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Neurology and Nervous System

MRI Brain Images

Feature Based Matching

Highlights

Nocturnal Panic Attack

Venous Sinus Thrombosis

Discovering Thoughts, Inventing Future

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Feature based Matching of CT & MRI Brain Images

By Ayush Dogra

Punjabi University, India

Abstract- Multimodal image matching calls or demands for feature based or object based matching. Feature used in matching can be edges, ridges, blobs, valleys etc. Feature based matching is considered as less tedious and low level image processing task whereas object based matching is considered as high level image processing task and complex.

GJMR-A Classification : NLMC Code: WI 368



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I. MATCHING

While integrating two multimodal and mono modal images, first step is matching (geometrical matching) and second step is fusion (combined display of data involved). In this paper we will concentrate on first step. Matching of CT and MRI images is useful in radiation therapy planning. This type matching is also used in skull base surgery and epilepsy surgery.

II. DIFFERENCE BETWEEN CAT AND MRI SCANS

CAT scans are a specialized type of x-ray. The patient lies down on a couch which slides into large circular opening. The x-ray tube rotate around the patient and computer collects the results. These results are translated into images that look like a slice of a person. CT is very good for imaging bone structure. "Fig." 1 shows CT slice.

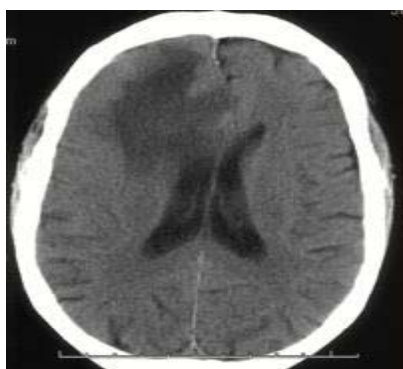


Figure 1 : A CT slice

MRI scan uses magnets and radio waves to locate the images. The patient lies on the couch that looks very similar the ones used for CT. they are then placed in a very long cylinder. The machine will produced a lot of noise and examinations typically run

minutes. MRI does not do very good job to bones but its advantage is ability to change the contrast of images. Most MRI machines can produced images in any plane. CT can not do this. "Fig." 2 and 3 are axial images whereas "Fig." 4 is coronal image.

Feature based matching of CT & MRI brain images

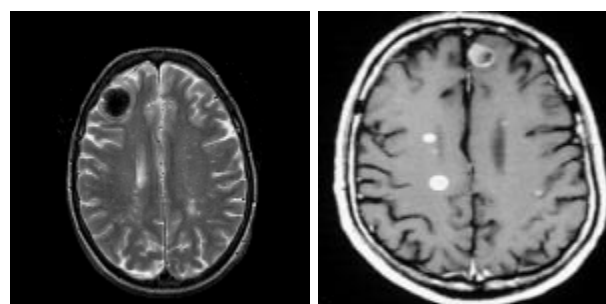


Figure 2 & 3 : Axial Images

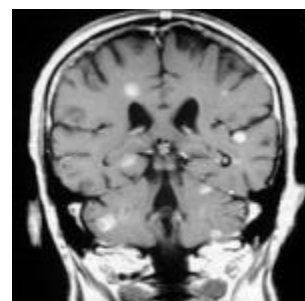


Figure 4 : Coronal Image

III. RIDGES

For matching of CT and MRI brain images we select skull ridge because nature of skull is in deformable. In "Fig" 5 CT slice is shown. In "Fig." 6 landscape of same depicted which is also called intensity landscape. "Fig." 7 shows the intensity of same CT slice but now smoothed by convolution with Gaussian. There are no. of geometrical invariants that extract ridges in a variety of images. Definition of L_{vv} [3,4] measure of 2D images

$$L_{vv} = \frac{1}{\|v\|^2} (v \cdot \nabla)^2 L,$$

(where ∇ is the nabla operator $(\frac{\partial}{\partial x}, \frac{\partial}{\partial y})$ and v is a right handed normal).

And the generalization of a 3D images by lvv operator can be found in[4]. When applying lvv operator to the CT set the resultant image show skull ridge. Then this ridgeness image is superimposed on to the original

CT slice to construct the 3D volume. "Fig." 8 shows ridged CT image. Similar example can be done in MRI image. "Fig." 9 shows a MRI image. "Fig." 10 shows the ridged MRI image (also called troughed image as in MRI image the skull area is dark).

