Chapter 12
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Brain Derived Neurotrophic Factor (BDNF) As a Predictive Biomarker of the Occurrence of Post Traumatic Stress Disorder (PTSD)

H. Belhadj-Tahar[1*] and N. Sadeg[2]

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ABSTRACT

The primary goal of the pilot study was to determine the rate of serum BDNF and the initial clinical course of a subject who had been exposed to a potentially traumatic incident over the course of three months. In this study 12 volunteers were recruited, 7 have been exposed to a traumatic event and 5 negative controls without psycho-trauma history. In this study, there is no correlation between circulating levels of cortisol and BDNF. The following are the findings of this study: In comparison to the control group, the rate of BDNF was substantially lower in the trauma group of volunteers: 6.20±1.73 ng / ml for the group with trauma *versus* 21.79±1.76 ng / ml for the control group with p<0.001. When compared to those who have experienced a traumatic event, the rate of serum BDNF is substantially reduced in victims of physical aggression: 4.36±0.37 ng / ml Assault group *versus* 6.94±1.44 ng / ml control group event with p = 0.03. The level of BDNF is significantly inversely correlated with the intensity of the Peritraumatic distress (r = -0.75, p <0.05). When compared to the group without PTSD, the rate of serum BDNF was significantly lower in the group with acute PTSD: 7.5±0.9 ng / ml in the absence of PTSD (n = 4) *versus* 4.5 ±0.4 in the presence of PTSD (n = 3), p = 0.001.

Keywords: Post traumatic stress; PTSD; brain-derived neurotrophic factor; BDNF; biomarker.

1. INTRODUCTION

The term Psychic trauma and their repercussions on the mental health of victims have been known since antiquity. In this regard, we find in the writings of Herodotus the case of unexplained blindness of the warrior Epizelos who was frightened by the brutal vision of the Persian giant who came to confront him [1]. Likewise, Lucretia (40 BC) reported in “De natura rerum” the nightmares of warriors who saw each other every night on the battlefield [2]. But the first medical observations identifying mental disorders resulting from traumatic exposures date back to the end of the 17th century thanks to the doctors of the French armies of the “Ancien Régime” who reported the cases of soldiers suffering from feelings of “nostalgia”, many of which were linked to distress, and the horror of the violence of the battles [1]. Contemporary of the wars of the Empire, Pinel established in his Medico-Philosophical nosography an inventory of the psychological disorders caused by the violence of the combats and the "moral emotions" of the terror or the war [3]. Among these disorders he cited melancholy, hypochondria and neurosis of circulation or respiration. On the other hand, surgeons of the Napoleonic armies, such as Desgenettes, Larrey and Percy, described "the syndrome of the wind of the ball" which indicated a state of neurosis, with acute stupor stupor, caused by the only fear felt by the soldiers during the passage of the projectile in the absence of any physical injury [1]. However, the concept of traumatic neurosis was not introduced until the end of the 19th century by Oppenheim, who described "lasting psychic alterations" in 42 victims of occupational or railway accidents [4].

[1]Mental health research group, French Association for Medical Research Advancement (AFPREMED), 9 rue du Pr Antoine Baisset, 31000 Toulouse, France.
[2]International Medical Institute of Toxicology and Pharmacology, Bat. B8, Rue Henri Becquerel, 60230 Chambly, France.
**Corresponding author: E-mail: hafid.bt@gmail.com;*

Noting in many cases a discrepancy between the minimal physical shock and a disproportionate psychic semiology, the psychology pathogenic hypothesis was adopted by the author to explain the sleep disorders, irritability and phobias resulting from the fright felt during the occurrence of the accident. Indeed, in his clinical analysis, he mainly identifies:

(a) a uniformity of the ideal content of the patients who were obsessed with the memory of the accident, (b) major anxiety triggered by anyone who can remind them of the accident, (c) sleep disorders with agitation and accident nightmares, (d) a profound modification of the affective sphere with a tendency to withdraw into oneself.

For Charcot, traumatic neurosis was indistinguishable from other neuroses, neurasthenia, or hystero-neurasthenia [5]. At the same time, Janet reported several cases of hysteria and neurasthenia following a traumatic event [6]. In 1892, Freud and Breuer argued that hysteria and traumatic neurosis resulted from superimposable pathogens, the reminiscence of which occupied a central place [1]. For Freud, the memory of the traumatic event is like a foreign body in the psyche of the victim, thus joining the postulate of Janet [6]. As a reminder, Janet referred to a phenomenon he called "dissociation" which corresponded to the coexistence of adapted behaviour and maladaptive behaviour resulting from the "raw recollection" of the event that had a traumatic impact. This term of dissociation will be taken up later by the Anglo-Saxons in this “Janetian” meaning.War trauma was particularly studied during the first half of the twentieth century, which saw the outbreak of two extremely destructive and murderous world wars, leaving 8 million people killed and 32 million injured in the two camps during the first war (1914 -1918) and 58 million dead as well as 35 million injured for the second (1939-1945). During the First World War, Salmon drew on the experience of the Russian chief medical officer Autocratov, and proposed "psychiatry of the front" (that is to say at the front and not practiced at the behind the lines) for the therapeutic care of psychic traumatism according to five principles: proximity, immediacy, centrality, simplicity and hope [7]. Salmon's principles were summarized as follows: Proximity was based on the advisability of keeping the subject in the atmosphere of the front to convince him that it was not a final withdrawal but only a short recovery period before finding his comrades as quickly as possible. The aim of immediacy was to not allow the latency period of a traumatic neurosis to set in. The hope implied that the subject had to be convinced that he would certainly be healed. Simplicity was reflected in the implementation of uncomplicated methods in a rustic but clean room equipped with appropriate means to dispense rudimentary hygiene (beds with clean sheets, water point, and toilet, which appeared to be a real problem. luxury in view of the living conditions in the trenches). The centrality implied a coherent general organization, staggered from the antennas in the front to the treatment and “channeling centers” in the rear then the hospitals in the interior and rehabilitation centers and finally repatriation from Europe to hospitals in the United States of America. After World War II, American psychiatrists implemented the DMS-I [8] based primarily on the identification of symptoms and evolutionary patterns. In this version, the diagnosis of "Gross Stress Reaction" was there [8].

