No. 16-2444

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**UNITED STATES COURT OF APPEALS**

**FOR THE FIRST CIRCUIT**

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JWAINUS PERRY,

*Plaintiff-Appellant,*

v.

LUIS S. SPENCER, Commissioner; THOMAS DICKAUT, Former Superintendent; ANTHONY MENDOSA, Former Deputy of Classification; JAMES SABA, Superintendent; ABBE NELLIGAN, Deputy of Classification; PATRICK TOOLIN, Correctional Program Officer; KRISTIE LADOUCER; CAROL MICI; THOMAS NEVILLE,

*Defendants-Appellees.*

JENS SWANSON, Property Officer,

*Defendant.*

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# BRIEF OF CENTER FOR LAW, BRAIN & BEHAVIOR AND NEUROSCIENTISTS AS *AMICI CURIAE* IN SUPPORT OF PLAINTIFF-APPELLANT JWAINUS PERRY

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## CORPORATE DISCLOSURE STATEMENT

Pursuant to Federal Rule of Appellate Procedure 26.1, the *amici curiae* state that none has had a corporate parent, none issues stock, and no publicly held corporation owns 10% or more of any of them, individually or collectively.

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## RULE 29(A)(4)(E) STATEMENT

No part of this brief was authored, in whole or in part, by counsel for any party. No person, including but not limited to any party or party's counsel, other than amici, contributed any money intended for the preparation or submission of this brief.

## IDENTITY AND INTEREST OF *AMICI CURIAE*[1]

The Center for Law, Brain & Behavior (CLBB) at Massachusetts General Hospital's mission is to put the most accurate and actionable neuroscience in the hands of people who shape the standards and practices of the legal system and affect its impact on people's lives. By equipping system actors in this way, CLBB works to make the legal system more effective and more just for all those affected by the law. To this end, CLBB provides expert training, tools, and counsel to help members of the legal community understand and apply the most relevant brain science to cases, courtroom procedures, and policies. The neuroscientists who have joined the proposed *amici curiae* brief share CLBB's interest in ensuring that the most accurate and current neuroscience informs the operation of law. *Amici* are uniquely positioned to provide this Court with the scientific community's current understanding of the brain, as related to solitary confinement.

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[1] This brief is filed with the consent of the parties pursuant to Federal Appellate Rule 29(a)(2).

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## SUMMARY OF ARGUMENT

The human nervous system is fundamentally plastic: Brain structure, functions, and connections all change in response to intrinsic and extrinsic stimuli by reorganizing, even in adulthood. This malleability makes us deeply vulnerable to harmful environments. And those environments have impacts that are more than "merely" psychological; they change the brain itself. They amount to a physical injury. Legal policies which suggest mental injury is somehow not physical are subscribing to outdated scientific doctrine, especially with respect to solitary confinement.

Research has shown that the conditions of prolonged isolation, chronic emotional stress, and disrupted sleep endemic to solitary confinement are capable of causing adverse anatomical and functional changes in the brain, including in areas core to memory and learning (hippocampal shrinkage in chronic emotional stress and chronic sleep deprivation); in areas core to the social and emotional brain (social deprivation and atrophy in the posterior superior temporal sulcus, chronic sleep deprivation and damage to the insula and amygdala); in disordered immune and stress systems (impaired sleep increasing the presence of brain tau plaques, social isolation

increasing amyloid and tau plaque presence and increasing cortisol levels); in functional disruptions related to emotional processing (chronic stress and post-traumatic stress disorder manifesting with hyperactivity in the amygdala), and shrinkage and dysfunction of areas of the brain core to learning, impulse control, reasoning, and social cognition (shrinkage of the medial prefrontal cortex and anterior cingulate cortex in PTSD, lowered connectivity in the corpus callosum and corona radiata in chronic stress, global reductions of cerebral blood flow tied to social isolation).

By any definition, such changes to the brain constitute physical injury.

## ARGUMENT

### I. Conditions Endemic to Solitary Confinement Inflict Structural and Functional Changes in the Human Brain.

#### A. Prolonged Isolation Can Inflict Structural and Functional Changes in the Brain.

Inmates in solitary confinement are subject to restrictions on visits from friends and family, as well as restricted interaction with other prisoners and prison staff.[2] The extent of isolation is difficult to comprehend; there is no communication with guards, no social group to speak of, no tie to the outside world, no television,

[2] Bruce A. Arrigo & Jennifer Leslie Bullock, *The Psychological Effects of Solitary Confinement on Prisoners in Supermax Units: Reviewing What We Know and Recommending What Should Change*, 52 Int'l J. Offender Therapy & Comp. Criminology 622 (2008).

no phone, no window. This extreme social isolation puts the brain and body at grave risk of isolation-mediated injuries ranging from impairment of heart health and sleep quality to brain shrinkage and cognitive decline.