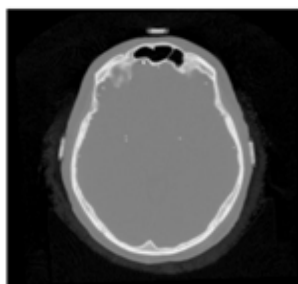


Figure 5 : CT slice

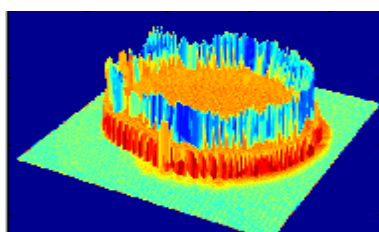


Figure 6 : Intensity landscape

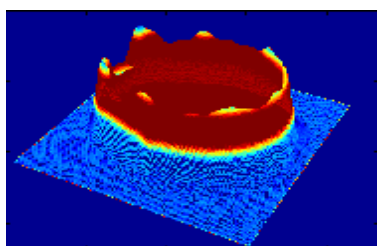


Figure 7 : Blurred by Gaussian Convolution

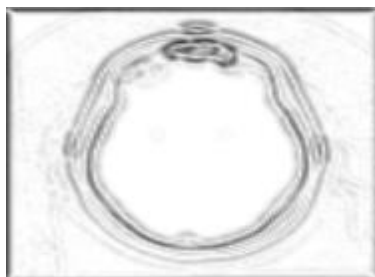


Figure 8 : Ridged CT image formed by superimposing the ridges on to the CT slice

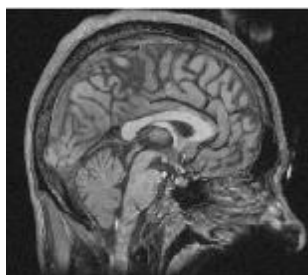


Figure 9 : MRI image

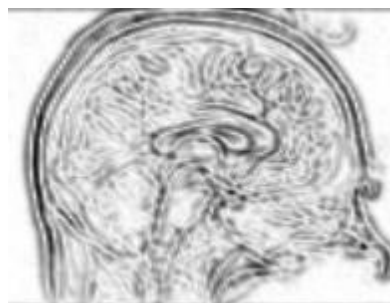


Figure 10 : Ridged MRI image

Feature based matching of CT & MRI brain images

IV. REGISTRATION METHOD

Now we need to register the feature volume. The technique used is cross correlation[5] since the two images have different physical realities. By using the grey values directly [1], avoid segmentation our feature images.

The correlation value $c(t)$ of CT feature volume L_1 and MR feature volume L_2 over all rigid transformations t , where $c(t)$ is defined

$$c(t) = \sum_{(x,y,z) \in L_1} L_1(x,y,z)L_2(t(x,y,z)).$$

Here next level is formed by maximizing the trough images or minimizing the ridge images. This method is also called multi resolution correlation [2,6]. The disadvantage of this approach is high computational effort required. "Fig." 11 shows resultant image after CT and MR volume matching using ridgeness correlation.

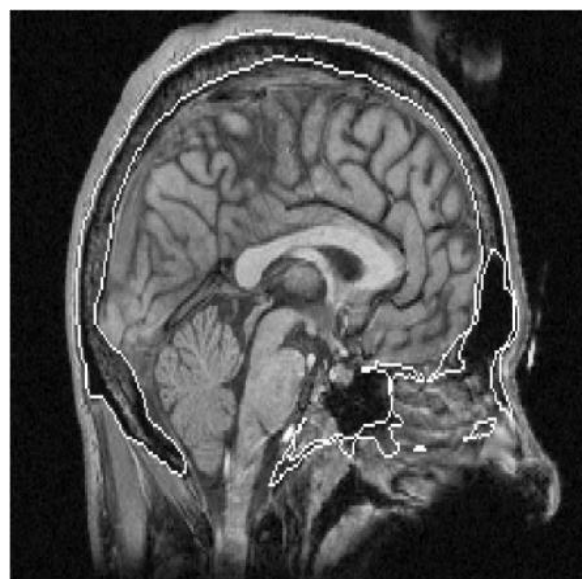


Figure 11 : CT and MRI matching using ridgeness correlation

V. CONCLUSION

The terms matching and registration are both used to denote the process of determining a transformation that relates the contents of two images in a meaningful way. The registration of MR and CT images was one of the first application of medical image registration. Further more the applicability of MR-CT registration is restricted primarily to the head. MR-CT registration is likely to become more widely used in future.