However, this diagnosis was deleted from the DSM in its second revision in the midst of the Vietnam War [9]. But from the 1980s several studies on the fate of the soldiers of Vietnam and which will show that the veterans still suffered 10 years after debilitating mental disorders [10]. In another register, many works have been published on post traumatic stress resulting from sexual assault in the 1980s [1]. The term Post Traumatic Stress Disorder (PTSD) was introduced in 1980 at the Third revision of the DSM [11]. It has undergone some changes in the DSM-III and DSM IV- R versions developed successively in 1987 and 1994 [12,13]. On the other hand, the "Acute Stress Disorders" diagnosis backwards from the 2nd day was added to it in the 1994 version DMS IV. This pathology appears in the 10th revision of International Classification of mental illness from 1992 [14]. Although significant progress has been made in terms of the diagnostic and therapeutic management, the fact remains that internationally, dramas supposedly related to the state of post-traumatic stress still not resolved. These tragedies highlight that remain some unknowns regarding prognostic factors to identify the victims exposed to a traumatic event. While it is estimated during life, 51% to 83% of the general population will be confronted with a traumatic event [15]. Some of the victims will develop a state of post-traumatic stress disorder (PTSD). The prevalence of PTSD differs considerably from one study to another: from 1 to about 10% probably due to the societal and cultural environment [16]. Indeed, first in the West countries, sexual assaults take first place, while traumatic event remains taboo and

hidden in Asian region and other societies. Nevertheless, some authors question the validity of the diagnosis of PTSD based on several combinations of symptoms from a list of diagnostic criteria for DSM IV-R [17,18]. According to these authors, the diagnosis of PTSD would be unreliable because it is based on subjective clinical criteria that occurred after exposure to an often unverifiable psycho-traumatic potential events reported by patients including research of secondary benefits [19].

The research for a biological indicator is a key objective evidence to verify the reality of post-traumatic stress and screening of individuals at risk in order to focus the resources used in providing the victim with a decision more effective, comprehensive and early treatment to prevent or limit the progression to PTSD. However, until now vulnerability and protective factors are only partially identified. One of these protective factors is BDNF that is a neurotrophin belonging to the family comprising the neurotrophin NGF (Nerve Growth Factor) and the neurotrophins NT3, NT4 / 5, NT6 and NT7 [20]. The major roles include regulation of BDNF activity through both the synapse plasticity facilitating synaptic transmission [21,22] and the trophicity acting as a promoter of the survival of neuronal populations during development and in adults and remodelling of neuronal populations factor [23,24].

In addition, the BDNF seems to be a potential biological indicator of PTSD [25]. The purpose of the present article is to quantify the concentration of serum BDNF in a group of victims in the early stages and follow clinically for 3 months in order to test the predictive power of BDNF versus the developed PTSD.

2. EXPERIMENTAL PROCEDURES

12 volunteers were enrolled in this prospective study; divided into two groups (i) 7 subjects have recently been exposed to a traumatic event (within 72 h), and have felt intense fear, helplessness, or horror (ii) and 5 subjects without trauma exposure as control group.

Excluded were those neurological illness; psychiatric disorders, alcohol or substance abuse or dependence, and serious medical illnesses, including cardiovascular, gastrointestinal, respiratory, endocrinologic, and genitourinary system diseases. They were not taking an anti-inflammatory medication during the previous two weeks. Some confounders of serum BDNF such as smoking and obesity are not included in this study. Effectively, these situations can interfere with the findings. All subjects included provided written informed consent, after receiving a complete description of the study and having the opportunity to ask questions.

The psychiatric assessments included: the Trauma History Questionnaire (THQ) at day1, Peritraumatic Distress Inventory (PDI) at day1, Peritraumatic Dissociative Experiences Questionnaire (PDEQ) at day 1, Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) at day 30 and day 90 ; PTSD CheckList - Specific (PCL-S) at day 30 and day 90.

