RESILIENCE AND DEPRESSIVE DISORDERS

Sandro Elisei¹, Tiziana Sciarma¹, Norma Verdolini² & Serena Anastasi²

¹Division of Psychiatry, Clinical Psychology and Rehabilitation, Department of Clinical and Experimental Medicine -University of Perugia, Santa Maria della Misericordia Hospital, Perugia, Italy
²School of Specialization in Psychiatry - University of Perugia, Perugia, Italy

SUMMARY

Introduction: There is considerable variability in the response of individuals to adverse environmental conditions, while some develop psychiatric illnesses like depression, others seem very capable of dealing with it. It is in this observation that the concepts of vulnerability and resilience are rooted.

Methods: We conducted a review of the literature by inserting in PubMed the keywords resilience, vulnerability and depressive disorders.

Discussion and conclusions: Freud formerly used the so-called crystal-principle to describe the concept of vulnerability: according to this, the different psychopathologies would arise depending on the different psychological weaknesses, just like a crystal thrown to the ground shatters along its lines of cleavage intrinsic to it, albeit invisible. The term resilience has been borrowed from physics where it is used to describe the ability of a material to withstand impact without cracking. In psychology, the term resilience refers to a complex and dynamic multidimensional construct, which derives from the interaction of neurobiological, social and personal factors and indicates the ability to adaptively cope with stress and adversity, preserving a normal physical and psychological functioning. Resilience has proven to be a protective factor against the development of psychiatric disorders such as depression. Making a conceptual leap, the concepts of vulnerability and resilience can be related to the psychodynamic classification of depression postulated by Gaetano Benedetti, who distinguished four kinds of depression: the first due to the failure of the ego, the second to the perversion of the superego, the third to the inhibition of the Id and the fourth to the collapse of the ego ideal.

It is possible to improve the resilience of depressed subjects through pharmacological and psychotherapeutic interventions.

Key words: resilience - vulnerability and depressive disorders

* * * * *

INTRODUCTION

Several studies have shown that early-life stress, including abuse, neglect and exposure to inter-parental violence, influences affective and cognitive function and is associated with a higher risk of developing depression (Seok et al. 2012). Animal research showed that the amount of care received in the first few days of life determines behavioral, hormonal and neurochemical aspects of the stress response. Moreover when the relationship between mother and pup is compromised there can be changes in SNC activation in response to chronic stress in adult life. These results can be extended to human beings (Silveira et al. 2011). However not everyone exposed to childhood abuse or other traumas experiences psychopathology (Wingo et al. 2010). The concepts of resilience and vulnerability exactly rise from the observation that there is considerable variability in the response of individuals to adverse environmental conditions (Carli et al. 2011).

METHODS

We conducted a review of the literature by inserting in PubMed the keywords resilience, vulnerability and depressive disorders. We selected articles published in the last five years. Furthermore we analyzed the psychodynamic aspects.

DISCUSSION

Freud formerly used the so-called crystal-principle to describe the concept of vulnerability: "If we throw a crystal to the floor, it breaks; but not into haphazard pieces. It comes apart along its lines of cleavage into fragments whose boundaries, though they were invisible, were predetermined by the crystal's structure. Mental patients are split and broken structures of this same kind." (Freud 1933).

According to this principle the different psychopathologies would arise depending on the different individual psychological weaknesses.

On the other hand, the concept of resilience refers to a dynamic and multilevel process of adaptively overcoming stress and adversity while maintaining normal psychological and physical functioning (Wu et al. 2013). This is not just a lack of stress susceptibility (Henningsen et al. 2012).

Another definition of resilience, given by the American Psychological Association is "the process of adapting well in the face of adversity, trauma, tragedy, threats or even significant sources of threat" (APA 2010).

