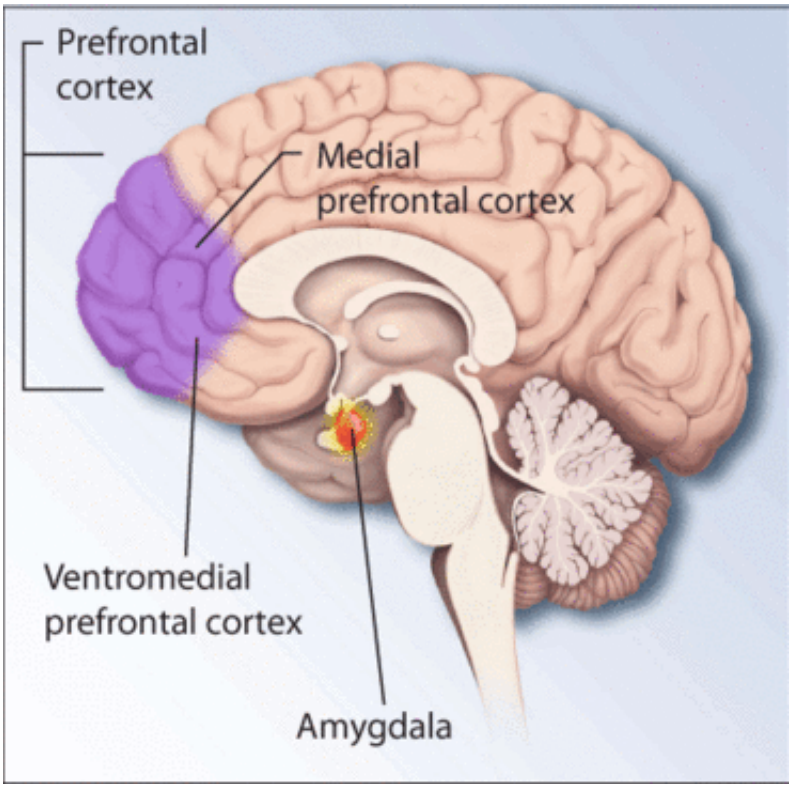
Alterations in blood-based miRNA in veterans affected with combat-related PTSD

September 4 2017



Regions of the brain associated with stress and posttraumatic stress disorder. Credit: National Institutes of Health

Individuals affected with PTSD (Post-Traumatic Stress Disorder) demonstrate changes in microRNA (miRNA) molecules associated with gene regulation. A controlled study, involving military personnel on deployment to a combat zone in Afghanistan, provided evidence for the

role of blood-based miRNAs as candidate biomarkers for symptoms of PTSD. This may offer an approach towards screening for symptoms of PTSD, and holds promise for understanding other trauma-related psychiatric disorders. Limitations of the study are that this was a small pilot study, and the findings need to be validated, extended and confirmed. First results will be presented at the ECNP conference in Paris.

PTSD is a psychiatric disorder which can manifest following exposure to a traumatic event, such as combat, assault or natural disaster. Among individuals exposed to traumatic events, only a minority of individuals will develop PTSD, while others will show resiliency. Little is known of the mechanisms behind these different responses. The last few years have seen much attention given to whether the modification and expression of genes - epigenetic modifications - might be involved. But there are several practical and ethical challenges in designing a research study on humans undergoing such experiences, meaning that designing relevant study approaches is difficult.

The research group from the Netherlands, worked with just over 1,000 Dutch soldiers and the Dutch Ministry of Defense to study changes in biology in relation to changes in presentations of symptoms of PTSD in soldiers who were deployed to combat zone in Afghanistan. In a longitudinal study they collected blood samples before deployment, as well as 6 months after deployment. Most of the soldiers had been exposed to trauma, and some of the soldiers had developed symptoms of PTSD.

For this pilot study, from the initial group, subgroups were selected of in total of 24 subjects; 8 of the soldiers had developed symptoms of PTSD; 8 had endorsed traumatic experiences but had not developed symptoms of PTSD; and another 8 had not been in serious traumatic circumstances and served as a control group. Using modern sequencing techniques,

several types of miRNAs of which the blood levels differed between the groups were identified.

MiRNAs (Micro RiboNucleic Acids) are small molecules with chemical building blocks similar to DNA. Unlike the more famous DNA, miRNAs are typically very short - comprising only around 20 to 25 base units (the building blocks of nucleic acids), and they do not code, in other words they do not specify the production of a protein or peptide. However, they have very important roles in biology (every miRNA regulates the expression, and thereby also the activity of several other genes), and they are known to regulate the impact of environmental factors on biology. In addition, brain-derived miRNA can circulate throughout the human body and can be detected in the blood.

Differences in miRNA levels have been associated with certain diseases, such as some cancers, kidney disease, and even alcoholism. This regulatory role makes them also a candidate for investigation in PTSD.

"We discovered that these small molecules, called miRNAs, are present in different amount in the blood of persons suffering from PTSD compared to trauma-exposed and control subjects without PTSD", said first author Dr Laurence de Nijs (Maastricht University).

"We identified over 900 different types of these small molecules. 40 of them were regulated differently in people who developed PTSD, whereas there were differences in 27 of the miRNAs in trauma-exposed individuals who did not develop PTSD."

"Interestingly, previous studies have found circulating miRNA levels to be not only correlated with different types of cancer, but also with certain psychiatric disorders including major depressive disorders. These preliminary results of our pilot study suggest that miRNAs might indeed be candidates as predictive blood markers (biomarker) to distinguish

between persons at high and low risk of developing PTSD. However, several steps need to be performed before such results can really have an impact on the larger field and in clinical practice. In addition to working towards biomarkers, the results may also provide novel information about the biological mechanisms underlying the development of PTSD".

Dr de Nijs explained:

"Most of our stressful experiences don't leave a long-lasting psychological scar. However, for some people who experience chronic severe stress or really terrible traumatic events, the stress does not go away. They are stuck with it and the body's stress response is stuck in 'on' mode. This can lead to the development of mental illness such as PTSD.

These individuals experience symptoms including re-experiencing of the traumatic event through flashbacks or recurrent nightmares, constant avoidance of reminders of the event, negative mood, and extreme arousal. This can manifest itself through insomnia and or hyper-alertness. Individuals with PTSD are six times more at risk of committing suicide and having marital problems, and the annual loss of productivity is estimated to be approximately $3 billion. Currently, there is no definite cure for patients with PTSD, and available treatments often are not effective".

Commenting, Professor Josef Zohar (Ex-ECNP Chair, Tel Aviv, Israel) said:

"The relevance of a better understanding of stress related events is unfortunately becoming clearer and clearer after each terror attack. This work points to an innovative avenue regarding the potential identification of risk factors for susceptibility to developing post-traumatic stress disorder".

Provided by European College of Neuropsychopharmacology