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A case of Foster Kennedy Syndrome (FKS) with Increase Intracranial Pressure (ICP) Attributed to Cerebral Venous Sinus Thrombosis (CVST)

By Madihah ALhubayshia & Tahir Obeidb

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Here we present a case of Foster Kennedy-like syndrome, in which meningioma compressed one optic nerve and cerebral venous sinus thrombosis impair cerebral venous drainage inducing intracranial hypertension, and papilledema in the other eye. This case emphasis the importance of considering of CVST as underlying pathogenesis of raised ICP in absence of cerebral edema or obstructed hydrocephalus.

Keywords: foster kennedy syndrome (FKS), raised intracranial (pressure (ICP), cerebral venous sinus thrombosis CVST).

GJMR-A Classification : NLMC Code: WI 355



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Madihah ALhubayshia^α & Tahir Obeidb^ο

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Keywords: foster kennedy syndrome (FKS), raised intracranial (pressure (ICP), cerebral venous sinus thrombosis CVST).

I. INTRODUCTION

The Foster Kennedy syndrome consists of optic disc pallor in one eye, optic disc edema in the other eye, and reduced olfaction caused by space-occupying lesion.^(1, 2)

Classically, The ophthalmological sign of Foster Kennedy syndrome (FKS) produced by direct compression of the ipsilateral optic nerve by basal frontal lobe, olfactory groove or sphenoid wing meningioma leading to optic atrophy with concomitant contralateral optic disc swelling secondary to raised (ICP) caused by the mass effect of the tumor.⁽¹⁻⁶⁾ Anosmia results from direct compression of the olfactory nerve.^(1, 2)

We describe a case report regarding the different pathogenic mechanisms, for which increased intracranial pressure (ICP) resulting from CVST. This is to suggest that not all FKS cases have the same underlying pathogenesis.

Our aim is to document this unique association and to draw attention on the importance of its presence. This is because the management in such situation advocates the use of anticoagulation.

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II. CASE STUDY

27 year old female referred to King AbdulAziz Medical City (KAAMC), Jeddah in 2004 with one week history of headache, diplopia and visual deterioration in both eyes, particularly in the left eye. She had occasional vomiting with no nausea. She had no symptoms to suggest underlying systemic diseases.

Examination showed visual acuity of 20/30 in the left eye and no light perception in the right eye. A right relative afferent pupillary defect was present with optic disc edema in the left eye, (fig.1.b) and an atrophic right optic disc (fig.1.a)

Slit lamp examination normal for both eyes.

There was left 6th cranial nerve palsy. Humphrey perimeter of the left eye revealed a superior nerve fiber bundle defect (fig.2.). The rest examination was normal.

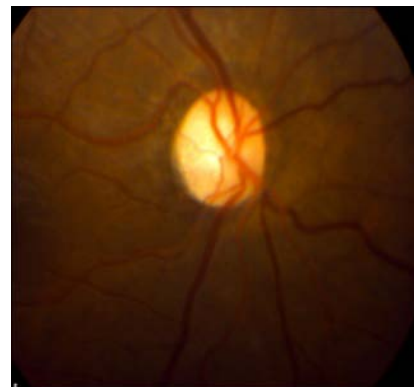


Figure 1.a : Atrophy of the right optic disc

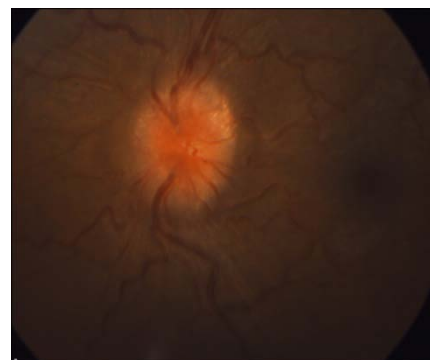


Figure 1.b : Edema of the left optic disc

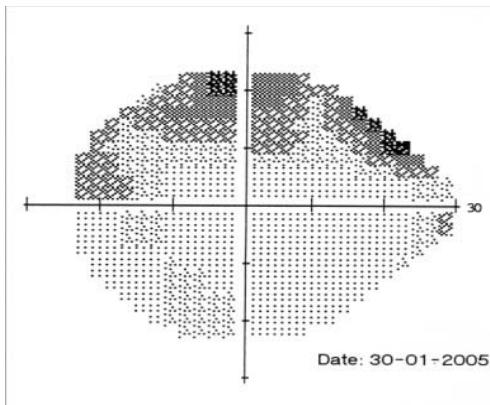


Figure 2 : Humphrey perimeter of the left eye disclosed an superior nerve fiber bundle defect

CT scan of the brain showed hyperostosis in right sphenoidal and right Occipitoparietal bone (**fig.3**).