The Venous blood was collected between 8 and 9 a.m. and centrifuged within 20 min after sampling at 2000×g for 20 min then aliquoted and stored at -80°C until analysis. Serum BDNF was quantified by ELISA (RayBio™ technique). BDNF assay employed an antibody specific for human BDNF coated on a 96-well plate. Cortisol concentration dosage was obtained by Electro-ChemiLuminescence immunoassay method (Cobas™, Roche Laoratories).

The statistical analysis (Student's test and Pearson’s correlation coefficients) were carried out by Microsoft Excel 2013™.

3. RESULTS

In this study 12 volunteers have been selected: 7 (5 men and 2 women) aged 34 $\pm$ 13.4 years have been exposed to a traumatic event and 5 negative controls (3 men and 2 women) aged 44 $\pm$ 14.2 years were without psycho-trauma history (Table 1 and Table 2). 2 volunteers were subjected to severe physical abuse and five witnesses hanging or fatal injury. The time between exposure to the

traumatic event and the consultation and therefore the collection of the blood sample for analysis including serum BDNF and serum cortisol collected between 2 h and 72 h.

Table 1. Characteristics of the group of volunteers exposed to trauma

Subject	Gender	Age (years)	Nature of the event	Delay* (h)	BDNF (ng / ml)	Cortisol (µg/dl)
V-1	F	45	Physical assault	18	4.62	Not measured
V-2	M	23	Physical assault	72	4.09	8.35
V-3	F	23	Witness hanging	72	6.99	6.04
V-4	F	47	Witness hanging	72	8.61	14.82
V-5	M	28	Witness of fatal injury	72	6.58	13.67
V-6	F	20	Witness of fatal injury	72	7.76	11.27
V-7	F	52	Witness hanging	2	4,78	39.12
Average		34.00		54.29	6.20	15.55
Standard deviation		13.47		30.60	1.73	12.00

**Delay: time between trauma event and blood collect*

Table 2. Characteristics of control group

Subject	Gender	Age (years)	BDNF (ng / ml)	Cortisol (µg / dl)
W-1	M	40	19.48	Not measured
W-2	M	55	22.79	8.89
W-3	F	53	23.19	7.21
W-4	F	21	20.31	31.47
W-5	M	52	23.19	10.08
Average		44.2	21.79	14.41
Standard deviation		14.24	1.76	11.43

3.1 Comparison of Serum Levels of BDNF and Cortisol:

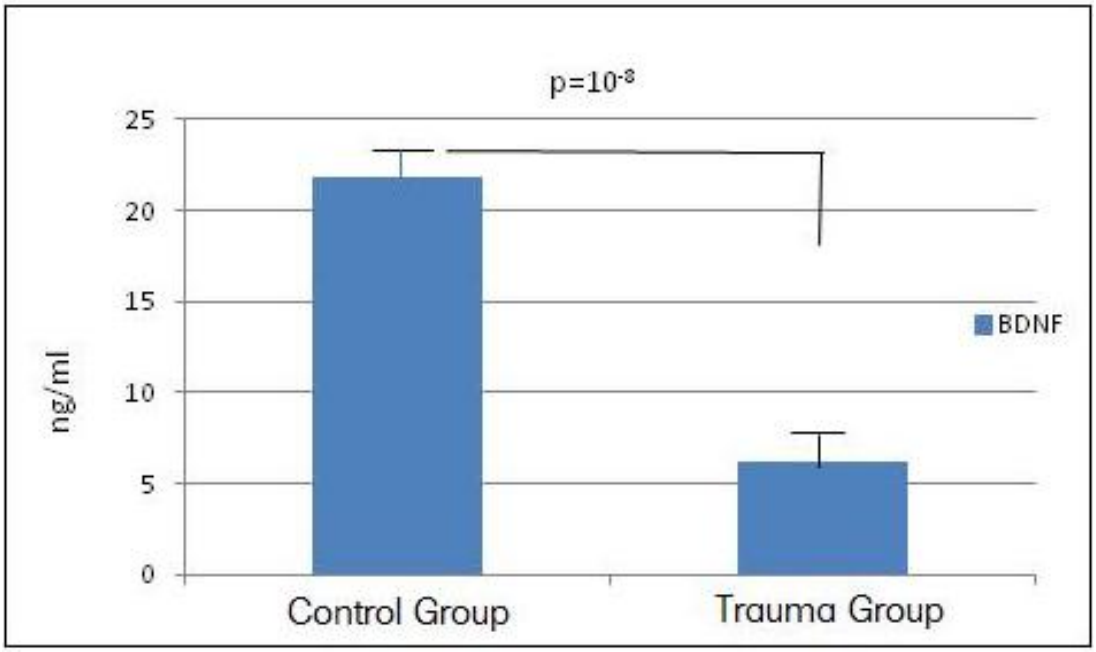
In the general population (exposed and unexposed, n = 12), the average rate of serum cortisol and serum BDNF were estimated respectively at 15.09 ± 11.13 µg/dl (for cortisol, n = 10) and 12.70 ± 8.20 ng / ml (for BDNF, n = 12). There is no correlation between the both levels of BDNF and cortisol.

