Perceived Stress and Brain Network Efficiency

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ABSTRACT

Introduction. *Literature about stress related neural correlates reported structural and functional alterations in brain regions associated to several processes including emotional, cognitive, and higher-order ones as well as psychological stress perception and regulation. Notwithstanding this literature, to the best of our knowledge and until now, no data are available about brain network properties such as local (E_{loc}) and global (E_{glob}) efficiency in perceived daily life stress in non-clinical samples by means of resting-state (RS) electroencephalography (EEG) functional connectivity analysis. Thus, the main aim of the current work was to exploratively investigate the associations among such brain network efficiency properties (i.e., E_{loc} and E_{glob}) and perceived daily life stress in a sample of university students through RS-EEG.* ***Methods.*** *A battery of questionnaires has been administered to a sample of university students after giving their written informed consent. The battery included the Italian version of Perceived Stress Scale (PSS-10). A checklist evaluating socio-demographic variables as well as exclusion/inclusion criteria was also administered to everyone. 31-channels EEG recordings have been performed during RS. Functional connectivity and frequency decomposition have been computed to obtain network matrices for each individual and for each frequency band, in which nodes were represented by Regions of Interest (ROIs, i.e., 84) and edges were weighted for functional connectivity lagged phase synchronization. Then we computed E_{loc} and E_{glob} brain network metrics by means of Brain Connectivity Toolbox (BCT). As regarding statistical analysis, partial correlations have been performed controlling for potential confounding variables such as age and sex.* ***Results.*** *Results reveal that PSS total score negatively and significantly correlated with E_{loc} metric in alpha frequency band ($r=-.245$, $p=.029$) controlling for age and sex. No significant correlations emerged for other network efficiency related metrics.* ***Discussion.*** *Our data suggests a decreased segregation in alpha frequency band associated to increased perceived stress. Notwithstanding there is not definitive accordance about the functional meaning of alpha oscillations, literature reports that their involvement includes top-down cortical control, cognitive and executive processes. Indeed, the association between high perceived stress and decreased alpha E_{loc} could be linked to stress related altered RS cognitive and executive processes. In conclusion, these results could help to shed light on stress related processes and orientate future research.*

Keywords: stress, network, EEG, connectivity, efficiency, alpha.

1.INTRODUCTION

Stress is a common daily life experience for humans and in certain conditions (e.g., when unmanaged and overwhelming) its consequences could be burdensome. Indeed, stress can alter subjective health both directly (by neuro-biological responses) and indirectly (e.g., by the adoption of health threatening behaviors) [1]. Research about stress has focused on a wide range of processes from different standpoints, including those of epidemiology, psychology, and neuro-biology [2]. In such multi-faceted approach, perceived stressful events, that are those perceived as characterized by unpredictability, uncontrollability, and overload [3], are acknowledged to activate processes leading to neuro-biological and behavioral responses which, if overwhelming, inappropriate or prolonged, could lead to negative consequences on both physical and mental health and, extremely, to disease [2, 4, 5]. In this regard, it has been recently reviewed that stress can affect multiple biological systems [1].

Among these consequences, stress has been reported to affect also cognitive domain. Indeed, several studies reported that individuals perceiving higher levels of stress often exhibit poorer cognitive performance [6-8] and cognitive complaints are also common [9]. From a neuroscientific standpoint, research has reported that stress is associated with modifications in structures (e.g., prefrontal cortex, hippocampus) and functions involved in cognitive processes [7, 10-16]. Cognitive functions are acknowledged to be sustained by the interplay among widespread brain areas which are known to work in a synergistic manner in large-scale brain networks [17]. Furthermore, literature about stress-related neural features reported both structural and functional alterations in brain regions related to emotion processing and regulation, saliency detection (e.g., the insula), psychological stress perception and regulation (e.g., prefrontal, limbic regions), and self-referential mental activity (e.g., the posterior cingulate cortex) [e.g., 18, 19-22].