Loneliness is tied to shrinkage in the brain. A recent study found loneliness to be correlated with decreased volume of the posterior superior temporal sulcus (pSTS), an area implicated in social cognition, while another found loneliness is tied to reduced gray matter (largely composed of the cell bodies of neurons) in the pSTS.[3] Another study related extended social isolation to lower hippocampal volumes, an especially plastic area of the brain core to learning and memory.[4] The volume of an individual's amygdala, an area core to emotional processing, is predicted by the size and complexity of their social networks in adults across the lifespan; as a social network is restricted, the amygdala shrinks.[5] These plasticity induced brain changes

[3] Ryota Kanai et al., *Brain Structure Links Loneliness to Social Perception*, 22 Current Biology 1975 (2012); Sandra Düzel et al., *Structural Brain Correlates of Loneliness among Older Adults*, 9 Sci. Rep. 13569 (2019).
[4] Alexander Choukèr, *Stress Challenges and Immunity in Space: From Mechanisms to Monitoring and Preventive Strategies* (2019); Niccolò Zovetti et al., *Neuroimaging Studies Exploring the Neural Basis of Social Isolation*, 30 Epidemiology & Psychiatric Sci. (2021).
[5] Kevin C. Bickart et al., *Amygdala Volume and Social Network Size in Humans*, 14 Nature Neuroscience 163 (2011); Seyul Kwak et al., *Social Brain Volume Is Associated with in-Degree Social Network Size among Older Adults*, 285 Proc. Royal Soc'y B (2018).

related to a given environment are probable mechanisms for the physical brain damage tied to social isolation. As social isolation changes brain anatomy, it can also create disordered brain function; prolonged isolation in conditions of confinement is associated with broad reductions in global brain activity.[6] Two studies found that higher loneliness scores were associated with (i) decreased blood flow from the dorsal to the ventral attentional network, (ii) decreased flow from the emotional to the visual network; indeed, these brain alterations in lonely subjects are so significant that neuroscientists can accurately predict subjective loneliness in subjects only by looking at objective altered brain activity.[7]

How can it be the case that extended social isolation causes such potentially devastating brain damage? Evidence from evolutionary psychology and neuroscience indicates that extended social isolation causes psychologically painful chronic

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[6] A. Jacubowski et al., *The Impact of Long-Term Confinement and Exercise on Central and Peripheral Stress Markers*, 152 Physiology & Behav. 106 (2015); Jan Weber et al., *Neurophysiological, Neuropsychological, and Cognitive Effects of 30 Days of Isolation*, 237 Experimental Brain Res. 1563 (2019).

[7] Yin Tian et al., *Causal Interactions in Resting-State Networks Predict Perceived Loneliness*, 12 PLoS ONE (2017); Chunliang Feng et al., *Connectome-Based Individualized Prediction of Loneliness*, 14 Soc. Cognitive & Affective Neuroscience 353 (2019).

stress signaling.[8] For social animals, being socially excluded was evolutionarily often equivalent to death.[9] The primate neuroscience literature establishes that separation from members of social groups in primates activates major behavioral and stress response systems.[10] For example, marmosets placed in isolation for a two-week period evidence increases in plasma cortisol concentrations (a stress-related hormone involved in preparation for physical defense), submissive crying, and weight loss averaging ten percent of body mass.[11]

Social stressors have been shown to evoke similarly strong physiological responses in humans. Humans' extraordinary reliance on other individuals has led to the characterization of humans as the "ultra-social animal." This reliance puts us at

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[8] Jaak Panksepp, *Affective neuroscience: The foundations of human and animal emotions* (Oxford Univ. Press 1998); Eric E. Nelson & Jaak Panksepp, *Brain Substrates of Infant-Mother Attachment: Contributions of Opioids, Oxytocin, and Norepinephrine*, 22 Neuroscience & Biobehavioral Rev. 437 (1998); Faiza Mumtaz et al., *Neurobiology and consequences of social isolation stress in animal model—A comprehensive review*, 105 Biomedicine & Pharmacotherapy 1205 (2018).

[9] Eric D. Wesselmann et al., *An Evolutionary Social Psychological Approach to Studying the Effects of Ostracism*, 6 J. Soc., Evolutionary & Cultural Psychol. 309 (2012).

[10] W. A. Mason & S. P. Mendoza, *Generic Aspects of Primate Attachments: Parents, Offspring and Mates*, 23 Psychoneuroendocrinology 765 (1998).

