EDITORIAL

Brain Basis of Resilience and its Effect on Mood Disorders in the Aging

A growing field of research has emerged on the concept of resilience among older adults and its role in successful aging. The successful aging has several components, but it is typically defined as *freedom from chronic disease and disability, as well as high physical and mental functioning* [1]. High resilience later in life has been associated with optimal outcomes, such as reduced depression and mortality risk [2-5], as well as better self-perception of successful aging [1, 6], increased quality of life and improved lifestyle behaviors. Therefore, in the present issue, we aimed to provide a comprehensive review of the literature on aging and resilience by selected experts.

Recent evidence has suggested that sedentary lifestyle and poor diet have a role in the onset and course of depression and anxiety disorders [7, 8]. Hence, Dr. Farioli-Vecchioli and Dr. Cutuli reviewed on the potential positive effects of physical exercise and nutritional factors, such as Omega-3 fatty acids, on psychiatric disorders during aging.

Gene-environment interactions can have lasting consequences on brain structure and function, potentially contributing to diverse neuropsychiatric phenotypes [9, 10]. Dr. Zannas revised the evidence showing how gene-stress interactions can impact the aging brain and related phenotypes in late life. The author also discussed the potential mechanisms underlying such gene-environment interactions and their implications for the prevention and treatment of late-life neuropsychiatric syndromes.

Thirdly, Dr. Faye *et al*. summarized neurobiological factors underlying stress resilience, with particular focus on the serotoninergic (5HT), glutamatergic, and γ-Aminobutyric acid (GABA) systems, as well as the hypothalamic-pituitary-adrenal (HPA) axis in rodents and humans [11-14]. Finally, they discussed stress resilience in the context of aging, as the likelihood of mood disorders increases in older adults. Interestingly, increased resilience has been shown to slow aging and improved overall health.

One of the greatest challenges of the neuroscience research is to identify biological agents that increase resistance to develop pathological responses to stress throughout life. Thus, Dr. Moreno-Fernández *et al*. suggest that LPA_1-receptor could be one of these agents [15, 16]. This receptor is one of the six G protein-coupled receptors through which lysophosphatidic acid acts and has been recently involved in emotional regulation. In fact, the reviewed evidence illustrate the relevance of the LPA-LPA1 pathway in adaptive stress coping and shed light on a potential specific mechanism of stress resilience in the aging.

On the other hand, many studies have shown an important role of glutamatergic system in major depressive disorder [17, 18]. Experimental and clinical data suggest that attenuation of N-methyl-D-aspartate (NMDA) receptor function exerts antidepressant effects. In this sense, Dr. Reús and Dr. Quevedo highlighted findings from animal and human studies identifying the role of glutamatergic system in resilience.

Finally, Dr. Sampedro-Piquero *et al*. helped the reader to improve their understanding about age-related changes in the brain mechanisms involved in regulating the stress response. Furthermore, this review focused on identifying the characteristics of a resilient brain (modifications in HPA structure and function, neurogenesis, specific neuron types, glia, neurotrophic factors, nitric oxide synthase or microRNAs, among others). For example, a better regulation of HPA axis [14], enhanced levels of postmitotic type-3 cells [19, 20] or changes in GABAergic neurotransmission [13] are some of the brain mechanisms involved in resilience.

In conclusion, the aim of this special issue was to give an insight into the current research of neurobiological mechanisms underlying resilience and its impact during aging.

ACKNOWLEDGMENTS

We would like to express our appreciation to all the authors for their contributions and the reviewers for their support and constructive critiques. All of them have made this Special Issue possible.

REFERENCES

[1] Jeste, D.V.; Savla, G.N.; Thompson, W.K.; Vahia, I.V.; Glorioso, D.K.; Martin, A.S.; Palmer, B.W.; Rock, D.; Golshan, S.; Kraemer, H.C.; Depp, C.A. Older age is associated with more successful aging: Role of resilience and depression. *Am. J. Psychiatry*, **2013**, *170*, 188-196. [DOI: 10.1176/appi.ajp.2012.12030386] [PMID: 23223917].

[2] Smith, J.L.; Hollinger-Smith, L. Savoring, resilience, and psychological well-being in older adults. *Aging Ment. Health*, **2015**, *19*, 192-200. [DOI: 10.1080/13607863.2014.986647] [PMID: 25471325].

[3] Bowling, A.; Iliffe S. Psychological approach to successful ageing predicts future quality of life in older adults. *Health Qual Life Outcomes*, **2011**, *9*, 9-13. [DOI: 10.1186/1477-7525-9-13] [PMID: 21388546].

[4] Gooding, P.A.; Hurst, A.; Johnson, J.; Tarrier, N. Psychological resilience in young and older adults. *Int. J. Geriatr. Psychiatry*, **2012**, *27*, 262-270. [DOI: 10.1002/gps.2712] [PMID: 21472780].

[5] Martin, A.S.; Distelberg, B.; Palmer, B.W.; Jeste, D.V. Development of a new multidimensional individual and interpersonal resilience measure for older adults. *Aging Ment. Health*, **2015**, *19*, 32-45. [DOI: 10.1080/13607863.2014.909383] [PMID: 24787701].