In neuroscience research area, networks approach has gained great attention among researchers providing an interesting framework into which orienting neuroscientific research focus. This approach could provide salient information about brain functioning including those underlying cognition [23]. Indeed, in the past years, networks have been proposed as the underlying "organizational elements of human brain architecture" [18, p. 281]. Based on Graph Theory, network analysis approach considers brain essential elements (e.g., brain regions) as nodes and links between them (e.g., functional interactions) as edges [23-25]. Network properties and features could be analyzed through this approach to obtain relevant data about brain functioning integrative features [26]. In fact, network analysis allows exploring brain network organization from the computation of metrics including those about its functional organization in terms of functional integration and segregation [24, 25]. Specifically, efficiency is a quantitative indicator of the extent into which information is exchanged efficiently in the network [27] and it is calculated in terms of global (E_{glob}) and local (E_{loc}) efficiency. Of them, E_{glob} is about efficient communication at long range level and E_{loc} is about short range one [27], the first is a measure linked to network integration while the latter is linked to segregation and it could be useful investigating network organization in these terms [28-31]. Indeed, it has been suggested that flexible cognitive processes and behaviors are promoted by the optimal balance between integration and segregation processes at brain level [29]. For these reasons, the study of these network properties could be interesting when dealing with stress-related processes which are known to be associated with alterations at neuro-biological, cognitive, affective, and behavioral level. Specifically, it has been suggested that the study of brain functioning associated with stress-related individual differences could be worth of importance in stress-related disorders [32].

In the past few years, some brain network analysis studies have been performed in clinical samples with stress-related disorders (e.g., PTSD) [33, 34]. However, there is poor similar literature on perceived stress levels in non-clinical samples and, although electroencephalography (EEG) is largely used in studies about stress related processes [e.g., 35, 36], to the best of our knowledge, there are no available data on brain network analysis during resting state (RS) in such non-clinical samples. Furthermore, even if fMRI is widely used for the analysis of brain networks functional connectivity, the EEG well fit with the study of brain network functional dynamics providing rich and salient data about neural synchronization across different frequency bands [37-40].

Therefore, the main aim of the current study was to exploratively investigate relationships among efficiency related network metrics such as E_{loc} and E_{glob} and perceived daily life stress levels in a sample of university students by means of RS-EEG.

2. METHODS

2.1 Participants

Study participants were undergraduate students recruited at university campus who voluntarily accepted to take part in the study. The final sample was composed by 81 university students [mean age (M±SD) = 22.24±2.56; females (N; %) = 49; 60.5%]. Inclusion criteria were: i) right handedness, ii) negative anamnesis for neurological or psychiatric disorders, iii) negative anamnesis for head trauma. Exclusion criteria were: i) age minor to 18 years old, ii) assumption of psychotropic drugs.

2.2 Assessment

All participants fulfill a checklist assessing socio-demographic variables (e.g., sex, age) and inclusion/exclusion criteria as well as a battery of questionnaires including the 10 item Perceived Stress Scale [PSS-10; 3]. In the current study, the PSS-10 was adopted in its Italian version [41]. It is one of the most used questionnaires to measure psychological perceived stress and it is composed of items rated on a Likert-type scale ranging from 0 to 4 (i.e., *never* to *very often*, respectively). Particularly, this scale measures the extent to which life circumstances are perceived as stressful in terms of overload, unpredictability, and uncontrollability with regard to the preceding month [3]. Higher scores reflect higher rates of perceived stress and, conversely, lower scores reflect lower levels of perceived stress. Total score ranges 0-40. In the current study Cronbach alpha was about .86 for PSS-10 total score.

2.3 EEG recording and analysis

Each participant underwent a single EEG recording during RS lasting at least 5 minutes. In order to obtain the optimal RS condition, participants were comfortably seated on an armchair in a quiet room with semi dark lighting. We ask participants to keep their eyes closed during EEG recording and they were previously asked to refrain from assuming central nervous system active substances (e.g., caffeine, theine) in the 4-6 hours prior to their recording session. EEG recordings were performed with a head cap consisting of 31 electrodes disposed on the standard 10-20 system. Other 4 electrodes were placed: 2 reference electrodes on right and left mastoids, 2 electrodes (left and right derivations) to record electrocardiogram (ECG) signal. Each EEG was visually cleaned from non-cerebral artifacts through EEG lab toolbox for MATLAB. A detailed description of artifact-rejection procedure has been described in previous works of our team [42, 43].

The eLORETA software has been used for connectivity analysis on EEG data. It is a validated and well corroborated tool for the localization of cerebral electrical activity [44] and several studies have shown that it has a localization agreement with diverse multi-modal imaging techniques which can be considered satisfactory [e.g., 45, 46, 47].

