Biological Psychology 112 (2015) 107–115

Contents lists available at ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

Sex commonalities and differences in the relationship between resilient personality and the intrinsic connectivity of the salience and default mode networks

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ARTICLE INFO

Article history:
Received 13 April 2015
Received in revised form 2 September 2015
Accepted 25 September 2015
Available online 9 October 2015

Keywords:
Resilience
NEO personality inventory
Resting state networks
Default mode network
Salience network
Sex differences

ABSTRACT

Increased resilience is associated with better health outcomes and reduced morbidity in response to injury and homeostatic perturbations. Proper functioning of the salience network (SN) and modulation of the default mode network (DMN) by SN may play a role in adaptively responding to stress. Here, we demonstrate that resilient personality in healthy subjects is associated with SN and DMN connectivity patterns and that these patterns are influenced by sex. While connectivity of SN with several brain regions including right anterior insula was significantly associated with resilient personality in both men and women, results suggest that increased functional integration of anterior DMN preferentially benefits women while increased functional integration of posterior DMN preferentially benefits men in terms of resilience. These findings may relate to previous demonstrations that men and women engage different information processing and behavioral strategies to achieve resilience and highlight the importance of considering sex in resilience research.

1. Introduction

While the great majority of behavioral and biopsychosocial research has focused on disease mechanisms and interventions for patients affected by disease, it is only during the past decade that there has been an increasing focus on the phenomenon of resilience. Although definitions of resilience vary in details, resilience is an adaptive response to adversity. A common feature is the ability to maintain normal psychological and physical functioning (homeostasis) and avoid serious mental or physical illness following exposure to even extraordinary levels of stress or trauma (Russo, Murrough, Han, Charney, & Nestler, 2012). Resilience is difficult to operationalize as it may include many different phenotypes, including psychological resilience (the ability to "bounce back" after a stressful situation) (Block & Kremen, 1996; Southwick & Charney, 2012), the tendency to not develop psychiatric disease despite genetic risk or stress exposure (Fredrickson, Tugade, Waugh, & Larkin, 2003; Stewart & Yuen, 2011), or the tendency to not develop chronic medical illness despite high risk exposure (Cohen, Janicki-Deverts, & Miller, 2007; Sutin et al., 2010). Thus, different approaches to quantify resilience have been proposed (Windle, Bennett, & Noyes, 2011).

The NEO Personality inventory (NEO) has been used to examine one factor influencing resilience: personality. Additional factors include: social resources, perceived economic resources, and cognitive skills. The NEO includes five dimensions of personality traits: neuroticism, extraversion, openness, agreeableness and conscientiousness (Costa & McCrae, 2008). A characteristic pattern of low neuroticism and above average extroversion, openness, agreeableness and conscientiousness on the NEO has been described as a 'resilient personality' (Berry, Elliott, & Rivera, 2007Campbell-Sills et al., 2006Hjemdal et al., 2012). Increased resilience as

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http://dx.doi.org/10.1016/j.biopsycho.2015.09.010
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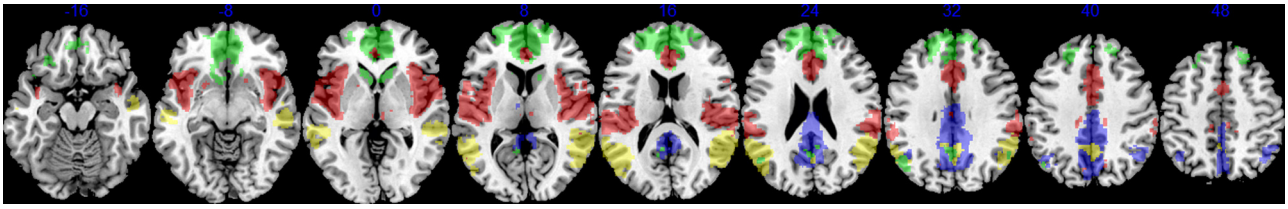

Fig. 1. Identified networks of interest (SN in red, aDMN in green, pDMN in blue, and latDMN in yellow) are depicted. (For interpretation of the reference to color in this figure legend, the reader is referred to the web version of this article.)

measured by the NEO has been associated with normal BMI, decreased violence and improved social problem solving abilities in recent veterans, and improved recovery in spinal cord injury patients (Berry et al., 2007; Elbogen et al., 2012), whereas reduced resilient personality has been linked to medical conditions, including chronic inflammation, obesity and metabolic syndrome (Karatsoreos & McEwen, 2011; Stewart-Knox et al., 2012). Thus, the NEO assesses an important aspect of resilience, even though it does not directly measure adaptation to specific instances of adversity.

