour to sit quietly. Researchers should therefore consider what they want to learn or promote, then how to do that in a low-impact way. As suggested by Dr. Baskin-Sommers' presentation, interventions that are not only brief, but also exciting or enjoyable, might be more likely to be adopted widely. The NIH Stage Model provides a framework for modifying interventions to promote their real-world acceptability and usefulness while remaining consistent with the principles that make that intervention potent.

The perception of the caregiver that their actions are helpful versus ineffectual could be a critical factor in developing interventions for caregivers, who face a deteriorating bond, taxing demands, and a situation where their efforts may not appear to help the person they are caring for. Thus, one question that could be addressed through research relates to the impact of interventions on the caregiver's perception of the success or failure of his or her efforts. For example, an intervention that reduces a caregiver's expectations of psychological reward by engaging their natural tendencies to help people they love may increase their perceived success during care. Interventions that aim to increase self-compassion, such that caregivers understand their situation and limitations and alleviate feelings of guilt, could also be practical to develop.

Structural or situational factors may also serve as targets, such that the onus is not on the caregiver alone, but support is built into health systems and communities. In Connecticut, LiveWell is a dementia services provider that focuses not only on relieving caregivers' stress, but also on integrating caregivers into a community and providing support. It is working with the Patient-Centered Outcomes Research Institute to empower partnerships between individuals with early-stage dementia and their caregivers, and to involve them in research design. Likewise, in parental care, low social support is a strong predictor of postpartum

depression. With an initiative called Mothers and Others, mothers are encouraged to form groups and to care for their babies together.

Session IV: Measurement

A clear ontology is needed to guide measurement and intervention development to promote empathy and compassion. That said, attempting to define empathy and compassion at this meeting is not feasible, as these are old constructs that have been described differently in various contexts. Nevertheless, researchers must be clear on what kind of empathy and compassion they want to measure and promote. The caregiver could have empathy toward the recipient, and vice versa. Likewise, caregivers and care recipients could have compassion toward each other or themselves. Researchers must consider how targets and outcomes of interventions can be accurately measured.

The caregiving population is heterogeneous. Therefore, when developing interventions, researchers should understand the nature and the needs of the population they are studying. Professional caregivers, such as doctors, nurses, or nursing assistants, may differ from non-professional caregivers, and spousal caregivers may differ from children caring for their parents. Research to develop interventions should account for variability even within the same setting. In addition, some mental health interventions seen in clinical psychology could be adapted for interventions to promote the wellbeing of caregivers.

Another important emphasis in intervention development involves the experiences and capacities of the person receiving care, as well as the nature and stage of that person's illness. The literature on caregiver burden suggests that individuals caring for individuals with dementia experience more negative outcomes than those caring for individuals with cancer or heart disease. Work by Dr. Levenson and his colleagues suggests that loss of cognitive empathy on the part of the care recipient predicts these negative outcomes. Other work has demonstrated that individuals with dementia vary in their impairments.

Researchers must consider which behavior or action they are trying to understand or modify and how best to measure it. For example, measuring one's ability to feel what others are feeling can be done at a behavioral or neural level, whereas action tendencies in caregiving might be measured by tasks performed under conditions of strong communication or stress. Self-report can be a valuable measure but also a problematic one, because empathy is a socially desirable trait, and obtaining honest answers is difficult. Although self-report can be useful for measures of emotional contagion, it might not offer an accurate measure of empathy. Work is under way to identify measures that correlate more strongly with behavioral outcomes. The Psychopathy Inventory is designed to accommodate dishonest answers. Perspective-taking can be measured by tasks that have individuals cultivate an intrinsic, automatic process or by tasks that push individuals to build deliberate, compensatory processes. The Self Scale, including items related to the "other," is another useful measure.