There is no significant difference between the cortisol group "exposed to a traumatic event" *versus* "unexposed" negative control group: level's group exposed showed an average value of 15.55 ± 10.95 µg / dl *versus* 14.41 ± 11.43 µg / dl for the unexposed group.

3.2 BDNF Levels and Nature of the Traumatic Event

The serum BDNF levels are significantly lower in volunteers exposed to trauma compared with the control group (Graph 1): 6.20 ± 1.73 ng / ml for the group with trauma *versus* 21.79 ± 1.76 ng / ml for the control group (witnesses), with $p<0.001$.

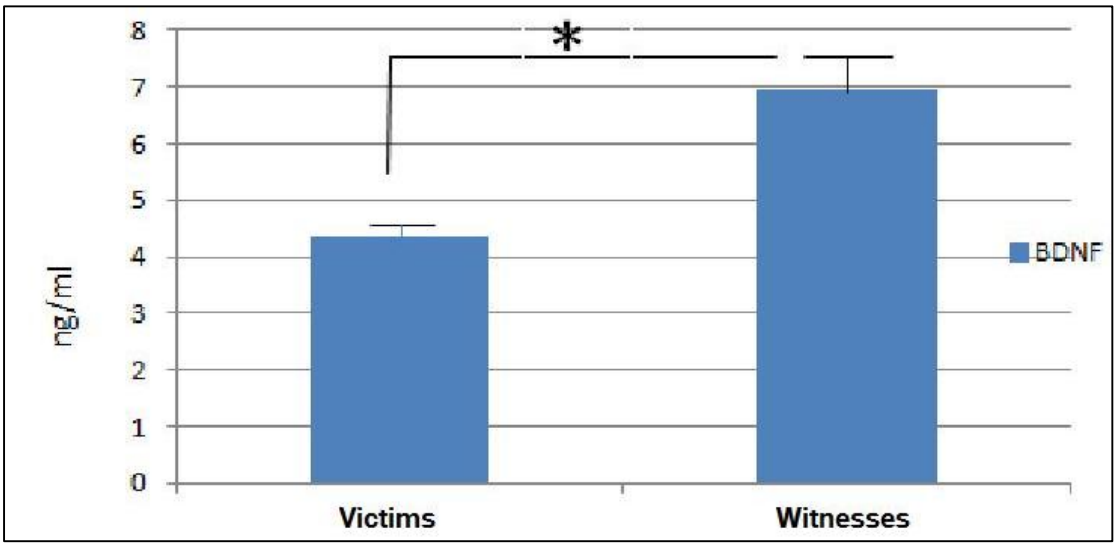
There is no correlation between BDNF levels and age of the subject. There is no correlation between BDNF levels and the delay between exposure to the event and the BDNF sampling (this period ranged from 2h to 72h) (see Graph 1).



Graph 1. Comparison of BDNF rate between the exposed and control

The values of serum BDNF women are not significantly different from those for men: the average of BDNF level for men is 5.34 ± 2.67 ng / ml *versus* 6.55 ± 1.48 ng / ml for women.

The BDNF levels were significantly lower in the group of victims of physical aggression compared to the group who have witnessed traumatic event: 4.36 ± 0.37 ng / ml for Assault group (n = 2) *versus* 6.94 ± 1.44 ng / ml for control group event and $p = 0.03$ (n = 5) (see Graph 2).



Graph 2. Comparison of BDNF rate between victims and witnesses of trauma event

3.3 BDNF and Peritraumatic Reactions

Table 3 shows the questionnaire results of Peritraumatic dissociative experiences (PDEQ) and Inventory of peritraumatic distress disorder (DPI).

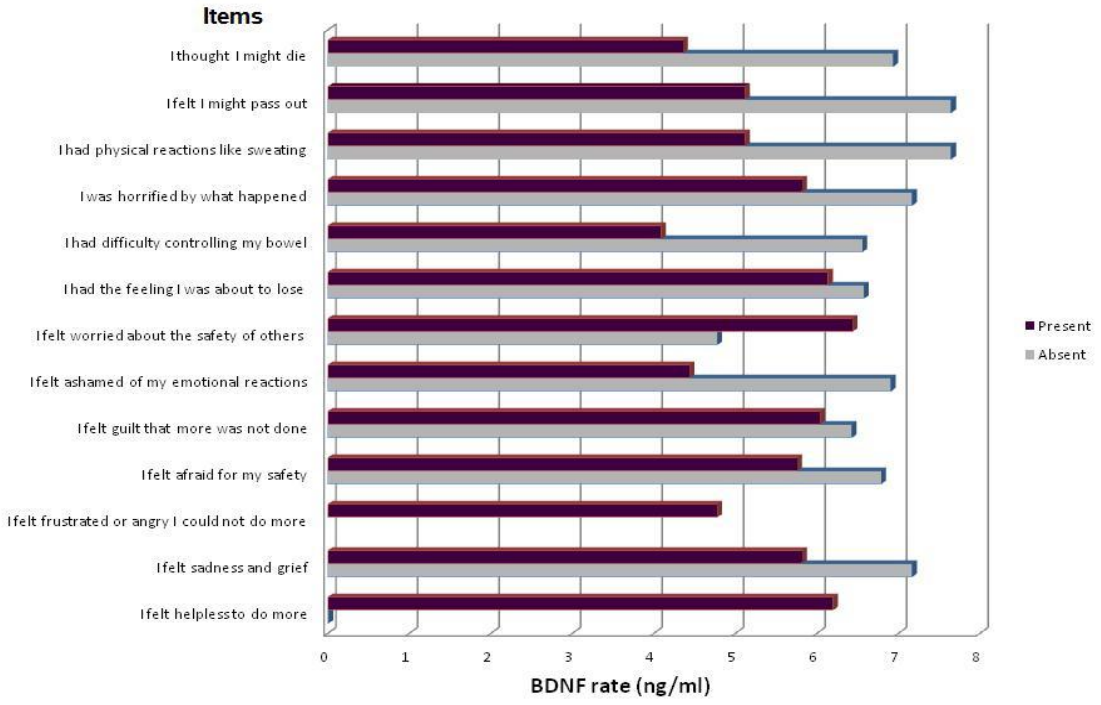
Table 3. Comparison between the levels of BDNF and scores of questionnaires peritraumatic dissociative experiences (Peritraumatic Dissociative Experiences Questionnaire, PDEQ) and Inventory of peritraumatic stress disorder (Peritraumatic Distress Inventory, PDI)