Although much attention has been paid to the psychological and organizational factors promoting resilience, much less work has focused, until recently, on the neurobiology of resilience (Karatsoreos & McEwen, 2011). A small number of functional brain imaging studies have reported findings suggesting resilience-related differences in brain structure (DeYoung et al., 2010), responses to acute experimental paradigms (Daniels et al., 2012; Peres et al., 2011; Reynaud et al., 2013; Vythilingam et al., 2009; Waugh, Wager, Fredrickson, Noll, & Taylor, 2008) and resting state brain activity (Kunisato et al., 2011). However these studies ignore the potential for sex differences in the neurobiology of resilience. There is considerable evidence that stress response patterns of men and women differ with women displaying greater tendency towards "tend and befriend" responses while males are more likely to engage in "flight or fight" responses (Taylor et al., 2000). Additional evidence shows that men and women differ in preferred coping and defense strategies with women reporting more social support strategies (Diehl, Coyle, & Labouvie-Vief, 1996; Kort-Butler, 2009). For example, female melanoma survivors reported more secure attachment styles while male survivors reported more secondary cognitive appraisal strategies to achieve the same level of well-being (Hamama-Raz, 2012). Thus, men and women may differ in the biological systems engaged and behavioral strategies taken to achieve resilience.

Even during resting conditions, brain activity is highly organized (Raichle, 2011). Examination of the brain through resting state fMRI has provided insights into the impact of experience, disease, and traits on the organization of large-scale brain networks (Guerra-Carrillo, Mackey, & Bunge, 2014). One widely recognized resting state network that may be relevant for resilience is the salience network (SN). SN is a brain network important for assessing the homeostatic relevance of stimuli (Seeley et al., 2007). Altered SN connectivity has been demonstrated in returning male veterans with PTSD (Sripada et al., 2012), social anxiety disorder (Pannekoek et al., 2013), and in patients with psychogenic non-epileptic seizures (van der Kruijs et al., 2012). The SN is also considered pivotal in regulating activity of other networks, including the default mode network (DMN) (Seeley et al., 2007). The DMN is engaged when individuals are left to think undisturbed, but has also been found to be engaged in tasks of theory of mind, social cognition, prospection and self-reflection (Buckner, Andrews-Hanna, & Schacter, 2008). Altered DMN connectivity was been seen in a wide variety of psychiatric and neurological disorders including Alzheimer's disease, depression, autism, and schizophrenia (Broyd et al., 2009; Greicius et al., 2007), and has also been related to traits such as pessimism (Alexopoulos et al., 2012). Thus, DMN integrity and interaction with other networks has become an interest in the study of mental health. Disrupted SN integrity following traumatic brain injury has been shown to impact DMN function supporting the concept that SN regulates dynamic changes in the DMN (Bonnelle et al., 2012). Proper SN functioning and modulation of the DMN by SN may function to adaptively respond to stress and may be a significant factor in resilience.

In the current study, we aimed to identify relationships between a NEO personality profile associated with high resilience and the resting scan connectivity of the SN and DMN in a large sample of male and female healthy subjects. We hypothesized that variations in resilience in terms of personality traits would be reflected in SN integrity and connectivity with the DMN. Furthermore, we hypothesized that sex differences exist in the neurobiology underlying a resilient personality.

2. Methods and materials

2.1. Subjects

82 healthy right-handed subjects (46 female; 36 male; ages 20–52) participated. Subjects were screened via medical exam and the MINI structured psychiatric interview (Sheehan et al., 1998) for absence of significant health or psychiatric conditions. Exclusion criteria also included pregnancy, substance abuse, and tobacco dependence. Study protocols were approved by UCLA's Office of Protection for Research Subjects and informed consent was obtained from all subjects.

2.2. Behavioral measures

All subjects completed the NEO PI-R, a 240 question survey designed to measure five dimensions of personality including: neuroticism, extraversion, openness, agreeableness and conscientiousness (Costa & McCrae, 2008). Scale scores for each dimension are expressed as *T*-scores that vary from 20 to 80 with higher numbers reflecting an individual with more characteristics of the specific trait.

2.3. fMRI acquisition

A high resolution structural image was acquired from each subject before the resting state scan with a magnetization-prepared rapid acquisition gradient echo (MP-RAGE) sequence, repetition time (TR) = 2200 ms, echo time (TE) = 3.26 ms, slice thickness = 1 mm, 176 slices, 256 × 256 voxel matrices, and 1.0 × 1.0 × 1.0 mm voxel size. Resting scan fMRI was performed on a Siemens 3 T Trio using the following parameters: Echo time (TE) = 28 ms, Repetition time (TR) = 2000 ms, flip angle = 77 degrees, FOV = 220, slice thickness = 4.0 mm, 40 slices were obtained with whole-brain coverage. The duration of the resting scan varied from 8–10 min. Subjects rested with eyes closed during the scan.

2.4. fMRI preprocessing

Using DPASRF (Chao-Gan & Yu-Feng, 2010) and SPM8 software (Welcome Department of Cognitive Neurology, London, UK), data were slice-time and motion corrected, spatially normalized to the MNI template using their structural image, and spatially smoothed with a 3 mm Gaussian kernel. The first two volumes were discarded to allow for stabilization of the magnetic field.

2.5. Statistical analyses

2.5.1. Resilient personality scores

The NEO subscale scores for all subjects were entered into a factor analysis using SPSS v22 (IBM Corp, Armonk, NY). The first principal component accounted for 49% of the variance and reflected a personality dimension consistent with the resilience dimension reported in previous studies: negative weight for neuroticism (−0.88)