Developing interventions for caregivers also requires that research explore the interpersonal dynamics of the caregiver–care recipient relationship and how those dynamics are affected by the recipient’s dementia. Dr. Monin and colleagues have developed a validated scale to capture the perspectives of the person who is suffering and of the person who is perceiving that suffering. However, it should be noted that nonverbal measures of perspective-taking and empathic accuracy are less accurate than some expect, for example because individuals often interpret others’ feelings incorrectly. Dr. Monin and her colleagues also have developed coding systems of social interactions and caregiving behaviors. Interventions for parents and children and emotion-focused therapy, an attachment-based approach used for spouses, may offer measures that could be adapted to the bond between caregiver and care recipient.

However, psychometric research by Dr. Brown and colleagues suggests that emotional dependence and attachment anxiety predict few outcomes related to the effects of the bond between caregiver and care recipient. They have therefore developed scales to disentangle the social bond from attachment anxiety and emotional dependence, including an interdependence scale that maps to genetic similarity, familiarity, and proximity. Among caregivers of individuals with AD, those who report higher scores on the interdependence scale are more likely to experience positive emotions when they help. Likewise, individuals who help but do not feel connected with the care recipients show worse physiologic and immune outcomes. Thus, the quality of the relationship between the caregiver and the care recipient serves as a moderator. In addition, an individual’s cognitive assessment of the relationship is associated with outcomes in a way that the emotional relationship itself is not.

Physiologic measures can add to the picture generated by subjective measures. Measures of one individual’s response to another’s experiences are difficult and can be relationship specific. However, other physiologic tools can measure the state of other orientation, assessing the degree not only to which someone is focused on another’s wellbeing, but also to which the person automatically assumes that perspective. Surprisingly, oxytocin is not an adequate measure of the strength of a bond, because it is recruited just as much for stress-enhancing processes as for stress-reducing processes. However, among physiologic biomarkers that predict long-term health outcomes, transforming growth factor beta, which is associated with several diseases, can be influenced by a 15-minute closeness induction.

Dr. Siegle and colleagues are measuring synchrony using electroencephalogram to assess the dynamics of a relationship in real time. They have found that brain activation in one individual may induce different locations and patterns of brain activity in their partner. These studies suggest that massive, dynamic multivariate neural networks are involved in interactions between partners. Thus, interdisciplinary teams, including statisticians with expertise in multivariate modeling, may be useful for understanding and targeting neural mechanisms of interpersonal interactions in interventions.

Although some aspects of empathy and compassion are universal, others might vary by culture. For example, some cultures are more collectivist and vary with respect to perceptions of burden. Families in these communities traditionally keep their loved ones at home; thus,

patients are not seen in the clinic until later stages in their disease. Cultures also vary in the level of government support for caregiving, as well as how they view suffering. In some cultures, sadness is viewed as a rich experience; interventions promoting acceptance might be especially helpful or could prove to be unnecessary in that context. Studies conducted within different cultures may help to shed light on understanding whether, how, and why interventions work the same or differently within these different cultural contexts. For example, it may be asked whether interventions based on meditation practices, which have been borrowed from other traditions and are part of a broader philosophy, work differently and have different effects within different cultures.

Breakout Sessions

Considerations in Study Design

Robert DeRubeis, PhD, University of Pennsylvania

Often, an intervention that appears promising shows only a modest effect, if any, when tested. This can arise from inaccurate assumptions about the intervention's potency or from weak or inconsistent evidence of benefit. An intervention can show a disappointingly small effect because the treatment target is incorrect or poorly defined/measured or because it is optimal only for a subset of individuals. Current intuitions about promising interventions do not account for individuals who remit spontaneously and therefore do not need a strong intervention, nor do they account for intractable individuals who are unlikely to benefit from the intervention. In clinical trials, therefore, inclusion and exclusion criteria need to be given careful consideration inasmuch as this will affect the likelihood that the strength of an intervention, or its strength relative to that of a comparator or control condition will be revealed. The most discriminating tests of an intervention are those that recruit from a population consisting primarily of "pliant patients," or patients who will exhibit a robust response to an intervention but will improve little, if at all, if they receive a weaker intervention, or no intervention at all.