[11] E. O. Johnson et al., *The Biobehavioral Consequences of Psychogenic Stress in a Small, Social Primate (Callithrix Jacchus Jacchus)*, 40 Biological Psychiatry 317 (1996).

extraordinary risk from social isolation.[12] A meta-analysis showed that in humans, the threat of social evaluation and exclusion is unique among psychological stressors in stimulating the release of high levels of cortisol (and this relation was particularly strong when stress was uncontrollable).[13] Chronically high levels of cortisol are linked to increase in blood cholesterol, triglycerides, blood sugar, and blood pressure, common risk factors for heart disease, as well as increasing the likelihood of cognitive decline.[14]

Evidence links perceived social isolation with adverse health consequences including depression, poor sleep quality, impaired executive function, accelerated cognitive decline, poor cardiovascular function and impaired immunity at every stage of life.[15] Incredibly, lack of social connection heightens health risks as much as smoking fifteen cigarettes a day or having alcohol use disorder.[16] A 2019 study

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[12] Michael Tomasello, *The Ultra-Social Animal*, 44 Euro. J. Soc. Psychol. 187 (2014); Jean Decety, *The Social Brain: A Developmental Perspective* (2020).
[13] Sally S. Dickerson et al., *When the Social Self Is Threatened: Shame, Physiology, and Health*, 72 J. Personality 1191 (2004).
[14] Guerry M. Peavy et al., *The Influence of Chronic Stress on Dementia-Related Diagnostic Change in Older Adults*, 26 Alzheimer Disease & Associated Disorders 260 (2012).
[15] Louise C. Hawkley & John P. Capitanio, *Perceived Social Isolation, Evolutionary Fitness and Health Outcomes: A Lifespan Approach*, 370 Phil. Transactions Royal Soc'y B (2015).
[16] Julianne Holt-Lunstad et al., *Loneliness and Social Isolation as Risk Factors for Mortality: A Meta-Analytic Review*, 10 Persp. on Psychol. Sci. 227 (2015).

from the American Cancer Society, analyzing data from more than 580,000 adults, found that social isolation increases the risk of premature death from every cause for every race and, among Black participants, social isolation doubled the risk of early death while it increased the risk among white participants by sixty to eighty-four percent.[17] A recent study surveying more than 12,000 U.S. adults ages fifty years and older found loneliness is associated with a forty percent increase in a person's risk of dementia.[18] Two recent studies investigated the neurobiological correlates of loneliness found that perceived loneliness was associated with increased amyloid and tau proteins, brain plaque aggregates commonly associated with the development of several neurocognitive diseases including dementia.[19]

### B. Chronic Emotional Stress Can Inflict Structural and Functional Changes in the Brain.

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[17] Kassandra I. Alcaraz et al., *Social Isolation and Mortality in US Black and White Men and Women*, 188 Am. J. Epidemiology 102 (2019).

[18] Angelina R. Sutin et al., *Loneliness and Risk of Dementia*, 75 J. Gerontology B Psychol. Sci. & Soc. Sci. 1414 (2020).

[19] Zovetti et al., *supra*; Nancy J. Donovan et al., *Association of Higher Cortical Amyloid Burden With Loneliness in Cognitively Normal Older Adults*, 73 JAMA Psychiatry 1230 (2016); Federico D'oleire Uquillas et al., *Regional Tau Pathology and Loneliness in Cognitively Normal Older Adults*, 8 Translational Psychiatry 282 (2018).

Five decades of neuroscientific research suggest chronic emotional stress is neurotoxic, with stress signaling affecting brain volume in the hippocampus, amygdala and frontal cortex.[20] Our biology respects no distinction between mind and brain; the emotional pain of chronic stress is brain activation, and prolonged patterns of brain activity cause physical brain changes.[21] Physical pain and psychological pain operate via shared mechanisms in the brain.[22] With respect to chronic physical pain, neuroscientific evidence indicates that prolonged bodily pain can lead to brain atrophy. For example, patients with chronic back pain show five to eleven percent less neocortical gray matter volume than control subjects.[23] Chronic back pain specifically reduces patients' bilateral hippocampal volume, a brain injury that is implicated in the learning and memory deficits commonly observed in such patients.[24]

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[20] Sonia J. Lupien et al., *The Effects of Chronic Stress on the Human Brain: From Neurotoxicity, to Vulnerability, to Opportunity*, 49 Frontiers Neuroendocrinology 91 (2018).

[21] Nina Smyth, *Stress and Brain Health: Across the Life Course* (2020).

[22] Geoff Macdonald & Mark R. Leary*, Why Does Social Exclusion Hurt? The Relationship between Social and Physical Pain*, 131 Psychol. Bull, 202 (2005).

[23] A. Vania Apkarian et al., *Chronic Back Pain is Associated with Decreased Prefrontal and Thalamic Gray Matter Density*, 24 J. Neuroscience 10410 (2004).

