

Thesis Title	The Effect of Stress and Anxiety on the Expression of the Peripheral Benzodiazepine Receptor Gene in Human Lymphocytes	
Name	Sutisa Nudmamud	
Degree	Master of Science (Neuroscience)	
Thesis supervisory Committee	Stefano O. Casalotti	Ph.D.
	Pongchai Harnyuttanakorn	Ph.D.
	Naiphinich Kotchabhakdi	Ph.D.
	Chittin Chindaduagrattana	M.D.
	Anan Srikiatkachorn	M.D.
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Abstract

Several studies have shown that PBR are sensitive to hormonal changes and stress. In general acute stress induced an increase in PBR density, while chronic stress decreased PBR density. In human studies, PBR density was decreased in lymphocytes of anxious patients and returned to normal after chronic diazepam treatment. These previous studies have used radioligand binding assay for quantification of PBR. The aim of this study was to determine whether "every day life" stressful experiences and prolonged periods of anxiety affect PBR expression at the mRNA level, and whether PBR mRNA alterations correlate with modulations in plasma levels of stress hormones such as cortisol and prolactin. Accordingly we have developed a semi-quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) technique for measuring the level of PBR gene expression in human lymphocytes. The RT-PCR products were labelled with fluorescein 12 dUTP, and were measured by a Dot blot assay using anti-fluorescein antibodies and

chemiluminescent detection. The level of PBR mRNA were expressed as a ratio of actin mRNA level.

PBR mRNA was measured in lymphocytes of students following University examinations and in clinically defined anxious patients and compared to control subjects. The results indicated that a group of the students taking examination had a significantly higher level of PBR mRNA. Cortisol but not prolactin was also elevated in this group. Anxious patient showed a wide range of PBR levels but on average they had lower PBR mRNA than the control group.

The molecular mechanism of PBR gene expression in lymphocytes was studied by dexamethasone treatment of B-lymphocyte cell line in culture. PBR gene expression changes could not be reliably detected at the various time points and concentrations tested. In contrast proliferation of B-lymphocyte cell line was suppressed by dexamethasone treatment.

The results of this study suggest that "examination" stress and prolonged periods of anxiety induce an alteration of PBR gene expression. PBR gene expression should be studied further in various types of stress or disease affected by stress before this procedure could be proposed as diagnostic methodology for stress. Moreover, the molecular mechanism and other factors that affect to the expression of PBR in lymphocytes should also be studied further.