Dr. DeRubeis and colleagues have conducted simulations of RCTs comparing a potent treatment condition and a control condition. They instantiated that the treatment condition would be 10 points better than the control in a situation where the advantage of the stronger treatment is relevant for all patients (thus excluding those who would remit spontaneously or whose problem is intractable). If the study is simulated thousands of times in an idealized population, the intervention will always show a significant effect. In a population predominated by pliant patients the average difference between the treatment and control condition will remain high. However, in study populations that are skewed such that a substantial proportion of the participants are likely to remit spontaneously or with only minimal treatment, very small differences can be expected between two treatments that would differ markedly in their effects if pliant patients comprised a substantial portion of the sample. Consequently, the power of any given study that fits this description to detect treatment differences will be very low. The same holds for populations that consist primarily of "very challenging" or intractable patients. In tests conducted with a broad sampling along this responsiveness dimension, it is still important to estimate the average effect of an intervention or of its advantage relative to a

comparator. However, a sole focus on the average effect can result in researchers missing what could be a very positive effect for a subset of dyads, in which a promising intervention could be deemed too weak to study further or disseminate. This risk again suggests the need for researchers to understand who the target population is for an intervention and to consider aspects of personalization.

With respect to caregiving, outcome studies have shown mixed results, but it is possible that some important benefits might have been obscured. Based on work by Dr. DeRubeis and colleagues, study populations will likely be skewed, and no one variable will inform on the strength of an intervention. In addition, because attrition among caregivers is high, researchers will need to account and predict for dropout in their studies. However, they will need to be clear about the goals that can be furthered by predicting dropout. The goal might simply be to predict who is likely to drop out and who is likely to complete the intervention. A practical use of a model that predicts dropout is that it can illuminate the characteristics of caregivers or recipients that make them prone to drop out. The intervention could then be modified to make it more compelling or engaging for these individuals, assuming this does not negatively affect the nature of the intervention for those who do not require the modification. Finally, a separate intervention could be offered to a caregiving pair that is predicted to be at high risk for dropout from the standard intervention. The care recipient and the dyad between caregiver and care recipient should also be considered in study design. This might include modeling the expected trajectory as dementia progresses in the care recipient. In this way, study designs can include “better than otherwise” as an outcome; this may reflect a decline or worsening, but at a slower rate than would occur without the intervention.

Overview of Breakouts

Expert panelists and participants from NIA and NASEM divided into two groups. Potential topics for discussion included optimal study designs for developing interventions to promote empathy and compassion among caregivers, how and where to recruit participants for intervention research, how to implement interventions related to empathy and compassion, and gaps in basic or intervention research.

Report-Outs

Group 1 acknowledged practical concerns with reaching caregivers, who are already busy, and the importance of considering disease stage and caregiving context in study design. The group therefore focused its discussion on early-stage dementia and on the individual within the dyad, including that individual’s interaction with the dyad and the health system. Group members noted a general lack of awareness of and preparation for situations caregivers will face. The group therefore proposed studies/interventions that would prepare caregivers and build their skills before “things fall apart.” The targets of skills-building would be intermediate or action-oriented states within the caregiver. The group considered the waiting room, when caregivers already have some down time, as a setting for interventions in general, and they considered the workplace as a place for skills-building, similar to what is done for retirement preparation. The

group also considered the importance of terminology, noting that not everyone wants to be called a caregiver. The group discussed a closed-loop detection model, based on ambulatory technologies and monitoring, to determine when interventions are needed; the need for a technique to monitor the progression of caregiver stress without relying on self-report; and integrating aspects of empathy and compassion into existing caregiving interventions such as Care of Persons with Dementia in their Environments.