Actually the term resilience has been borrowed from physics where it is used to describe the ability of a material to withstand impact without cracking and regain its original shape. Although the understanding of this concept is still at an early stage, several researches on this field showed that resilience is the result of the interplay between genetic, epigenetic, developmental, psychological and neurochemical factors (Wu et al. 2013).

Genetic factors

Genetic factors significantly influence resilience responses to trauma and stress. Among these, there are genetic variations determining altered expression of Neuropeptide Y (NPY), which produces anxiolytic effects and promotes protective responses to stress. Alterations in genes that regulate the hypothalamicpituitary-adrenal (HPA) axis also play a role in determining resilience, in particular polymorphisms in corticotropin-releasing hormone (CRH) receptor gene 1 (CRHR1) and FK506-binding protein 5 gene (FKBP5) seem to influence susceptibility to psychiatric illnesses (Wu et al. 2013), mainly depression together with early life stress (Zimmerman et al. 2011). Vulnerability to psychiatric illnesses is also associated to polymorphisms in the noradrenergic (Cathechol-O-Methyltransferase gene COMT) and dopaminergic systems (Cathechol-O-Methyltransferase gene COMT, Dopamine transporter gene DAT1, Dopamine receptor gene e.g. DRD2, DRD4), as well as in the serotonergic one, especially in case of depression (Promoter region of serotonin transporter gene 5-HTTLPR, Serotonin receptor genes e.g. HTR1A, HTR3A, HTR2C) (Wu et al. 2013).

Epigenetic factors

Differences in epigenetic factors, that is functional modifications to the genome without changing the DNA sequence, which regulate gene expression and phenotype through mechanisms such as methylation and demethylation as well as histone modifications, can be a consequence of stress-related factors during critical periods of development, thus influencing susceptibility to psychiatric disorders (Dudley et al. 2011).

Developmental factors

The characteristics of environment during the developmental period significantly influence resilience. As we have already seen, adverse events in early life can negatively affect the development of stress response systems, sometimes causing enduring damage (Wu et al. 2013), such as hyperactive HPA axis (Frodl & O'Keane 2013), hyperfunctioning of the locus coeruleus—norepinephrine system (Feder et al. 2011), reduction of hippocampal volume (Davidson & McEwen 2012), shorter telomeres associated to further develop of several illnesses including depression (Price et al. 2013).

Childhood traumatic events can lead to vulnerability or resilience and this is influenced by specific factors associated with the degree of the stress control of a person. On the one hand there is the so-called "learned helplessness", that is the tendency to believe that it is impossible to change an adverse condition (Wu et al. 2013). This is the consequence of repeated episodes of uncontrollable or overwhelming stress during infancy and childhood (Southwick & Charney 2012). On the other there is the "stress inoculation" phenomenon which occurs when the person develops an adaptative response to mild or moderate stressors and a greater resilience to negative effects of future stressors (Southwick & Charney 2012), just like vaccines induce immunity against diseases.

The significant effects of developmental environment have important implications on promoting resilience and protect against learned helplessness and depression (Southwick & Charney 2012) Key factors in child rearing are positive family functioning and peer relationships, connections to supportive adults and prosocial romantic partners, planfulness, self-discipline and cognitive ability (Burt & Paysnick 2012).

Psychological factors

Positive affect has proven to have a protective effect in the face of stress, as well as being associated with quicker recovery times and better overall psychical health after stress exposure (Geschwind et al. 2010). Also optimism, that is the expectation for good outcomes, has been associated with active coping strategy, subjective well-being, physical health and more fulfilling social networks and connections. (Wu et al. 2013).

Another factor strongly associated to resilience is cognitive reappraisal, that is the ability to monitor and assess negative thoughts and replace them with more positive ones. These factors are both positively influenced by a positive attachment style. Women seem more prone to the use of cognitive reappraisal (Wu et al. 2013).

Adaptability and psychological resilience have been also associated with active coping, which involves behavioral and/or psychological strategies to change qualities of the stressor, the stressor itself or how this is perceived (Feder et al. 2009). A form of active coping contributing to resilience is humor, not only for its capability of alleviating tension but also for its ability to attract social support (Southwick & Charney 2012).