MRI/MRV(**fig.4**) showed right sphenoidal wing strongly enhanced mass that consistent with the diagnosis of meningiomatosis. It extended from the right orbital apex through the optic canal and into the intracranial space. MRV study showed thrombosis of the posterior third of the superior sagittal sinus and the right sigmoidal sinus (**fig.5**)

Diagnostic Angiogram showed tow tumor blushes highly suggestive of meningiomas (**fig.6**)

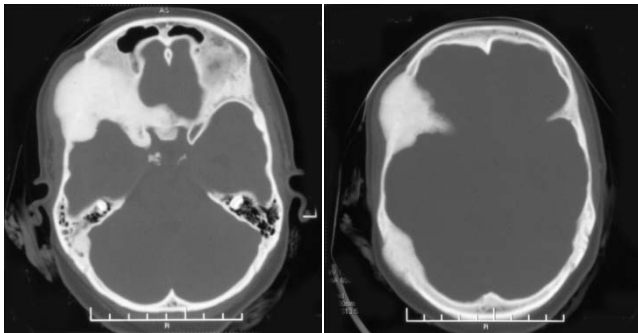


Figure 3 : CT scan of the brain bone window showed Hyperostosis in right sphenoidal and right Occipitoparietal bone

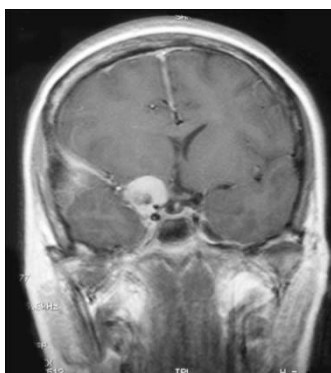


Figure 4 : MRI/ T1 with contrast Showing Right sphenoidal Wing strongly enhanced mass

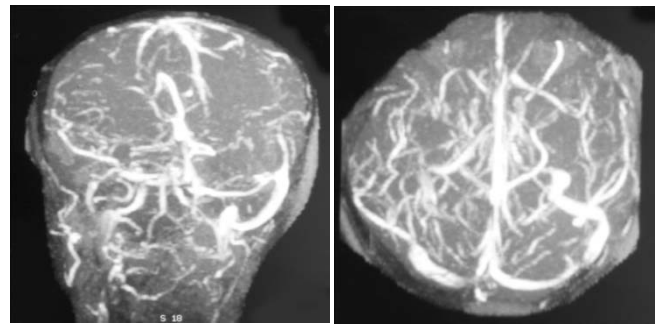


Figure 5 : MRVthrombosis of the posterior third of the SSS

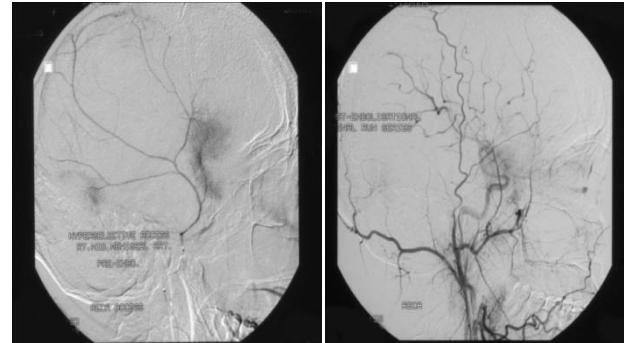


Figure 6 : Angiogram showed tow tumor blushes highly suggestive of meningiomas

The patient was treated with enoxoparine 1mg/kg subcutaneous BID, acetazolamid 500mg BID.