Group 2 discussed intervention development within the context of the NIH Stage Model, noting the need for a rigorous way to understand the principles underlying the effects of the intervention. Depending on the availability of resources, the new intervention could be added to existing approaches, such as educational or informational interventions, to determine whether the intervention is better than, or at least adds value to, what is already done. In addition, basic science questions about mechanisms could be added to the study of existing interventions. Consistent with discussions throughout the meeting, the group noted that caregivers are heterogeneous and that researchers must therefore specify the target population for their intervention, for example individuals suspected of having AD and their partners, or children caring for their parents. Regarding implementation, participants suggested using Web-, phone-, or video-based interventions. The computer-based pre-training used to prepare individuals for change in CBT, used by Dr. Carrol's CBT4CBT program, was cited as a model for an intervention that is efficacious and easily implemented. The group also expressed caution regarding interpretation of intervention studies reporting many outcomes; group members suggested combining outcomes or ordering them hierarchically. Participants also discussed consulting with clients about feasibility and considering the different stages of dementia (early stages, when the recipient is a capable partner; midpoint, when the caregiver is overwhelmed by changes; and end of care, which involves grieving).

Final Discussion and Synthesis

The word "empathy" encompasses many definitions. As the panel discussed, empathy that reflects an affective response to someone else's affect is good for building rapport and a strong bond, and it serves as an entry point to compassion. Researchers must distinguish among empathic care, emotional empathy, and tenderness; regarding compassion, researchers must distinguish intention or motivation to act versus observed behavior. The method and type of measurement is also critically important. For example, self-report measures of empathy may differ substantially from other measures of empathy, as is the case with emotion. To develop targeted, principle-driven interventions facilitating the optimal levels and types of empathy among caregivers, where mechanisms of behavior change are understood, researchers must clearly define and measure the type of empathy being targeted.

Knowledge Gaps and Potential Research Questions

- What multilevel approaches are available for measuring empathy and compassion?
- How is empathy related to motivation to act? How is motivation to act related to compassion? Does motivation to act translate into action? How can this knowledge inform intervention development?
- What basic mechanisms explain reduced affective activity and empathy following overexposure to others' suffering, compared with the increased tenderness without increased empathic distress observed after compassion meditation? How can these findings relate to intervention development?
- What is the impact of lower cognitive empathy in the individual with ADRD? What is the impact of higher emotional empathy in the caregiver? How do these two states contribute to poor caregiver health?
- Who becomes a caregiver? What paths and processes determine who becomes a caregiver and who does not? How much of the process of becoming a caregiver is determined by empathy? Can this inform intervention development?
- Do individuals' responses to stressors in the caregiving context differ from their responses to other stressors? How do stressors impact empathy and compassion of caregivers, and how do the empathy and compassion of caregivers affect response to stress?
- What is the role of acceptance in compassion and self-compassion, for both the caregiver and the care recipient, and how is this knowledge relevant to intervention development?
- What is the role of touch in fostering empathy and compassion? Can targeted interventions be developed to harness the power of touch, and how might these interventions promote the wellbeing of the caregiver and care recipient?
- What impact does the caregiver's cognitive capacity have on their empathy, compassion, and caregiving, and how might this relate to intervention development?
- How is exploitation related to empathy and compassion? Can psychometrically sound measures of exploitation be developed, and can they help to identify who most needs support and advocacy?
- Can social media data be mined to develop interventions targeting empathy and compassion for caregivers?
- Given the relevance of empathy and compassion to caregiving, what kinds of interventions targeting empathy or compassion can help prepare individuals for caregiving? What is the best timing to administer such interventions and how can unintentional negative outcomes be monitored and avoided?
- Does compassion provide a means to alleviate, or respond to, emotions that arise from empathy? If compassion involves helping, when does helping provide a benefit? Is helping worthwhile only when the caregiver perceives that it led to an improvement?
- What aspects of compassion meditation should future research investigate? How might outcome measures be derived from past research on explicit attention to intention, affective elements that generate warmth, tenderness, and well-wishing, and perspective-taking?