Other factors associated with psychological hardiness in the face of major adverse life events are: the presence of social support as well as the behavior of seeking social support (Ozbay et al. 2008), physical exercise (Fleshner et al. 2011), prosocial behavior, that is altruism (Southwick & Charney 2012), moral compass or an internal belief system guiding values and ethics (Southwick & Charney 2012) and trait mindfulness which may help prevent ruminative depressogenic thinking (Thompson et al. 2011). Mindfulness originated as a Buddhist meditation practice which

involves moment-to-moment awareness of bodily activities, feelings, emotions or sensations, while purposely perceiving and discarding any distracting thoughts that come into awareness (Thompson et al. 2011).

Neurochemical factors

Numerous neurochemicals have been found to be involved in resilience. As previously mentioned among these: Neuropeptide Y, hormones of HPA axis, norepinephrine, dopamine, serotonin, BDNF, glutamate, GABA and endocannabinoids. (Wu et al. 2013)

Neural circuits of resilience

The neural circuits involved in the development of resilient character traits and adaptive social responses to stress are the reward and fear circuits. A key reward circuit is the mesolimbic dopamine pathway and functional abnormalities in this pathway can contribute to key depressive symptomatology such as anhedonia, decreased energy and reduced motivation. (Nestler & Carlezon 2006) The neural circuitry of fear response includes amygdala, hippocampus, medial prefrontal cortex, nucleus accumbens, ventromedial hypothalamus and numerous brain stem nuclei (Wu et al. 2013)

Psychodynamic perspective

Making a conceptual leap, we can find the concepts of vulnerability and resilience in the theory formulated by Gaetano Benedetti about the pathogenesis of depression (Benedetti et al. 1979). The author distinguishes four kinds of depression:

- one due to failure of the ego: the failure is a subjective experience, not an objective failure (which not necessarily provokes depression). The failure of the ego is experienced as an absolute inability to cope with the tasks posed by the outside world. Any liability is then too high for an ego that feels unable to respond to it and that, therefore, is accused of nullity. The depressive ego that is deemed insufficient in the reality is actually unable to fulfill his unconscious desires, present in the id, but the failure of the depressive ego also exists in relation to the super-ego, which means inability to approach its high standards;
- one due to perversion of the superego, which is characterized by the presence of a destructive and sadistic superego, that rages against the ego and hates it even before any of its actions;
- one due to inhibition of the Id which represents the most complex part of the psychodynamics of depression because an acute frustration of vital needs, even in normal subjects, can have a depressogenic effect. Depression, however, occurs only when there is a transposition of an oral tendency from the id to the ego, that is when a chronic sense of

- frustration of dependency needs in the ego creates a sense of helplessness and futility of his own existence:
- one due to the collapse of the ego ideal, in which depression is linked to the collapse of an ideal figure which corresponds to the collapse of the ego ideal. (Benedetti 1979).

CONCLUSIONS

As we discussed, since resilience is a multidimensional construct, there are many interventions and strategies for its improvement that can be used for the prevention and treatment of depression. Several areas have been studied. (Southwick & Charney 2012)

Genetic and epigenetic studies showed that vulnerability genes or "risk alleles" interact with the environment and that resilience can be promoted in some cases by changing the biological and/or psychosocial environment (Rende 2012).

As regards child rearing, it is critical to offer children a supporting and loving environment to protect them against learned helplessness and depression, as well as to promote resilience.

In a similar way, high levels of social support have been positively associated with active coping, sense of control and predictability in life, self-esteem, motivation, resilience and lower levels of depression (Southwick & Charney 2012).