As vision of the left eye continued to deteriorate, the decision was taken to relief the pressure surgically and the patient underwent lumboperitoneal shunt, CSF examination done intra operatively showed opening pressure of 450 mm with normal compositions and negative cultures for bacterial and fungal infections, there was no evidence of malignant cell.

Other diagnostic tests including complete blood count, complete metabolic panel, erythrocyte sedimentation rate, c-reactive protein, and were unremarkable.

Post operatively, The patient received warfarin with therapeutic INR (2-3).

One month later the papilledema and visual field had improved on the left eye, and visual acuity was stable.

After 5 years, the patient vision stabilized and developed no shunt complication.

III. DISCUSSION

The mechanism and underlying pathology of ophthalmic feature of the FKS is variable. The classical pattern is caused by unilateral direct compression of the optic nerve fiber by meningioma and secondary increased intracranial pressure (ICP) causing papilledema of the contralateral eye. ^(1,2,4) Other mechanism have been suggested to explain the underlying pathology due to bilateral direct optic nerve fiber compression with normal ICP while atrophic

changes resulting from asymmetrical compression of both optic nerve by tumor.⁽⁷⁾

It may also results from chronic increased ICP which initially gives bilateral papilledema, with one optic disc subsequently developing pallor as a result of axonal death while the other optic disc remains swollen.⁽⁷⁾

This case of FKS meningioma cause direct compression of the right optic nerve, and presence of CVST impair cerebral venous drainage that round the other optic nerve by thrombus in which CSF is at a higher pressure than normal and which becomes responsible for papilloedema on the opposite side.

The treatment of visual loss due to Papilledem depends largely on the underlying pathology hence it is important to look for CVST when obvious brain edema and obstructed hydrocephalus are lacking, Prompt use of anticoagulation and cerebrospinal fluid diversion is critical in prevented visual loss in our case.

There is a previous report a patient with FKS in which meningiomas compressed the superior sagittal sinus to block cerebral venous drainage causes increased intracranial pressure, and papilledema in the other eye.⁽⁸⁾ Our case differ from this patient by having CVST.

We may postulate that some of the previous cases of FKS may have CVST as a cause of ophthalmic feature of this syndrome rather than a direct compression and/or an intracranial hypertension while MRI, MRV were lacking it emphasizes the importance of looking for this association as adding anticoagulation among other measures.

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Nocturnal Panic attack : Is it an Another Sub type?

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Abstract- Objective: The aim of this study is to investigate whether the nocturnal panic attack has different features and might be considered as a sub type or not.

Methods: Socio demo graphic data form, SCID-I, SCID-II, Panic and Agoraphobia Scale (PAS), Hamilton Depression Scale (HAM-D), Beck Anxiety Scale, and Bakirkoy Panic Disorder Behavioral Changes Form we reapplied to the participants. Fifty-one of the 98 patients were suffering from Nocturnal Panic Attacks according to the inclusion/exclusion criteria.

Results: It was revealed that 47.9% of the panic disorder patients were suffering from nocturnal panic attacks. The most frequent symptoms in nocturnal panic disorder cas-es were experiences of feelings like drowning, lethargy, palpit-ation, vertigo, fear of death, and anxiety. The existence of noct-urnal panic attacks was found to be related with severity of the disorder and com or bid depression.

Keywords: *nocturnal panic attack, sub type, panic disorder.*

GJMR-A Classification : NLMC Code: WI 370



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Results: It was revealed that 47.9% of the panic disorder patients were suffering from nocturnal panic attacks. The most frequent symptoms in nocturnal panic disorder cases were experiences of feelings like drowning, lethargy, palpitation, vertigo, fear of death, and anxiety. The existence of nocturnal panic attacks was found to be related with severity of the disorder and com or bid depression. Moreover, com or bid sleep disturbances characterized with troubles in falling sleep, difficulty in sustaining sleep, feeling tired in the morning were observed. There were sleep related avoidance and behavioral changes. Panic disorder patients with nocturnal panic attacks were found to avoid sleeping, or going to bed at one.

Conclusions: Panic disorder cases with nocturnal panic attacks had more severe symptoms. From here, it can be concluded that it might be a subtype of panic disorder.

Keywords: nocturnal panic attack, sub type, panic disorder.