Subject	BDNF (ng / ml)	PDEQ	DPI
V-01	4.62	41	35
V-2	4.09	42	43
V-03	6.99	46	32
V-04	8.61	28	18
V-05	6.58	14	8
V-06	7.76	17	16
V-07	4.78	20	33
Average	6.20	29.25	26.43
Standard deviation	1.73	12.31	12.53

Peritraumatic dissociative experiences and BDNF: The score of peritraumatic dissociative experiences questionnaires (PDEQ) was estimated at 29.25/50 (29.25±12.31) with a minimum of 14/50 and a maximum of 46/50 (see Table 3). There is no correlation between BDNF levels and PDEQ's score.

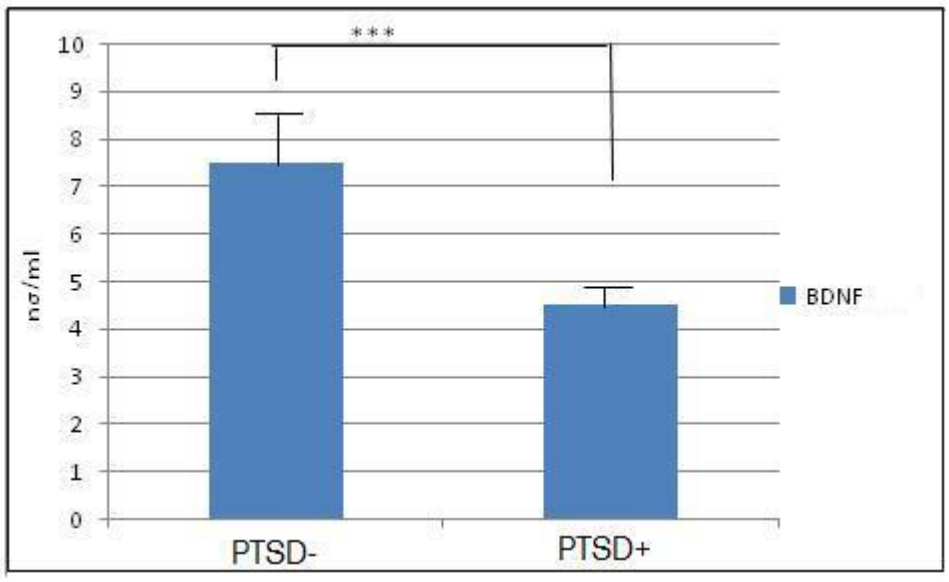
BDNF and peritraumatic distress: The average score of the Inventory of peritraumatic distress disorder (DPI) was estimated at 26.87 / 52 (26.87±11.70) with a minimum of 8/52 and a maximum of 43/52. There is a good correlation between the rate of BDNF and PDI score ($r = -0.74$, $p < 0.05$). These results support our hypothesis: the severity of post-traumatic distress is inversely proportional to the rate of BDNF.

The BDNF levels are lower in the presence of symptoms in all peritraumatic distress items with the exception of Item 7 "I was worried for the safety of others" (Graph 3).



Graph 3. Comparison between clinical symptoms and BDNF levels after the DPI

BDNF rate and diagnosis of PTSD in the first month: Based on SCID-I (Structured Clinical Interview for DSM-IV Axis I Disorders), the diagnosis of PTSD was selected in 3 cases. The average concentration of BDNF was significantly higher in the absence of PTSD: 7.5 ± 0.9 ng / ml in the absence of PTSD (n = 4) *versus* 4.5 ± 0.4 ng / ml in the presence of PTSD (n = 3), $p = 0.001$ (Graph 4).



Graph 4. Comparison of BDNF in the presence versus absence of PTSD in the first month rate

BDNF rate and diagnosis of PTSD in the third month: The diagnosis of PTSD was retained in one case. In the absence of PTSD, the mean concentration was 6.44 ± 1.41 ng / ml. In the presence of PTSD, the average serum BDNF becomes 4.78 ng / ml and it's statistically different.

