The mechanism of emotion regulation in response to stress using an fMRI study and a biological mathematical model*

Yukihiro Suzuki

Abstract

Stress is inevitable in our society. The ability to cope appropriately with the stress of social life is essential for adapting to complex environments. However, it is still unclear which brain regions and neural level characteristics contribute appropriately to adaptive responses under stress. The thesis examined two approaches to investigate the mechanisms of adaptation processing under stress by brain studies using fMRI and neuronal simulations.

First, during emotional regulation under stress in fMRI studies, the ventromedial prefrontal cortex (vmPFC) and pre-SMA showed significantly different activity in response to image valence. The midbrain showed differences with and without stress during assessing emotional images. Significant negative correlations with trait anxiety were confirmed for vmPFC, and correlations were obtained for pre-SMA, mainly for negative affect. Furthermore, functional coupling between vmPFC and midbrain was negatively correlated with acute stress-induced changes in anxiety. These results indicate that activity and functional connectivity, including vmPFC, in emotion regulation reflect individual differences in response to stress.

Second, we focused on two distinctive firing types to understand the locus coeruleus (LC) mechanisms, a noradrenergic resource that is important for controlling the arousal that occurs in stress. We assumed two modes, homogeneous and inhomogeneous, to understand how these firing characteristics function as a

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neural population. Combining these modes with a feed-forward neural network model revealed that the homogeneous mode detects more significant spike coherence than the inhomogeneous mode. On the other hand, the inhomogeneous mode was found to have the ability to suppress spike coherence. These functions support previous studies in biological experiments, indicating that these two modes are dynamically responsible for controlling cognitive processing, including stress.

Keywords:

fMRI, Stress, Emotion Regulation, Neural Population Coding, vmPFC, Locus coeruleus

氏　名	鈴木 文丈

（論文審査結果の要旨）

現代社会では至るところにストレスがあり、ストレスに対する耐性が重要である。にもかかわらず、ストレス適応の脳内メカニズムは不明のままであった。本論文はこの問題に対し、２つのアプローチで迫ったものである。

１つめはストレス適応に関与する脳部位を特定するfMRI研究であり、画像を見た時のストレスの有無によって活動に差がある部位を特定したところ、vmPFCおよびpre-SMAがストレス適応に関与することがわかった。

２つめはストレス適応の数理モデル研究であり、青斑核におけるニューロンの入力発火パターンの違いからその機能の差を調べたところ、均一な入力発火パターンの方が発火の同期を検知しやすく、逆にバースト状の入力発火パターンは発火の同期を抑える機能があることがわかった。

以上をまとめると，本論文はストレス適応の脳内メカニズムの解明に、fMRI研究および数理モデル研究の２つのアプローチで迫ったものであり、ストレス適応に関与する脳部位を特定するとともに入力発火パターンでその機能の違いを説明できることを数理モデルによって示したものであり、ストレス適応の理解に大いに資するものである．よって，博士（工学）の学位に値するものと認められる．