I. INTRODUCTION

Panic disorder (PD) is an anxiety disorder characterized by spontaneous, recurrent and unexpected panic attacks and accompanying anxiety for another possible attack between attacks (anticipatory anxiety) (1). Panic attack (PA) is an intense anxiety episode primarily seen in panic disorder as well as other psychiatric disorders in anxiety spectrum disorders (social phobia, post-traumatic stress disorder, acute stress disorder, obsessive compulsive disorder, separation anxiety disorder) (2). In recent studies about panic disorder, it was reported that patients with PD had different clusters of symptoms and they presented with different characteristics accordingly (3). It is well understood that panic disorder is not a uniform disorder, rather it is a heterogeneous group of many subtypes. It is thought that every subtype might be different in terms

of clinical presentation, behavioral change and socio demo graphic features (4). Identifying subtypes of panic disorder and its characteristics is essential for evaluating some elements such as severity of disorder, psychiatric and physical comorbidity and response and prognosis to different therapeutic approaches (5, 6). "Masked anxiety" or "alexithymic panic" was first defined as a subtype of panic disorder (7,8). Following years, "nonscognitive" panics (8,9) and "nocturnal panic attacks" (10) which both lacked cognitions associated with fear were defined. In 1989 Mellman Craske and Barlow began studying nocturnal panic attack and afterwards many researchers made contributions to studies of nocturnal panic attack (11-14).

Nocturnal panic attack (NPA), a subtype of panic disorder, occurs without an obvious trigger, awakens patient from his sleep and consists of recurrent frightening panic attack. Studies show that recurrent nocturnal panic attacks occur 18-33% of patients with panic disorder (8). The most common symptoms in NPA are dyspnea, flushing and subsequent palpitation (3, 15). Many researchers have reported that nocturnal panic attack cases compared with common panic disorder cases, experienced more severe symptoms, more attacks during the day and more intense somatic complaints (15-17). Norton et al. claimed that nocturnal panic attack cases experience more signs and symptoms especially more chest pain while there is no significant difference in fear of dying, shortness of breath or sensations of smothering (3). Agargun and Kara (4) reported that patients with NPA have greater comorbidity with major depression, worse prognosis and higher risk of committing suicide. Melman and Uhde (10) in their study of comparing triggering situations between classic and nocturnal panic attacks, found that both relaxation and sleep deprivation have greater roles in precipitating nocturnal panic attacks.

In this study it is aimed to define the relationship between NPA and some variables such as behavioral changes, classification and clinical presentation of the defined behavioral change, age of onset, severity, duration, avoidance and socio demo graphic characteristics and to compare these with classic-panic disorder-patients.

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II. METHODS AND MATERIAL

Specimen

Study sample included 98 patients who administered to outpatient clinic of Prof. Dr. Mazhar Osman Bakirkoy Research and Training Hospital of Psychiatry, Neurology and Neurosurgery, were diagnosed with panic disorder by a psychiatry specialist during the sessions, were between the ages of 18-65, were at least an elementary school graduate and voluntarily participated. The inclusion criteria for nocturnal PD group were NPA experience at least 6 months ago and twice within previous month or 2 attacks within previous two months accompanying moderate anticipatory anxiety of NPA (13,14). Patients who had panic disorder due to general medical condition or direct physical effects of alcohol-substance abuse according to DSM-IV criteria, serious neurologic disorders, pathological electroencephalography results or physical diseases were excluded from this study.

III. METHOD

In order to confirm Axis I diagnosis and to determine comorbid diagnosis, Structured Clinical Interview for DSM-IV Axis I Disorders/Clinical Version (SCID-I) were administered to all patients with panic disorder and patients with comorbid psychiatric diagnoses were excluded.

Out of 98 patients included in this study, 51 had NPA according to the criteria mentioned in the specimen section. Personal, familial and clinical features were defined by administering socio demo graphic questionnaire, developed for this study, to included participants. During psychiatric interviews, diagnosis of panic disorder was confirmed and possible com or bid diagnoses were determined by using SCID-I Clinical Version oriented with DSM-IV. Whether a personality disorder coexists or not and if exists its effects on behavior and disorder were explored by using DSM-IV oriented SCID-II Clinical Version during psychiatric interview. Moreover, in order to evaluate anticipatory anxiety, agoraphobic avoidance, familial, occupational and social functionality, and thoughts of physical illness, Panic Agoraphobia Scale; in order to evaluate behavioral changes Bakirkoy Panic Disorder Behavioral Changes Form were applied.