Confrontation of BDNF levels and symptoms of PTSD: Table 4 shows the scores of questionnaires PTSD Checklist-Specific (PCL-S) at the first months (PCLS30) and at the 3rd month (PCLS90).

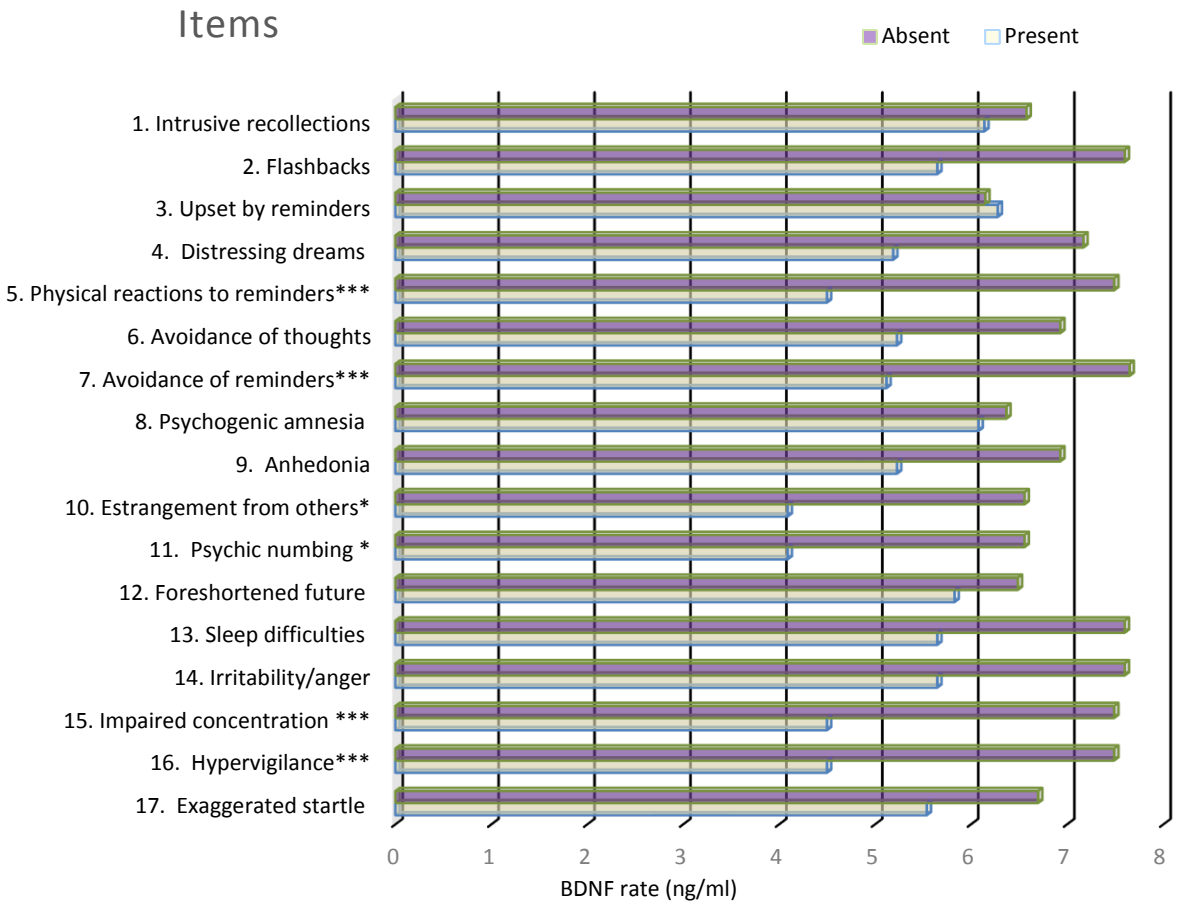
Table 4. Comparison between the levels of BDNF and PTSD Checklist scores questionnaires-specific (PCL-S) on the first month (PCLS30) and 3rd month (PCLS90)

	BDNF (ng / ml)	**Scores PCLS30**	**Scores PCLS90**
V-01	4.62	37	33
V-2	4.09	27	0
V-03	6.99	14	7
V-05	8.61	12	2
V-06	6.58	0	0
V-07	7.76	9	3
V-08	4.78	33	4
Average	6.20	22.76	7.01
Standard deviation	1.73	16.74	11.70

The average score PCL30 is estimated at 22.76 / 68 (22.76±16.74) with a minimum of 0/50 and a maximum of 37/50. There was a good correlation between the BDNF level and the PCL30 score ($r = -0.77$, $p < 0.05$). The severity of PTSD symptoms is inversely proportional to the levels of BDNF in the peritraumatic period.

The average score PCL90 is estimated at 13.51 / 68 (13.51±21.01) with minimum of 0/50 and a maximum of 35/50. There is no correlation between the BDNF level and the PCL30 score (r = 0.36, NS).

The Graphic 5 shows the results on PCLS questionnaire in the symptom is present or absent regardless of its intensity achieved in the first month. In general, the levels of BDNF is higher each time when the PCLS is absent in the symptom list.