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[6] Montross, L.P.; Depp, C.; Daly, J.; Reichstadt, J.; Golshan, S.; Moore, D.; Sitzer, D.; Jeste, D.V. Correlates of self-rated successful aging among community-dwelling older adults. *Am. J. Geriatr. Psychiatry*, **2006**, *14*, 43-51. [DOI: 10.1097/01.JGP.0000192489.43179.31] [PMID: 16407581].
[7] Ciucurel, C.; Iconaru, E. The importance of sedentarism in the development of depression in elderly people. *Procedia Soc. Behav. Sci.,* **2012**, *33*, 722-726. [DOI: 10.1016/j.sbspro.2012.01.216]
[8] Rao, T.S.; Asha, M.R.; Ramesh, B.N.; Rao, K.S. Understanding nutrition, depression and mental illness. *Indian J. Psychiatry,* **2008**, *50*, 77-82. [DOI: 10.4103/0019-5545.42391] [PMID: 19742217].
[9] Uchida, S.; Yamagata, H.; Seki, T.; Watanabe, Y. Epigenetic mechanisms of major depression: targeting neuronal plasticity. *Psychiatry Clin. Neurosci.*, **2017**, doi: 10.1111/pcn.12621. [PMID: 29154458].
[10] Moran, P.; Stokes, J.; Marr, J.; Bock, G.; Desbonnet, L.; Waddington, J.; O´Tuathaigh. Gene x Environment interactions in schizophrenia: evidence from genetic mouse models. *Neural Plast.,* **2016**, *2016,* 2173748. [DOI: 10.1155/2016/2173748] [PMID: 27725886].
[11] Duman, E.A.; Canli, T. Influence of life stress, 5-HTTLPR genotype, and SLC6A4 methylation on gene expression and stress response in healthy Caucasian males. *Biol. Mood Anxiety Disord.,* **2015**, *5,* 2. [DOI: 10.1186/s13587-015-0017-x] [PMID: 25995833].
[12] Nasca, C.; Bigio, B.; Zelli, D.; de Angelis, P.; Lau, T.; Okamoto, M.; Soya, H.; Ni, J.; Brichta, L.; Greengard, P.; Neve, R.L.; Lee, F.S.; McEwen, B.S. Role of the astroglial glutamate exchanger xCT in ventral hippocampus in resilience to stress. *Neuron*, **2017**, *96*, 402-413. [DOI: 10.1016/j.neuron.2017.09.020] [PMID: 29024663].
[13] Zhu, Z.; Wang, G.; Ma, K.; Cui, S.; Wang, J.H. GABAergic neurons in nucleus accumbens are correlated to resilience and vulnerability to chronic stress for major depression. *Oncotarget*, **2017**, *8*, 35933-35945. [DOI: 10.18632/oncotarget.16411] [PMID: 28415589].
[14] Gaffey, A.E.; Bergeman, C.S.; Clark, L.A.; Wirth, M.M. Aging and the HPA axis: stress and resilience in older adults. *Neurosci. Biobehav. Rev.,* **2016**, *68*, 928-945. [DOI:10.1016/j.neubiorev.2016.05.036] [PMID: 27377692].
[15] Pedraza, C.; Sánchez-López, J.; Castilla-Ortega, E.; Rosell-Valle, C.; Zambrana-Infantes, E.; García-Fernández, M.; Rodríguez de Fonseca, F.; Chun, J.; Santín, L.J.; Estivill-Torrús, G. Fear extinction and acute stress reactivity reveal a role for LPA (1) receptor in regulating emotional-like behaviors. *Brain Struct. Funct.*, **2014**, *219*, 1659-1672. [DOI: 10.1007/s00429-013-0592-9] [PMID: 23775489].
[16] Moreno-Fernández, R.D.; Pérez-Martín, M.; Castilla-Ortega, E.; Rossel-Valle, C.; García-Fernández, M.I.; Chun, J.; Estivill-Torrús, G.; Rodríguez de Fonseca, F.; Santín, L.J.; Pedraza, C. malLPA1-null mice as an endophenotype of anxious depression. *Transl. Psychiatry*, **2017**, *7*, e1077. [DOI: 10.1038/tp.2017.24] [PMID: 28375206].
[17] Shin, S.; Kwon, O.; Kang, J.I.; Kwon, S.; Oh, S.; Choi, J.; Kim, C.H.; Kim, D.G. mGLuR5 in the nucleus accumbens is critical for promoting resilience to chronic stress. *Nat. Neurosci.*, **2015**, *18*, 1017-1024. [DOI: 10.1038/nn.4028] [PMID: 26005851].
[18] Nasca, C.; Bigio, B.; Zelli, D.; Niconetti, F.; McEwen, B.S. Mind the gap: glucocorticoids modulate hippocampal glutamate tone underlying individual differences in stress susceptibility. *Mol. Psychiatry*, **2015**, *20*, 755-763. [DOI: 10.1038/mp.2014.96] [PMID: 25178162].
[19] Birch, A.M.; McGarry, N.B.; Kelly, A.M. Short-term environmental enrichment, in the absence of exercise, improves memory, and increases NGF concentration, early neuronal survival, and synaptogenesis in the dentate gyrus in a time-dependent manner. *Hippocampus*, **2013**, *23*, 437-450. [DOI: 10.1002/hipo.22103] [PMID: 23460346].
[20] Clemenson, G.D.; Deng, W.; Gage, F.H. Environmental enrichment and neurogenesis: from mice to humans. *Curr. Opin. Behav. Neurosci*., **2015**, *4*, 56-62. [DOI: 10.1016/j.cobeha.2015.02.005].

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