Hamilton Depression Rating Scale and Beck Anxiety Scale were applied to two groups in order to assess the severity of depressive symptoms and anxiety, to compare the level of depressive symptoms and anxiety of two groups and to find the relationship between severity of anxiety and depressive symptoms and if exist, behavioral changes within the same group.

IV. MATERIAL

1. Socio demo graphic Data Form: This form, consists of 28 questions, is used by the researchers to

interpret participants' socio demo graphic data and their clinical presentations.

2. DSM-IV Axis I Disorders/Clinical Version (SCID-I): It is used to scan DSM-IV criteria and to systematically inquire the symptoms (18,19).
3. DSM-IV Axis II Disorders/Clinical Version (SCID-II): It is a structured interview to diagnose personality disorders (20).
4. Panic Disorder Behavioral Changes Form (App 1): It is a questionnaire which was developed by Ozer to detect the behavioral changes of panic disorder patients in our country. This questionnaire is based upon clinical experience, patients' statements and "Lifetime Panic Agoraphobia Scale" whose validity and confidentiality for Turkish was established by Tural et al (21). Behavioral changes are divided to three categories: avoidance behavior, prevention behavior and seeking reassurance. This questionnaire consists of 88 multiple choice questions of 4 options for each. Option a is for inexistence of any behavioral change before or after the panic disorder; option b is for any behavioral change that existed before panic disorder and has never changed after; option c is for the behavioral change that has intensified after panic disorder and lastly option d is for any new behavioral change, that has not existed before panic disorder, after panic disorder.
5. Panic Agoraphobia Scale (PAS):
It is applied to patients with panic disorder, with or without agoraphobia. It has five sub-scales:
 - a) Characteristics of the panic attack: 3 questions are rated and 1 question is not rated.
 - b) Agoraphobia/ avoidance: 3 questions.
 - c) Anticipatory anxiety: 2 questions.
 - d) Disability: 3 questions.
 - e) Health concerns: 2 questions.

Every subscale determines its own rating and the sum of all ratings determine the total severity. Tural et al. revised this scale for Turkish (21-23).

6. Beck Anxiety Scale: It is used to rate the anxiety. It totally includes 21 somatic and anxiety complaints (23).
7. Hamilton Depression Rating Scale (HAM-D): It is used to measure the severity of depression and the changes in severity.

V. STATISTICAL ANALYSIS

SPSS for Windows Software was used for statistical analysis. For categorical data chi-square test, for non-categorical data that shows normal distribution two sample student t test and for non-categorical data showing non-normal distribution Mann-Whitney-U test are used. For all tests used, significance was evaluated at $p < 0.05$ level.

VI. RESULTS

It was revealed that 52 patients (52.1%) out of 98 patients with panic disorder also suffer from NPA. Most of the patients with panic disorder were women (NPA group 84.3% and non-NPA group 70.2%), most of the participants were married (NPA group: 86.3% and non-NPA group 63.8%) and the average age in NPA group was found to be 40.6 ± 8.4 , in non-NPA group it was 37.7 ± 9.5 . No statistically significant difference was emerged between the groups in terms of gender ($\chi^2 = 2.79$, $p = 0.09$), age ($t = 1.62$, $p = 0.10$) and marital status ($\chi^2 = 6.76$, $p = 0.08$). However there was statistically significant difference between two groups regarding education level ($\chi^2 = 8.26$, $p = 0.041$) and occupational life ($\chi^2 = 8.41$, $p = 0.004$). 70.6% of NPA group was graduated from elementary school while of non-NPA group, 42.6% was elementary school, 14.9% was junior high school and 31.9% was high school graduates. It was found that the education level is lower and unemployment is higher in NPA group.

While average duration of illness was 104 ± 98.3 months in NPA group, it was 99.4 ± 92.9 months in non-NPA group. This difference was not statistically significant ($Z = -0.06$, $p = 0.94$). If the groups are compared in terms of first attacks, average duration of an attack was 34.9 ± 27.3 minutes in NPA group and 36.2 ± 33.5 minutes in non-NPA group. This difference was not statistically significant either ($z = -0.02$, $p = 0.85$).