Numerous therapeutic approaches have been conceived in order to make the individual believe that he/she has the skills, experience and resources to overcome an adverse situation, appraising the situation as challenging, without developing depression. Among these:

- interventions in attention control, which teaches individuals how to control the focus of their attention;
- cognitive reappraisal, that is the ability to cognitively reframe adverse and negative events in a more positive light; this is also a central component of cognitive-behavioral therapies which teach individuals to observe their cognitive and behavioral reactions to stress, to challenge distorted negative appraisals of self and the situation and to replace distortions with more positive appraisals;
- strategies to increase coping self-efficacy which refers to perceived capacity to successfully manage and recover from stressful situations. (Southwick & Charney 2012)

It is also possible to do neurobiological intervenetions, such as enhancing NPY functioning which might improve resilience by helping to maintain the sympathetic nervous system and HPA axis high enough to respond to danger without stimulating excessive fear, anxiety and depression (Southwick & Charney 2012). Actually all the aforementioned neurochemical mediators could serve as potential therapeutic targets for reducing the likelihood of developing stress-related depression (Covington et al. 2010).

It may also be possible to develop pharmacological and psychotherapeutic interventions to help regulate neural pathways which underlie resilience (those involved in emotion regulation, attention, reward and motivation, adaptive social behaviors etc.). There are also many practical aspects, concerning physical health, that should be taken into account in order to guarantee a good response to stress: quality of diet, amount of exercise, capacity to relax, quality and quantity of sleep (Southwick & Charney 2012).

In conclusion, even though the study of resilience is a relatively young area of scientific investigation, it is already possible to do the aforementioned interventions to enhance stress-protective factors through practice and training, thus improving adaptation to stress, increase speed of recovery, decrease the likelihood of developing depression (Southwick & Charney 2012) and contribute to better treatment outcomes in already depressed patients (Min et al. 2012).

Acknowledgements: None.

Conflict of interest: None to declare.

References

- 1. American Psychological Association: The Road to Resilience. APA, Washington, DC, 2010
- 2. Benedetti G: Introduzione a una psicoterapia della depressione. In Benedetti G, Corsi Piacentini T, D'Alfonso L, Elia C, Medri G, Saviotti M.: Paziente e analista nella terapia delle psicosi. Dalla non-esistenza all'incontro terapeutico, 235-257. Feltrinelli, Milano, 1979.
- 3. Burt KB, Paysnick AA: Resilience in the transition to adulthood. Dev Psychopathol 2012; 24:493-505.
- 4. Carli V, Mandelli L, Zaninotto L, Roy A, Recchia L, Stoppia L, Gatta V, Sarchiapone M & Serretti A: Eur Psychiatry. A protective genetic variant for adverse environments? The role of childhood traumas and serotonin transporter gene on resilience and depressive severity in a high-risk population 2011; 26:471-8.
- 5. Covington HE 3rd, Vialou V & Nestler EJ: From synapse to nucleus: novel targets for treating depression. Neuropharmacology 2010; 58:683-93.
- 6. Davidson RJ & McEwen BS: Social influences on neuroplasticity: stress and interventions to promote wellbeing. Nat Neurosci 2012; 15:689-95.
- 7. Dudley KJ, Li X, Kobor MS, Kippin TE & Bredy TW: Epigenetic mechanisms mediating vulnerability and resilience to psychiatric disorders. Neurosci Biobehav Rev 2011; 35:1544-51.
- 8. Feder A, Charney DS & Collins K: "Neurobiology of resilience," in Resilience and Mental Health, eds S.M. Southwick, B.T. Litz, D.S. Charney and M.J. Friedman. NewYork, NY: Cambridge University Press, 2011.