[24] Amelia A. Mutso et al., *Abnormalities in Hippocampal Functioning with Persistent Pain*, 32 J. Neuroscience 5747 (2012).

Chronic headaches, back pain, and phantom limb pain are further associated with decreased gray matter density in the prefrontal cortex and thalamus.[25]

As emotional and physical pain are processed by overlapping brain networks, chronic emotional pain, too, is associated with brain atrophy. Exposure to chronic emotional stress, either repeated acute or moderate sustained stress, is one of the strongest risk factors for the development of psychopathologies such as post-traumatic stress disorder (PTSD), as well as a robust risk factor for many medical conditions including cardiovascular disease, obesity, cancer, and immune disorders.[26] Chronic stress can manifest behaviorally as emotional numbing, concentration deficits, substance use disorders and sleep disturbances, among other symptoms.[27] Measures of chronic emotional stress, and linked levels of chronically elevated cortisol, are correlated with shrinkage in brain volume as well as lowered connectivity in the corpus callosum and corona radiata.[28] A chronically stressful environment can cause stress-induced regression of the length of dendrites of pyramidal neurons in

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[25] A. Vania Apkarian, *The Brain Adapting with Pain: Contribution of Neuroimaging Technology to Pain Mechanisms* (2015).

[26] Macdonald & Leary*, supra*; Natalie Matosin, *Preclinical and Clinical Evidence of DNA Methylation Changes in Response to Trauma and Chronic Stress*, 1 Chronic Stress (2017).

[27] Rajita Sinha, *Chronic Stress, Drug Use, and Vulnerability to Addiction*, 1141 Annals N.Y. Acad. of Sci. 105 (2008).

[28] Justin B. Echouffo-Tcheugui et al., *Circulating Cortisol and Cognitive and Structural Brain Measures: The Framingham Heart Study*, 91 Neurology 1961 (2018).

the hippocampus, an area of the brain critical for memory, learning, and memory formation in wake and sleep.[29]

If acute or chronic stress develops into PTSD, it can manifest neurally as brain atrophy, disordered network connectivity in the brain, and altered brain chemistry. Patients with post-traumatic stress disorder (PTSD) show smaller hippocampal and anterior cingulate volumes, hyperactive amygdala function, and diminished medial prefrontal and anterior cingulate function.[30] Patients with PTSD show abnormally increased cortisol and norepinephrine responses to stress.[31] The medial prefrontal cortex, which exerts inhibitory control over stress responses and emotional reactivity, is reduced in volume in patients with PTSD, with reduction degree associated with PTSD symptom severity.[32] The hippocampus, implicated in the control of stress responses and one of the most plastic regions in the brain,[33] atrophies in proportion

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[29] B. Czéh et al., *Stress-Induced Changes in Cerebral Metabolites, Hippocampal Volume, and Cell Proliferation Are Prevented by Antidepressant Treatment with Tianeptine*, 98 Proc. Nat'l Acad. Sci. U.S. Am. 12796 (2001).

[30] Noriyuki Kitayama et al., *Smaller Volume of Anterior Cingulate Cortex in Abuse-Related Posttraumatic Stress Disorder*, 90 J. Affective Disorders 171 (2006).

[31] Sutin et al., *supra*; J. Douglas Bremner, *Traumatic Stress: Effects on the Brain*, 8 Dialogues Clinical Neuroscience 445 (2006).

[32] Scott L. Rauch et al., *Selectively Reduced Regional Cortical Volumes in Post-Traumatic Stress Disorder*, 14 Neuroreport 913 (2003); Jonathan E. Sherin & Charles B. Nemeroff, *Post-Traumatic Stress Disorder: The Neurobiological Impact of Psychological Trauma*, 13 Dialogues Clinical Neuroscience 263 (2011).

[33] E. Fuchs & E. Gould, *Mini-Review: In Vivo Neurogenesis in the Adult Brain: Regulation and Functional Implications*, 12 Euro. J. Neuroscience 2211 (2020).

to the severity of emotional trauma experienced. These injuries to the brain are inseparable from concomitant injuries to the mind, as the degree of hippocampal atrophy related to emotional trauma predicts future memory impairments, and chronic stress can impair hippocampal neurogenesis and inhibit future learning and future healing.[34] Degree of cortical atrophy in stress-relevant brain regions predicts a progressive shortening of lifespan.[35]

Solitary confinement creates an unbearably stressful environment. Prolonged social isolation is a constant stressor, diminished generalized perception of control over one's environment is associated with PTSD symptom severity,[36] and disruption in normal rhythms of exercise and sleep exacerbate stressor effects. Individuals in solitary confinement report high levels of anxiety and fear,[37] and experiencing soli-

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[34] M. B. Stein et al., *Hippocampal Volume in Women Victimized by Childhood Sexual Abuse*, 27 Psychol. Med. 95 (1997); R. M. Sapolsky, *Why Stress Is Bad for Your Brain*, 273 Science 749 (1996); D. M. Diamond et al., *Psychological Stress Impairs Spatial Working Memory: Relevance to Electrophysiological Studies of Hippocampal Function*, 110 Behav. Neuroscience 661 (1996).

