Social context affects posttraumatic stress disorder: modulation of the medial-prefrontal cortex and amygdala neural circuitry

(社會情境因素對於創傷後壓力症候疾患的影響：內側前額葉皮質區與杏仁核神經回路的調控)

1. 摘要

創傷後壓力症候疾患是常見的、經由壓力導致的焦慮疾患。無論是 921 大地震、莫拉克風災、戰爭、或是罹患癌症重大疾病等，都可能促使個案發病，導致社會以及家庭的壓力，並且造成病患家人的負擔。因此，台灣以及世界各國，對於心理創傷疾患的研究以及治療都非常重視。在過去研究中，我們發現社會情境可以改善創傷行為症狀，但是對於其機制並不了解。因此，**本研究將檢驗兩個議題。第一，檢驗社會情境對於創傷後壓力症候疾患之行為症狀及相關生物指標變化的影響。第二，調控有關之生物指標，來增強社會情境對創傷後壓力症候疾患行為症狀之有益的影響，並且集中研究內側前額葉皮質區與杏仁核神經回路之功能角色，藉此發展新的介入方法。**

第一個研究將檢驗社會情境對於創傷後壓力症候疾患之行為症狀與生物指標的影響，包括人類以及動物實驗。在人類實驗方面，將透過各種不同的社會支持型態，來當作社會情境，檢驗創傷後壓力症候疾患在前額葉皮質區之腦波(Electroencephalography, EEG)反應及心跳變異率(Heart rate variability, HRV)反應，並以 phase-amplitude coupling 演算法來分析腦波變化與創傷後壓力症候疾患的關係。而動物實驗採用環境豐富化以及群居、獨居等不同居住型態，來當作社會情境，模擬人類情形，並且檢驗社會情境對於創傷後壓力症候疾患行為症狀以及生物指標，在內側前額葉皮質區及杏仁核回路的反應表現，所要測量生物指標包括：c-Fos, 神經生長滋養因子、發炎反應蛋白、微小膠質細胞、多巴胺受體數量以及鴉片類 mu 受體數量。

第二個研究根據第一個研究之生物指標結果，來發展新的介入治療法。在人類實驗方面，將採取生理回饋方法，訓練受試者學習改變 EEG、HRV 變化，來改變社會情境對創傷後症候疾患的行為症狀影響，並找出增強效果的指標。在動物實驗方面，將採取行為藥理學、光學遺傳學、化學遺傳學、神經內分泌學等方法，操弄針對前額葉皮質區與杏仁核神經回路的生物指標（包括：c-Fos, 神經生長滋養因子、發炎反應蛋白、微小膠質細胞、多巴胺受體數量以及鴉片類 mu 受體數量）來找出社會情境對創傷後壓力症候疾患的行為症狀、改善的因素，藉此發展新的介入方法。

本研究將是跨領域研究，橫跨心理學、神經科學、生物醫學工程。預期社會情境會改變創傷後壓力症候疾患的行為症狀（包括害怕、憂鬱、焦慮）及生物指標，並檢測內側前額葉皮質區及杏仁核神經細胞回路在這些生物指標改變中所扮演的角色。創傷後壓力症候疾患的有效治療，應該立基於對其神經機制的瞭解，因此本研究提供創傷後壓力症候疾患治療的神經生物學基理，根據調控神經生物指標，以及對針對前額葉皮質區與杏仁核神經回路的調控，可以發展出新的有效

治療方法。

2. Abstract

The pre-proposal will examine two issues: (a). whether social context affect PTSD symptoms in fear, depression, and anxiety. Moreover, social context affect all selected biomarkers including EEG in the mPFC, HRV, corticosterone secretions, and c-Fos, BDNF, inflammatory cytokine, microglia activations, dopamine receptors, and mu-opioid receptors in the medial prefrontal cortex and amygdala neural circuitry. (b). We will manipulate the factor of biomarkers including EEG, HRV, corticosterone secretions, c-Fos, BDNF, inflammatory cytokine, microglia, dopamine receptor, and m-opioid-receptor to modulate the effect of social context in PTSD symptoms in behavior. Therefore, the novel interventions will be developed for the multiple brain system to increase the effect of social context in the PTSD symptoms.

The first issue of the present pre-proposal will involve human and animal investigations. In the human study, the different social supporting will be served as the social context to examine whether social context affect PTSD symptoms in depression and anxiety. In the animal study, environmental enrichment or different housing styles will be served as the social context to elucidate PTSD symptoms in fear, depression, and anxiety. Also, the animal study will test environmental enrichment or different housing styles affect biomarkers including EEG in the mPFC, HRV, corticosterone secretions in plasma, and c-Fos, BDNF, inflammatory cytokine, microglia, dopamine receptor, and mu-opioid-receptor in the mPFC and amygdala neural circuitry.

The second issue of the pre-proposal will link the multi-disciplines approaches among psychology, neuroscience, and biomedical engineering studies. In psychological studies, the biofeedback, behavioral pharmacology-dopamine-receptor, and behavioral pharmacology-mu-opioid-receptor approaches will be used to facilitate the effect of social context to PTSD symptoms. In neuroscience studies, the opto- and chemo-genetic methods will be utilized to increase the effect of social context to reduce PTSD. In the neuroendocrinology study, we will administer an artificial corticosterone, dexamethasone, to change the effect of social context to decrease PTSD. In the biomedical engineering study, it will analyze EEG data with phase-amplitude coupling algorithm to increase the effect of social context to reduce PTSD. Therefore, the second pre-proposal will be designed to modulate all biomarkers such as EEG, HRV, corticosterone secretion, c-Fos, BDNF, inflammatory cytokine, microglia, dopamine receptors, and mu-opioid-receptors and then facilitate effect of social context to PTSD symptoms in fear, depression, and anxiety. Dependent on the findings, the novel interventions will be developed to ameliorate the PTSD symptoms.