Functional connectivity has been computed by means of the lagged phase synchronization (LPS) index, a useful neurophysiological index when addressing functional connectivity at inter-regional level [48-50]. The advantage of this index is that it eliminates the instantaneous zero-lag component thus reducing artifacts such as volume-conduction [51]. This index is a measure of "*similarity of two time series by means of the phases of the analyzed signal*" [49] ranging from 0 to 1, which are values corresponding respectively to no synchronization and the maximum one. Specifically, in accordance with previous studies [52-54] and with the aim to obtain a general view of cerebral connectivity [52], LPS has been computed for all 84 Regions of Interest (ROIs; respectively 42 for right and 42 for left hemisphere) according to the Montreal Neurological Institute (MNI) atlas [55].

Functional connectivity and frequency decomposition (i.e., Fast Fourier Transform) computations have been performed to obtain network matrices i) for each individual and ii) for each standard frequency band (i.e., delta, theta, alpha, beta, and gamma). In these network matrices, nodes were represented by ROIs (i.e., 84) and edges were weighted for functional connectivity LPS index.

Once performed network construction, the "ECOfilter" topological threshold [56] has been used to get binarized matrices. Then, E_{glob} and E_{loc} metrics have been computed on these binarized matrices. E_{glob} and E_{loc} have been computed by means of Brain Connectivity Toolbox (BCT) (http://www.brain-connectivity-toolbox.net) for MATLAB [57]. Specifically, E_{glob} is a measure of how efficiently distant information is exchanged in the network and it is defined as the mean inverse shortest path length between all nodes pairs within the network [27, 57]. Thus, E_{glob} is considered a functional integration metric [57]. On the other hand, E_{loc} is defined as "*the average efficiency of the local subgraphs*" [27; p. 2] and it is considered a measure of segregation [57]. In the current research, E_{loc} has been calculated with respect to the entire network as the mean E_{loc} across all network nodes.

2.4 Statistical analyses

All statistical analyses were performed using SPSS software (v. 18). In order to investigate relationships between perceived stress and both global and local network efficiency metrics for each frequency band, partial correlations have been performed controlling for age and sex. Descriptive statistics about socio-demographical and psychological variables of the sample have been also calculated.

3.0 RESULTS

Socio-demographical and psychological variables of the sample are reported in **Table 1**. Results of the current study show that PSS total score was negatively and significantly correlated with E_{loc} metric in alpha frequency band (r_p =-.245, p =.029) controlling for potentially confounding variables such as age and sex (**Figure 1**). No statistically significant correlations emerged for the other network efficiency related metrics (i.e., neither E_{loc} in the other frequency bands nor E_{glob} metrics). E_{loc} related results are shown in **Table 2**, E_{glob} related ones are showed in **Table 3**.

Table 1. Socio-demographical and psychological features of the sample (N=81).

Variables	Values
Age - M±SD	22.24±2.56
Sex - F (%)	49 (60.5%)
PSS total score - M±SD	17.96±7.18

Abbreviations: PSS (Perceived Stress Scale); F (Females); M (Mean); SD (Standard Deviation).

Table 2. Partial correlations between PSS total score and E_{loc} in all considered frequency bands.

	E_{loc} Delta	E_{loc} Theta	E_{loc} Alpha	E_{loc} Beta	E_{loc} Gamma
PSS total score	-.068	.058	-.245*	.084	-.109

Abbreviations: E_{loc} (Local Efficiency), PSS (Perceived Stress Scale). *Note*: correlations are controlled for age and sex; *p <.05, **p >.01.

Table 3. Partial correlations between PSS total score and E_{glob} in all considered frequency bands.

	E_{glob} Delta	E_{glob} Theta	E_{glob} Alpha	E_{glob} Beta	E_{glob} Gamma
PSS total score	-.027	.121	-.124	.007	.005

Abbreviations: E_{glob} (Global Efficiency), PSS (Perceived Stress Scale). *Note*: correlations are controlled for age and sex.