- Feder A, Nestler EJ & Charney DS: Psychobiology and molecular genetics of resilience. Nat Rev Neurosci 2009; 10:446-57.
- Fleshner M, Maier SF, Lyons DM & Raskind MA: The neurobiology of the stress-resistant brain. Stress 2011; 14:498-502.
- 11. Freud S: New Introductory Lectures On Psycho-Analysis. The Standard Edition of the Complete Psychological Works of Sigmund Freud, Volume XXII (1932-1936): New Introductory Lectures on Psycho-Analysis and Other Works, 1933; 1-182.
- 12. Frodl T & O'Keane V: How does the brain deal with cumulative stress? A review with focus on developmental stress, HPA axis function and hippocampal structure in humans. Neurobiol Dis 2013; 52:24-37.
- 13. Geschwind N, Peeters F, Jacobs N, Delespaul P, Derom C, Thiery E, van Os J & Wichers M. Meeting risk with resilience: high daily life reward experience preserves mental health. Acta Psychiatr Scand 2010; 122:129-38.
- 14. Henningsen K, Palmfeldt J, Christiansen S, Baiges I, Bak S, Jensen ON, Gregersen N & Wiborg O: Candidate hippocampal biomarkers of susceptibility and resilience to stress in a rat model of depression. Mol Cell Proteomics 2012; 11:M111.016428.
- 15. Min JA, Lee NB, Lee CU, Lee C & Chae JH: Low trait anxiety, high resilience, and their interaction as possible predictors for treatment response in patients with depression. J Affect Disord 2012; 137:61-9.
- Nestler EJ & Carlezon WA Jr: The mesolimbic dopamine reward circuit in depression. Biol Psychiatry 2006; 59:1151-9. Epub 2006 Mar 29.
- 17. Ozbay F, Fitterling H, Charney D & Southwick S: Social support and resilience to stress across the life span: a neurobiologic framework. Curr Psychiatry Rep 2008; 10:304-10.
- Price LH, Kao HT, Burgers DE, Carpenter LL & Tyrka AR: Telomeres and early-life stress: an overview. Biol Psychiatry 2013; 73:15-23.
- 19. Rende R: Behavioral resilience in the post-genomic era: emerging models linking genes with environment. Front Hum Neurosci 2012; 6:50.
- 20. Seok JH, Lee KU, Kim W, Lee SH, Kang EH, Ham BJ, Yang JC & Chae JH: Impact of early-life stress and resilience on patients with major depressive disorder. Yonsei Med J 2012; 53:1093-8.
- 21. Silveira PP, Portella AK, Benetti Cda S, Zugno AI, Scherer EB, Mattos CB, Wyse AT, Lucion AB & Dalmaz C: Association between Na+,K+-ATPase activity and the vulnerability/resilience to mood disorders induced by early life experience. Neurochem Res 2011; 36:2075-82.
- 22. Southwick SM & Charney DS: The science of resilience: implications for the prevention and treatment of depression. Science 2012: 338:79-82.
- 23. Thompson RW, Arnkoff DB & Glass CR: Conceptualizing mindfulness and acceptance as components of psychological resilience to trauma. Trauma Violence Abuse 2011; 12:220-35.
- 24. Wingo AP, Wrenn G, Pelletier T, Gutman AR, Bradley B & Ressler KJ: Moderating effects of resilience on depression in individuals with a history of childhood abuse or trauma exposure. J Affect Disord 2010; 126:411-4.
- 25. Wu G, Feder A, Cohen H, Kim JJ, Calderon S, Charney DS & Mathé AA: Understanding resilience. Front Behav Neurosci 2013; 7:10.

26. Zimmermann P, Brückl T, Nocon A, Pfister H, Binder EB, Uhr M, Lieb R, Moffitt TE, Caspi A, Holsboer F & Ising M: Interaction of FKBP5 gene variants and adverse life

events in predicting depression onset: results from a 10-year prospective community study. Am J Psychiatry 2011; 168:1107-16.

Correspondence:

Sandro Elisei Division of Psychiatry, Clinical Psychology and Rehabilitation Department of Clinical and Experimental Medicine - University of Perugia Santa Maria della Misericordia Hospital, Perugia, Italy E-mail: sandro.elisei@unipg.it