- What is the social context (including cultural, interpersonal, and emotional factors) in which the caregiver provides care? How do levels and types of empathy and compassion relate to these factors? What interventions might be developed to prevent and address social isolation?
- How does culture influence empathy, compassion, altruism, and caregiving? What can be learned from group-centered cultures, and how can this knowledge be leveraged into new interventions? What functions might social expectations (e.g., communal motivation versus exchange motivation) play in empathy, compassion, and caregiving? How do these relate to development of effective interventions?
- How might interventions be developed to target empathy and compassion in contexts of dyad interactions (e.g., when a caregiver listens to a physician) to support and facilitate information processing?
- Can interventions targeting empathy and compassion be developed to help train clinicians and researchers to provide patients and caregivers with information about dementia in a sensitive way?

Potential Barriers

- Practical issues must be considered for all behavioral interventions under development. For caregivers, there are unique needs, and this is especially important as caregivers may not have enough time or energy for elaborate interventions.
- In developing interventions, researchers should keep in mind what systems will pay for. In some cases, this may mean considering what a system might support in the future, even if it does not pay for it at present.
- NIH policies governing clinical trials require that studies adhere to new definitions and requirements regarding data and safety monitoring and registration in [clinicaltrials.gov](https://www.clinicaltrials.gov).
- Laws such as the Health Insurance Portability and Accountability Act may have an impact when treating the caregiver–care recipient dyad in ADRD, yet to what extent is not clear.

Appendix A: Meeting Participants

Expert Panel

Robert DeRubeis, PhD, University of Pennsylvania (Co-Chair)
Sona Dimidjian, PhD, University of Colorado, Boulder (Co-Chair)
Arielle Baskin-Sommers, PhD, Yale University
Stephanie Brown, PhD, Stony Brook University
Stefan Hofmann, PhD, Boston University
Robert Levenson, PhD, University of California, Berkeley
Abigail Marsh, PhD, MA, Georgetown University
Joan K. Monin, PhD, Yale School of Public Health
Greg J. Siegle, PhD, University of Pittsburgh School of Medicine

NIA

Audie Atienza, PhD
Basil Eldadah, MD, PhD
Jonathan King, PhD
Melissa Gerald, PhD
Lis Nielsen, PhD
Lisa Onken, PhD
Luke Stoeckel, PhD

NASEM

Barbara Wanchisen, PhD, Director, Board on Behavioral, Cognitive, and Sensory Sciences
Adrienne Stith Butler, PhD, Associate Director, Board on Behavioral, Cognitive, and Sensory Sciences
Jacqueline Cole Miles, Senior Program Assistant

NIH Office of Behavioral and Social Science Research

William Riley, PhD, Director
William Elwood, PhD

Appendix B: Agenda

Day One: September 16, 2019

Please note: No food, coffee, or water will be provided. Please purchase these items in the cafeteria on the 3rd floor in advance of the meeting. Please save receipts for reimbursement.

- 9:00 am** **Welcome to the National Academies**
Barbara Wanchisen, Director, BBCSS
- 9:15** **Introductions and Setting the Stage for the Meeting**
Sona Dimidjian (Meeting Co-lead), University of Colorado, Boulder
Robert DeRubeis (Meeting Co-lead), University of Pennsylvania
- 9:30** **Background and Context**
Lis Nielsen, Division of Behavioral and Social Research, National Institute on Aging
- Orientation to NIA/BSR Research Agenda
- Lisa Onken, Division of Behavioral and Social Research, National Institute on Aging*
- Need for shared conceptual framework of behavioral intervention development to help participants. Overview of the NIH Stage Model
<https://www.nia.nih.gov/research/BSR/stage-model-behavioral-intervention-development>
- 10:30** **BREAK**
- 10:45** **Session I. The Caregiving Context: Problems and Needs**
Moderator: Robert DeRubeis
- Challenges and needs of the population: aging population is vulnerable to changing relationships, physical health and mental health of caregivers, emotional wellbeing of caregivers (unhappiness, guilt)
 - What are the interpersonal, social, and structural relationships within which caregiving occurs? Within these relationships, how are empathy and compassion relevant to both the caregiver and care receiver?
- Robert DeRubeis (20 min)*
- Challenges/hurdles encountered (interpersonal challenges that are relatively distinct but interact)
- Joan Monin (20 min)*
- Review basic relationship processes (including extent to which the person with dementia is able to cope with their transition to losing

the ability to have empathy/compassion/insight) and how this shifts over time. Then discuss potential next steps.