Graphic 5. Comparison between clinical symptoms and BDNF levels after the 30th day PCLS questionnaire

4. DISCUSSION

In another pilot study, we showed that there is a good correlation between blood and CSF BDNF levels [26]. The CSF sampling is difficult to obtain in routine and the serum is a good alternative for sampling. The limit of our study is the small size of patients. We consider that this study is a pilot and prospective approach to test the serum BDNF as biomarker for trauma events. A new study with a great number of patients is necessary to confirm our finding. The inclusion of such patient is difficult because of the multiple reasons of exclusion states (obesity, smoking, psychiatric disorder…).

In this study, there is no correlation between circulating levels of cortisol and BDNF. The BDNF levels were significantly lower in the group of volunteers exposed to trauma compared with the control group: 6.20 ± 1.73 ng / ml for the group with trauma *versus* 21.79 ± 1.76 ng / ml for control group. The same rate is significantly collapsed in victims of physical aggression compared to those who have witnessed a traumatic event: 4.36 ± 0.37 ng / ml for Assault group *versus* 6.94 ±1.44 ng / ml for control group event with p = 0.03. The peritraumatic reactions were explored via questionnaires

"Peritraumatic Dissociative Experiences Questionnaire" (PDEQ) and "Peritraumatic Distress Inventory (PDI)" during the visit of inclusion.

The level of BDNF is not significantly correlated with the intensity of dissociation of peritraumatic reactions. But so far, the immediate effects peritraumatic dissociation is discussed as well as some authors [27,28,29]. The peritraumatic dissociation can protect the individual from intense emotions such as feelings of fear, helplessness and horror. However, the peritraumatic dissociation would increase the risk of developing PTSD [30].

As against the BDNF levels were significantly inversely correlated with the score of the inventory of peritraumatic stress (DPI) with r = -0.75, p <0.05. Thus a diminution of BDNF levels is observed whenever distress symptom is present with the exception of the item 7 in relation to the other concern. The increase in BDNF seems to be related to the concern for others, while the "collapse on itself" would lead to the collapse of this neurotrophin.

According Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), 3 patients had PTSD at the end of the first month of which continued after the third month. Hence the establishment of diagnosis according to the criteria DSM-IV-R 3 cases of acute PTSD (1 month <symptom duration <3 months) and 1 chronic PTSD (symptom duration> 3 months). The BDNF levels were significantly lower in the group with acute PTSD compared to the group with no PTSD: 7.5±0.9 ng / ml in the absence of PTSD (n = 4) *versus* 4.5±0.4 ng/ml in the presence of PTSD (n = 3), p = 0.001.

Similarly, the levels of BDNF in the presence of only one case of chronic PTSD in 4.78 ng / ml was outside the 95% confidence interval concentrations of BDNF group of people free of chronic PTSD [from 5.03 to 7.86 ng / ml]. The BDNF values found in volunteers exposed to a traumatic event match those reported by Dell'Osso team that are similar to the BDNF values in people suffering from PTSD (5.3 ± 1.1 ng / ml) [25].

Finally, although this study involved only a small sample of volunteers (n = 7), the results highlight the importance of BDNF assay to better target victims at high risk of developing PTSD and what outperformed the support. A prospective study with more volunteers is in progress to confirm the results of this pilot study.

COMPETING INTERESTS

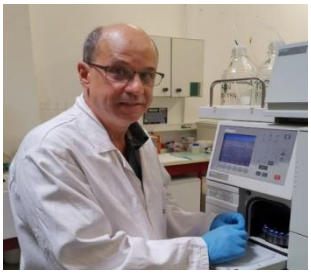
Authors have declared that no competing interests exist.

REFERENCES

1. Crocq L. Les traumatismes psychologiques de guerre. Paris, Odile Jacob édition; 1999.
2. Lucrece. De la nature (De natura rerum). Paris, Garnier; 1964.
3. Pinel P. Traité médico-philosophique sur l'aliénation mentale, Paris J.Ant. Brosson; 1909.
4. Oppenheim H. Die traumatischen Neurosen, Berlin, V. von August Hirschwald ed., (2e édition). 1892;1.
5. Charcot J-M. Leçons du mardi à la Salpêtrière 1888-1889. Paris, Progrès médical;1889.
6. Janet P. L'automatisme psychologique. Paris, Odile Jacob; 1998.
7. Salmon CK. The care and treatment of mental diseases and war neuroses ("shell shock") in the British army. New York City, War Work Committee of the National Committee for Mental Hygiene, Inc; 1917.
8. American Psychiatric Association: Diagnostic and statistical manual mental disorders. Washington, American Psychiatric Association Mental Hospital Service; 1952.
9. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. 2 edition. Washington, DC: American Psychiatric Association; 1968.
10. Gabriel R. No More Heroes: Madness and Psychiatry In War. Hill and Wang publication; 1987
11. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, third edition. American Psychiatric Association, Washington, DC; 1980.

12. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, third ed.American Psychiatric Association, Washington, DC; 1987.
13. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, fourth ed. American Psychiatric Association, Washington, DC; 1994.
14. WHO. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines, World Health Organization, Geneva; 1992.
15. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry. 1995;52:1048-60.
16. Klein S, Alexander DA. Epidemiology and presentation of posttraumatic disorders. Psychiatry. 2009;8(8):282-287.
17. Rosen GM, Spitzer RL, McHugh PR. Problems with the post-traumatic stress disorder diagnosis and its future in DSM–V. Br J Psychiatry. 2008;192:3–4.
18. Richardson L, Frueh C, Acierno R. Prevalence Estimates of Combat-Related PTSD: A Critical Review. Aust N Z J Psychiatry. 2010;44:4–19.
19. Frueh BC, Elhai JD, Grubaugh AL, Monnier J, Kashdan TB, Sauvageot JA, Hamner MB, Burkett BG, Arana GW. Documented combat exposure of US veterans seeking treatment for combat-related post-traumatic stress disorder. Br. J. Psychiatry. 2005;186:467-72.
20. Nilsson AS, Fainzilber M, Falck P, Ibanez CF. Neurotrophin-7: a novel member of the neurotrophin family from the zebrafish. FEBS Lett. 1998;424:285-290.
21. Lessmann V. Neurotrophin-dependent modulation of glutamatergic synaptic transmission in the mammalian CNS. Gen Pharmacol. 1998;31:667-674.
22. Lu B, Chow A. Neurotrophins and hippocampal synaptic transmission and plasticity. J Neurosci Res. 1999;58:76-87.
23. Connor B, Dragunow M. The role of neuronal growth factors in neurodegenerative disorders of the human brain. Brain Res Rev. 1998;27:1-39.
24. Murer MG, Yan Q, Raisman-Vozari R. Brain-derived neurotrophic factor in the control human brain, and in Alzheimer's disease and Parkinson's disease. Prog Neurobiol. 2001;63:71-124.
25. Dell'Osso L, Carmassi C, Del Debbio A, Catena Dell'Osso M, Bianchi C, da Pozzo E, Origlia N, Domenici L, Massimetti G, Marazziti D, Piccinni A. Brain-derived neurotrophic factor plasma levels in patients suffering from post-traumatic stress disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2009;33:899-902.
26. Belhadj-Tahar H, Vilamot B, Granberg M, Passamar M. Brain-derived neurotrophic factor (BDNF) as a predictive factor for post-traumatic stress disorder (PTSD). European Neuropsychopharmacology. 2014;24:S594-S595.
27. Marmar CR, Weiss DS, Metzler TJ, Delucchi K. Characteristics of emergency services personnel related to peritraumatic dissociation during critical incident exposure. American Journal of Psychiatry. 1996;153:94-102.
28. Briere J, Scott C, Weathers F. Peritraumatic and persistent dissociation in the presumed etiology of PTSD. American Journal of Psychiatry. 2005;162:2295-2301.
29. Van der Hart O, Van Ochten JM, Van Son MJ, Steele K, Lensvelt-Mulders G. Relations among peritraumatic dissociation and posttraumatic stress: a critical review. Journal of Trauma & Dissociation. 2008;9:481-505.
30. Ozer EJ, Best SR, Lipsey TL, Weiss DS. Predictors of posttraumatic stress disorder and symptoms in adults: a meta-analysis. Psychological Bulletin. 2003;129:52-73.

Biography of author(s)



Dr. H. Belhadj-Tahar
Mental health research group, French Association for Medical Research Advancement (AFPREMED), 9 rue du Pr Antoine Baisset, 31000 Toulouse, France.

He is a doctor in Medicine and specialized in Oncology (from Toulouse University) and Psychiatry (from Bordeaux University). He got PhD in radiochemistry (Grenoble University) in 1996 and engaged as researcher in radiopharmaceutics and *In vivo* exploration field in national center of scientific research (CNRS of Toulouse). He has been the director of Clinical Research Development in biomedical investigation center "Groupe Sante Recherche" and the Head of Psychiatric Emergency Department in Fondation Bon sauveur (Albi). He is the president of French Association of Medical Research Advancement (AFPREMED) since 2007 and current president of COLCOM (laboratory of Nanotechnology for biological applications). He is member of the World Health Organization's (WHO) Global Clinical Practice Network (GCPN) in Mental Health and Substance Abuse department. He has been board member and specialist in several medical societies, such as clinical and analytical toxicology, nanomedicine, nanotoxicology, toxicology, neurosciences and oncology. He was the author of several scientific publications in radiopharmaceutics, toxicology and neurosciences and 2 world patents in nanomedicine and cerebral radiotracer.

Dr. N. Sadeg
International Medical Institute of Toxicology and Pharmacology, Bat. B8, Rue Henri Becquerel, 60230 Chambly, France.

He is a doctor in Pharmaceutical sciences and PhD in Toxicology. He is the President of International Medical Institute of Toxicology and Pharmacology (IMITOX), the TOXseek scientific board chairman and vice President of French Association of Medical Research Advancement (AFPREMED). He has been board member and specialist in several medical societies, such as clinical and analytical toxicology, the International Association of Forensic Toxicologists, nanotoxicology, toxicology. He was the author of several scientific publications in toxicology and neurosciences.

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