[35] Seyma Katrinli et al., *Evaluating the Impact of Trauma and PTSD on Epigenetic Prediction of Lifespan and Neural Integrity*, 45 Neuropsychopharmacology (2020).

[36] B. R. Bolstad & R. E. Zinbarg, *Sexual Victimization, Generalized Perception of Control, and Posttraumatic Stress Disorder Symptom Severity*, 11 J. Anxiety Disorders 523 (1997).

[37] Huda Akil, *The Brain in Isolation: A Neuroscientist's Perspective on Solitary Confinement*, *in Solitary Confinement: Effects, Practices, and Pathways toward Reform* (Jules Lobel & Peter Scharff Smith eds., Oxford Univ. Press 2019).

tary confinement is significantly associated with PTSD symptoms among individuals accessing primary care following release from prison.[38] These effects have rippling effects: A study of more than 200,000 people released from prison found that those who had spent any time in solitary were seventy-eight percent more likely to die from suicide within the first year after their release than those incarcerated but not placed in solitary.[39]

### C. Disrupted Sleep Can Inflict Structural and Functional Changes in the Brain.

The conditions in solitary confinement contribute to disruption of sleep and circadian cycles, potentiating both sleep-specific brain injury and disruption of normal healing effects of a natural sleep cycle. Individuals in solitary experience reduced natural light; limited artificial lighting; or constant artificial illumination.[40] Excessive exposure to light at night and limited exposure to natural light during the

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[38] Brian O. Hagan et al., *History of Solitary Confinement Is Associated with Post-Traumatic Stress Disorder Symptoms among Individuals Recently Released from Prison*, 95 J. Urb. Health 141 (2018).
[39] Lauren Brinkley-Rubinstein et al., *Association of Restrictive Housing During Incarceration With Mortality After Release*, 2 JAMA Network Open (2019).
[40] Petition for Writ of Certiorai, *Grenning v. Miller-Stout*, No. 18-9052 (2019).

day can disrupt the transitions between cycles of sleep, diminish sleep quality, and decrease the amount of time one spends in essential REM sleep and deep sleep.[41]

Such sleep loss can beget structural changes in the brain. Sleep deprivation affects concentrations of neuron-specific enolase (NSE) and S100 calcium binding protein B (S-100B) in the human brain, in one night increasing them by up to twenty percent. Increasing concentrations of these factors in blood is indicative of neuronal damage and impaired blood brain barrier function.[42] Worse sleep quality, efficiency, and daytime tiredness are related to greater hippocampal volume loss over time.[43]

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[41] Emma J. Wams et al., *Linking Light Exposure and Subsequent Sleep: A Field Polysomnography Study in Humans*, 40 Sleep (2017); Mirjam Münch et al., *Wavelength-Dependent Effects of Evening Light Exposure on Sleep Architecture and Sleep EEG Power Density in Men*, 290 Am. J. Physiology, Regulatory, Integrative & Comp. Physiology (2006).

[42] Christian Benedict et al., *Acute Sleep Deprivation Increases Serum Levels of Neuron-Specific Enolase (NSE) and S100 Calcium Binding Protein B (S-100B) in Healthy Young Men*, 37 Sleep 195 (2014).

[43] Yuki Motomura et al., *Sleep Debt Elicits Negative Emotional Reaction through Diminished Amygdala-Anterior Cingulate Functional Connectivity*, 8 PloS ONE (2013); Anders M. Fjell et al., *Self-Reported Sleep Relates to Hippocampal Atrophy across the Adult Lifespan: Results from the Lifebrain Consortium*, 43 Sleep (2020).

Regional gray matter volume of the bilateral hippocampal body is significantly correlated with sleep duration.[44] There is a clear association between sleep loss, hippocampal volume changes, and impairment of memory function.[45]

Sleep loss is linked to memory pathologies ranging from mild cognitive impairment to Alzheimer's pathology. Sleep, but not wakefulness, allows removal of waste metabolites from the brain.[46] Sleep typically clears the brain of toxins and plaques which accelerate cognitive decline, but disturbed sleep instead increases these dangerous concentrations. Accordingly, there is a bidirectional relationship between sleep and Alzheimer's disease. Sleep loss increases the cerebrospinal fluid concentration of insoluble brain plaques (amyloid-β and tau) which are associated with neuronal loss, synaptic loss, and cognitive dysfunction in Alzheimer's Disease by nearly thirty percent.[47] Chronic sleep deprivation accelerates the spread of tau

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[44] Yasuyuki Taki et al., *Sleep Duration during Weekdays Affects Hippocampal Gray Matter Volume in Healthy Children*, 60 NeuroImage 471 (2012).