Bob Levenson (20 min)

- Different types of empathy in individuals with dementia and their caregivers and effects on caregiver health.

Discussion 30 min

12:15 pm **BREAK TO PURCHASE LUNCH (Available for sale in 3rd floor cafeteria)**

1:15 **Session II. Basic Research on Empathy and Compassion**

Moderator: Sona Dimidjian

- Types and definitions of empathy and compassion
- What are the components of empathy and compassion
- How have empathy and compassion have been investigated
- What basic science on empathy and compassion is ripe for translation into interventions for caregivers?

Stephanie Brown

Abigail Marsh

Greg Siegle

- Empathy and compassion in context of affective science and affective neuroscience frameworks.

2:45 Break

3:00 **Session III: Interventions to Increase Empathy and Compassion & Support Caregiver Wellbeing**

Co-Moderators: Robert DeRubeis and Sona Dimidjian

- What intervention research is currently happening?
- Who can benefit from interventions?
- What are the strengths and gaps in the evidence base?
- Can we target components of empathy and compassion?

Robert DeRubeis and Sona Dimidjian (10 min)

- Framing and brief overview of most widely used caregiving interventions

Stefan Hofmann (25 min)

- Review of literature on interventions based in meditation – focused on compassion, self-compassion, loving-kindness

Arielle Baskin-Sommers (25 min)

- Cognitive and affective processes

Discussion 30 min

4:30 **Summary of Day One**
Sona Dimidjian

5:00 **Adjourn Day One**

Day Two: September 17, 2019

Please note: No food, coffee, or water will be provided. Please purchase these items in the cafeteria on the 3rd floor in advance of the meeting. Please save receipts for reimbursement.

9:00 a.m. **Overview of Day Two & Reflections on Day 1**
Robert DeRubeis

9:15 **Session IV: Measurement**
Moderator: Sona Dimidjian

Each participant will present for 2 min on their top candidates for measurement of empathy and/or compassion

- What are the most promising methods to measure empathy and compassion?
- What are the priority outcomes of empathy and compassion interventions and how are these measured?
- What are populations of interest for studies of empathy and compassion?

10:15 **Organize Break Out Groups**

10:30 **BREAK**

10:45 **Break Out Sessions: Design and Implementation**

Potential topics for breakouts. We envision participants breaking into no more than three groups. Topics will also be informed by discussions that occur on day 1.

1. What designs are best suited when conducting research on developing interventions to help caregivers achieve optimal types and levels of empathy and compassion?
2. How and where do we find and recruit people with whom to conduct intervention research?
3. What would various forms of implementation related to empathy and compassion eventually look like (e.g., web-based, how teachable, ease of administration with fidelity in the real world)

4. What kinds of study designs are most informative given the current state of the field (e.g., informative for understanding mechanisms of behavior change in interventions to optimize type and level of empathy/compassion, or for developing the most potent types of interventions)? How do we tailor a study design to have real-world application?
5. What are the gaps in basic or intervention research and what designs best address these gaps? How can behavioral intervention development inform basic research on empathy/compassion and how can basic research inform intervention development?

12:00 pm **LUNCH**

1:00 **Report-out from Breakout Groups**

2:00 **Synthesis**
Robert DeRubeis
Sona Dimidjian

2:30 **Closing Remarks from the National Institute on Aging**
Lis Nielsen
Lisa Onken

2:45 **Adjourn**