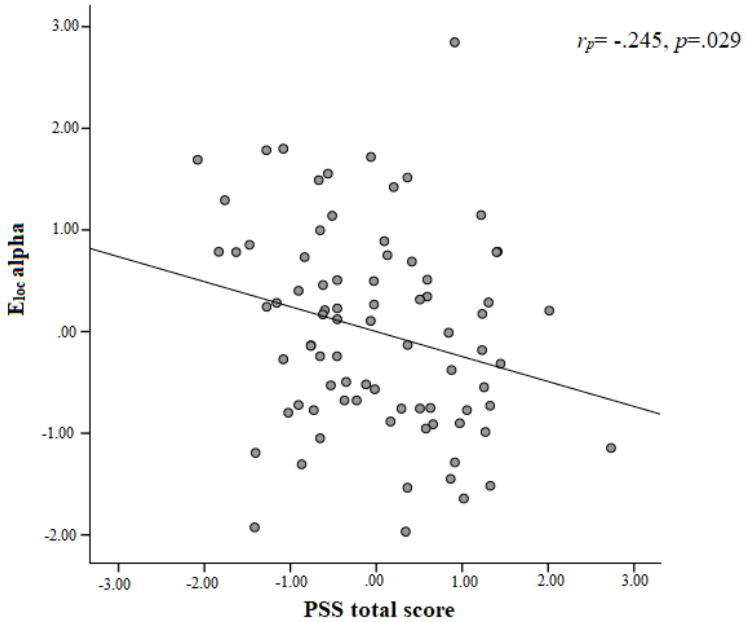

Figure 1. Scatterplot of partial correlations (controlled for age and sex) between E_{loc} in alpha frequency band and PSS total score. Abbreviations: PSS= Perceived Stress Scale; E_{loc}= Local Efficiency.

4.0 DISCUSSION

The main aim of the current study was to exploratively investigate relationships between perceived daily life stress and both global and local efficiency during RS by means of EEG. Due to the explorative nature of the study, no a-priori hypotheses have been drawn. Results show a significant negative correlation between E_{loc} in alpha frequency band and PSS total score controlling for age and sex. No statistically significant correlations between PSS total score and E_{loc} in the other frequency bands or E_{glob} have emerged. This result could suggest a decreased brain network segregation and poor short range efficient information exchanging associated with high perceived stress.

Perceived stress is known to affect both physical and mental health, passing by alterations on several biological systems [1] as well as on affective, cognitive, and behavioral domains [e.g., 2, 4, 5]. From a cognitive point of view, it has been reported that individuals experiencing high levels of perceived stress often report cognitive complaints and show poor cognitive performance during tasks [6-9]. Cognition is known to be sustained by the integrated and synergistic interplay among different brain structures [17]. From a network perspective, it has been suggested that RS brain networks functional organization is balanced, and flexibly switch, between integration and segregation to support different cognitive demands [58]. Furthermore, it has been suggested that segregation, integration, as well as integration-segregation balance could predict various cognitive abilities [58]. For example, memory seems to be supported by integration-segregation balance, while a shift toward higher segregation seems to be linked to cognitive aspects such as higher crystallized intelligence, and a shift toward higher integration seems to be associated to higher overall cognitive abilities [58]. In this perspective, local and global efficiency metrics have been proposed as measures of segregation and integration, respectively. More particularly, they measure efficient short (E_{loc}) or long (E_{glob}) range information exchanging. Furthermore, even if there is not clear accordance on alpha oscillations functional interpretation, previous literature suggest that alpha is involved in top-down control and, more in general, in attentional and cognitive processes including memory and stored information accessing, and in cognitive load [59-62]. Interestingly, a previous study reports that diminished frontal short-range connectivity in upper alpha frequency band is associated with increased involvement of executive functions (Sauseng, Klimesch et al., 2005).

According to this literature, we could speculate that the association between high perceived stress and decreased alpha local efficiency could be linked to stress related altered cognitive and executive processes during RS. However, the explorative nature of the current study does not allow us to draw further interpretations. Further studies of experimental nature are needed to investigate causal relationships that in the current study cannot be inferred.

Indeed, although potentially interesting, these results should be accounted considering several limitations such as i) the limited number of participants, ii) the intrinsic spatial limitation of EEG and the low number of electrodes considered, iii) the fact that no other graph theoretical related metrics have been taken into account. Indeed, considering other brain network metrics such as, for example, small-worldness, or nodal related metrics would have enlarged the explanation of our results and would help us to better understand these results. Future studies should examine a more complete range of network measures encompassing both nodal and global ones. In addition, although 31 scalp electrodes could be considered acceptable for brain network analysis, taking into account more electrodes might contribute to a broader view on brain network RS connectivity [40].

In conclusion, to the best of our knowledge and until the time we are writing, this remains the first study addressing brain network efficiency related metrics associated to overall perceived daily life stress in a non-clinical sample performed through RS-EEG. Our results show a negative and statistically significant correlation between perceived stress and local efficiency in alpha frequency band during RS controlling for potentially confounding variables such as age and sex. Taken together, these results could help to shed light on stress related processes and orientate future research.

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