[45] *Id.*; Hyun Jin Noh et al., *The Relationship between Hippocampal Volume and Cognition in Patients with Chronic Primary Insomnia*, 8 J. Clinical Neurology 130 (2012); Eun Yeon Joo et al., *Hippocampal Substructural Vulnerability to Sleep Disturbance and Cognitive Impairment in Patients with Chronic Primary Insomnia: Magnetic Resonance Imaging Morphometry*, 37 Sleep 1189 (2014).

[46] Natalie L. Hauglund et al., *Cleaning the Sleeping Brain – the Potential Restorative Function of the Glymphatic System*, 15 Current Opinion Physiology (2020).

[47] Nicolas R. Barthélemy et al., *Sleep Deprivation Affects Tau Phosphorylation in Human Cerebrospinal Fluid*, 87 Annals Neurology 700 (2020).

protein aggregations throughout the brain.[48] After extended sleep loss, the brain's immune system turns against itself: "portions of synapses are literally eaten by astrocytes because of sleep loss."[49] Chronic sleep loss can lead to permanent cell damage and neuronal death.[50]

Again, structural changes in the brain are linked to functional changes, and in turn are related to changes in behavior: The mind is inseparable from the brain. Sleep loss can beget functional changes including a significant decrease in the functional connectivity between the amygdala and the ventral anterior cingulate cortex (vACC), and hyperactivity of the left amygdala, in proportion to the degree of sleep debt. This decrease is significantly correlated with deterioration of subjective mood state.[51] Sleep quality can significantly predict changes in depression and PTSD

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[48] Jerrah K. Holth, et al., *The Sleep-Wake Cycle Regulates Brain Interstitial Fluid Tau in Mice and CSF Tau in Humans*, 363 Science 880 (2019); Chanung Wang & David M. Holtzman, *Bidirectional Relationship between Sleep and Alzheimer's Disease: Role of Amyloid, Tau, and Other Factors*, 45 Neuropsychopharmacology 104 (2020).

[49] Andy Coghlan, *The brain starts to eat itself after chronic sleep deprivation*, NewScience (May 23, 2017), https://www.newscientist.com/article/2132258-the-brain-starts-to-eat-itself-after-chronic-sleep-deprivation/#ixzz6qFwUWJXK.

[50] James E. Jan et al., Long-term sleep disturbances in children: A cause of neuronal loss, 14 Euro. J. Paediatric Neurology (2010).

[51] Motomura et al., *supra*.

symptoms, supporting the causal role of insomnia in the development of psychological issues.[52]

Sleep loss not only damages the brain, but also impairs the brain's repair systems. Sleep disruptions, as well as chronic stress, are both associated with impaired secretion of trophic factors, including brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1 (IGF-1). These trophic factors modulate learning, memory processes, neuronal plasticity, and tissue repair. Studies have found that increased concentrations of BDNF and IGF-1 facilitate cognitive and physical rehabilitation following brain injury.[53] Concentration levels can resume to baseline following the cessation of stress, but only if sleep is restored as sleep is a mediating factor in this return to baseline. In a recent study of combat veterans with PTSD, improved sleep quality was shown to be associated with significant declines in depression and posttraumatic symptoms, and a significant increase in concentrations

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[52] Kathleen M. Wright et al., *Insomnia as Predictor versus Outcome of PTSD and Depression among Iraq Combat Veterans*, 67 J. Clinical Psychol. 1240 (2011).

[53] Heather L. Rusch et al., *Improved Sleep Quality Is Associated with Reductions in Depression and PTSD Arousal Symptoms and Increases in IGF-1 Concentrations*, 11 J. Clinical Sleep Med. 615 (2015); Emily R. Rosario et al., *Hypothalamic-Pituitary Dysfunction Following Traumatic Brain Injury Affects Functional Improvement during Acute Inpatient Rehabilitation*, 28 J. Head Trauma Rehabilitation 390 (2013).

of IGF-1.[54] Sleep loss damages brain structure and brain function, impairs brain waste removal, and impairs opportunities for brain repair.

## II. Structural and Functional Changes in the Brain are Physical Injuries.

Brain injuries from each of these conditions compound; increased loneliness is strongly associated with insomnia symptoms and shorter sleep duration.[55] In turn, studies suggest that sleep deprivation lowers the psychological threshold for the perception of stress.[56] Chronic stress atrophies and shrinks the brain while chronic sleep disturbance fills it with insoluble plaque and disturbs systems which heal and protect. These brain injuries are not only debilitating but can further impede prisoners' effective rehabilitation and reintegration into society.[57] Mental injuries can often be as severe, long lasting, and treatment resistant as so-called physical injuries.[58] As

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[54] Rusch et al., *supra*.
[55] John T. Cacioppo & William Patrick, *Loneliness: Human Nature and the Need for Social Connection* (2009); Jade A. Benson et al., *Associations of loneliness and social isolation with actigraph and self-reported sleep quality in a national sample of older adults*, 44 Sleep (2021).
[56] Jared D. Minkel et al., *Sleep Deprivation and Stressors: Evidence for Elevated Negative Affect in Response to Mild Stressors When Sleep Deprived*, 12 Emotion 1015 (2012).
[57] Sadie Dingfelder, *Psychologist Testifies about the Dangers of Solitary Confinement*, 43 Monitor on Psychology (2012) ("One of the very serious psychological consequences of solitary confinement is that it renders many people incapable of living anywhere else.").
[58] *See In re* Medley, 134 U.S. 160, 168 (1890) ("A considerable number of the prisoners fell, after even a short confinement, into a semi-fatuous condition, from which

with other physical injuries, some brain injuries can be remediated using self-repair mechanisms that fall under the umbrella of 'neural plasticity', but like tissue injuries to other parts of the body, the law should not devalue a physical injury simply because of the possibility of future improvement. Mental injuries from chronic injury, i.e., chronic stressors, are extremely durable and difficult to overcome.[59]

A brain abnormality such as pSTS shrinkage related to social isolation could not only result from impoverished social interaction, but indeed could cause future social impairment: pSTS volume predicts the ability to recognize social signals, and lonely individuals showed difficulty in recognizing social cues.[60] Within the realm of social cognition, the ability to decode others' intentions is a crucial prerequisite

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it was next to impossible to arouse them, and others became violently insane; others still, committed suicide; while those who stood the ordeal better were generally not reformed, and in most cases did not recover sufficient mental activity to be of any subsequent service to the community.").

[59] *See* Stuart Grassian, *Psychiatric Effects of Solitary Confinement*, 22 Wash. U. J.L. & Pol'y 325, 332 (2006) ("Although many of the acute symptoms suffered by inmates are likely to subside upon termination of solitary confinement many [prisoners], including some who did not become overtly psychiatrically ill during their confinement in solitary, will likely suffer permanent harm… this harm is most commonly manifested by a continued intolerance to social interaction, a handicap which often prevents the inmate from successfully readjusting to … general population prison and often severely impairs the inmate's capacity to reintegrate into the broader society upon release from imprisonment.").

[60] Maria Arioli et al., *Increased pSTS Activity and Decreased pSTS-mPFC Connectivity When Processing Negative Social Interactions*, 399 Behav. Brain Res. 113027 (2021).

for appropriate behaviors, predicting successful interactions and good quality of life in healthy conditions, and their breakdown in neuro-psychiatric conditions.[61] Thus the injury is cyclical, both caused by an environment lacking social ties, and increasing the likelihood of future failed social interaction.

The longer solitary confinement lasts, the more likely ill effects will emerge. The Bureau of Justice Statistics reported that approximately twenty-five percent of people in prison and thirty-five percent of those in jail who had spent thirty days or longer in solitary confinement during the previous year had symptoms of serious psychological distress.[62] Conditions of social isolation, chronic sleep loss, trauma and chronic stress in solitary confinement leave enduring marks on those incarcerated, and effects can then further spread beyond those subjected to these torturous conditions: Recent studies show children of chronically stressed or trauma-exposed parents are at greater risk for physical, behavioral, and cognitive problems, including

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[61] Elliot A. Layden et al., *Perceived Social Isolation Is Associated with Altered Functional Connectivity in Neural Networks Associated with Tonic Alertness and Executive Control*, 145 NeuroImage 58 (2017); Stephanie Cacioppo et al., *Implicit Attention to Negative Social, in Contrast to Nonsocial, Words in the Stroop Task Differs between Individuals High and Low in Loneliness: Evidence from Event-Related Brain Microstates*, 70 Cortex 213 (2015).

[62] Bureau of Justice Statistics, *Use of Restrictive Housing in U.S. Prisons and Jails, 2011-12* (Oct. 23, 2015), https://www.bjs.gov/content/pub/press/urhuspj1112pr.cfm.

psychopathologies such as PTSD and depression. Research has illuminated mechanisms for intergenerational transmission of trauma--chronic stress and PTSD alter the epigenomes of parents, cortisol affects gene transcription--and biological correlates of parental stress include neuroendocrine, epigenetic, and neuroanatomical abnormalities in children.[63] The trauma inflicted by conditions of confinement may impose intergenerational impediments to whole communities, not just to individuals.

## III. The Distinction between Physical and Mental is Inapposite in the Brain.

Key to understanding brain injury related to conditions of confinement is the fact that modern neuroscience has long abandoned the distinction between a brain and mind. The distinction between mind and brain, called "substance dualism", was most famously defended by René Descartes in the seventeenth century as part of his argument for the existence of a human soul. As a contemporary scientific question of categories, substance dualism is roundly rejected by brain scientists and cognitive

[63] Mallory E. Bowers & Rachel Yehuda, *Intergenerational Transmission of Stress in Humans*, 41 Neuropsychopharmacology 232 (2016).

scientists alike.[64] There simply is no longer a substantive debate about whether psychology has a physical origin and whether mental processes manifest physically.[65] Legal policies which suggest mental injury is somehow not physical are subscribing to outdated scientific doctrine.

Mind, body, and brain are inseparable, and research has demonstrated that any attempt to separate feeling (in the mind) from physiology (in the body and brain) is scientifically incoherent. Brain-imaging techniques can reveal which specific brain regions are involved in mental efforts, such as face recognition, and in turn imaging of these brain regions can accurately predict the mental content in a subject's brain even without their verbal report (even when they are asleep and dreaming of faces[66]). Focal physical brain lesions can impact specific categories of emotion processing--creating, for instance, an inability to empathize in those injured, a brain injury manifest as altered feeling.

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[64] Dov Fox & Alex Stein, *Dualism and Doctrine*, 90 Ind. L.J. 975, 975 (2015) (describing dualism as "empirically flawed and conceptually bankrupt . . . a person cannot be reduced to his mind or separated from his body. He is, inescapably, both at once").

[65] Panagiotis C. Petrantonakis & Leontios J. Hadjileontiadis, *Emotion Recognition from EEG Using Higher Order Crossings*, 14 IEEE Transactions Info. Tech. Biomedicine 186 (2010); Argye E. Hillis, *Inability to Empathize: Brain Lesions That Disrupt Sharing and Understanding Another's Emotions*, 137 Brain 981 (2014).

[66] T. Horikawa, et al., *Neural Decoding of Visual Imagery during Sleep*, 340 Science 639 (2013).

Mind and brain are known to overlap in modern medicine; Medications designed to treat emotional pain and physical pain overlap, reflecting knowledge that the body itself does not respect a distinction between these targets. The active ingredient in Tylenol, acetaminophen, has a blunting effect on emotional as well as physical pain, and reduces neural responses to social rejection in brain regions associated with social and emotional pain. Clinicians commonly treat chronic physical pain using tricyclic antidepressants.[67] These treatments have effects of dulling both emotional and bodily pain because of the overlap in neural substrates underlying the experience of mental and physical pain.[68]

A mental experience is necessarily generated in the physical substrate of the brain and body. We are material beings, and our emotions are processed physically; psychological pain is physical pain, registered as such in the physical brain, and vice versa. Emotions related to trauma, environmental deprivation, social isolation, and chronic stress can cause physical brain injuries.

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[67] Mayo Clinic, *Antidepressants: Another weapon against chronic pain* (Sept. 7, 2019), https://www.mayoclinic.org/pain-medications/art-20045647.

[68] Specifically, psychological pain of social isolation and physical pain both involve the anterior cingulate cortex and periaqueductal gray brain structures and the opioid and oxytocin neuroendocrine systems. *See* Macdonald & Leary, *supra*; *Social Pain: Neuropsychological & Health Implications Loss & Exclusion* (Geoff MacDonald & Lauri A. Jensen-Campbell eds., Am. Psychol. Ass'n, 2011); Selma Rudert et al., *Current Directions in Ostracism, Social Exclusion and Rejection Research* (2019).

## CONCLUSION

The understanding of mental injury as other than physical is obsolete. Because the mind is the brain, any mental injury must be instantiated in the brain. Research demonstrates that the conditions of solitary confinement cause enduring mental injuries, and that the physical instantiation of those mental injuries are debilitating structural and functional brain changes. These changes to the physical brain constitute physical injury.

Respectfully submitted,

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*s/ Nancy Gertner*

Nancy Gertner

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I hereby certify that on this 11th day of March, 2022, a copy of the foregoing brief was filed electronically and is available for viewing and downloading on the Court's CM/ECF system, and service was made on all counsel of record via the Court's CM/ECF system.

*s/ Nancy Gertner*

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