Clinical Characteristics Related to Background and Family History: No statistically significant difference was found between the groups in terms of loss of parents ($\chi^2 = 0.00$, $p = 0.99$), divorce of parents ($\chi^2 = 0.37$, $p = 0.53$), school phobia ($\chi^2 = 3.60$, $p = 0.05$), separation anxiety ($\chi^2 = 0.50$, $p = 0.47$), intention to suicide ($\chi^2 = 1.13$, $p = 0.28$) and stress factor within last year ($\chi^2 = 0.07$, $p = 0.77$). However, compared with non-NPA group, NPA group reported to have more stress factor within last year ($\chi^2 = 3.93$, $p = 0.04$).

Alcohol and Psychoactive Substance Use: No significant difference was found between NPA and non-NPA group in terms of alcohol use ($\chi^2 = 0.89$, $p = 0.34$), psychoactive substance use ($\chi^2 = 0.93$, $p = 0.33$), panic disorder in family history ($\chi^2 = 0.10$, $p = 0.74$) and general medical condition ($\chi^2 = 0.02$, $p = 0.86$). However, there was statistically significant difference considering other psychiatric diseases in family history ($\chi^2 = 5.20$, $p = 0.02$).

Sleep Disorders: Significant difference was revealed between NPA and non-NPA groups regarding difficulty falling in sleep ($\chi^2 = 39.5$, $p < 0.001$), difficulty in maintaining sleep ($\chi^2 = 56.1$, $p < 0.001$) and morning fatigue ($\chi^2 = 56.1$, $p < 0.001$). Compared with non-NPA group, NPA group experienced more difficulty in falling and maintaining sleep, more fatigue in the morning ($p < 0.001$) and also more avoidance in sleeping ($\chi^2 = 33.8$, $p < 0.001$) and living alone ($\chi^2 = 39.9$, $p < 0.001$).

The hours of attacks in NPA group were found to be mostly at 3.00 A.M. (28%), more common at 02.00 A.M. (10%) and at least 04.00 A.M. (5%).

The Characteristics of First Panic Attack: There was no statistically significant difference between the NPA and non-NPA groups considering the place of first panic attack ($\chi^2 = 8.8$, $p = 0.11$), the activity during the first panic attack ($\chi^2 = 11.9$, $p = 0.06$) and the reaction towards the first panic attack ($\chi^2 = 2.2$, $p = 0.82$). It was found that both groups have experienced their first panic attacks at home (NPA: 68.6%, non-NPA: 44.7%), at rest (NPA: 45.1%, non-NPA: 55.3%) and have administered to emergency departments (NPA: 56.9%, non-NPA: 57.4%).

Panic Agoraphobia Scale (PAS) and Hamilton Depression Rating Scale (HAM-D): There was a significant difference between NPA and non-NPA groups in terms of PAS ($t = 3.2$, $p < 0.001$) and HAM-D ($t = 4.3$, $p < 0.01$) scores. NPA group had higher scores in both of the scales.

The Relationship between the Anxiety Symptoms and Beck Anxiety Scale: Compared to non-NPA group, in NPA group numbness ($t = 2.17$, $p = 0.03$), feeling that bad things will happen ($t = 2.6$, $p = 0.01$), palpitation ($t = 3.2$, $p = 0.002$), loss of balance ($t = 2.1$, $p = 0.04$), trembling ($t = 2.05$, $p = 0.04$), fear of death ($t = 2.3$, $p = 0.02$), fright ($t = 3.07$, $p < 0.001$), sensations of choking or smothering ($t = 3.3$, $p < 0.001$) were more frequent while hot flushes, weakness in legs, nervousness, losing control, shortness of breath, dizziness, facial flush and sweating were found to have no statistically significant difference (Table 1).

Behaviors of Avoidance-Prevention: According to the responses to 32 questions in behavior of prevention part of Panic Disorder Behavioral Changes Form, NPA patients display more behaviors of avoidance-prevention ($p < 0.05$) such as inability to stay alone, need of an accompanier most of the time, always carrying some pills (in their bags, pockets or cars) when outside, carrying their home addresses or phone numbers or addresses of their spouses, needing someone nearby during sleep, paying attention to sit close to the exit in places like movie theaters (Table 2).

Table 1 : Anxiety Symptoms - Scores of Beck Anxiety Scale

	NPA	n	Average	S.D.	t	p
Beck Anxiety Total Score	NPA +	51	34.75	2.44	0.43	0.67
	NPA -	47	31.21	5.47		
Numbness	NPA +	51	1.53	1.16	2.17	0.03
	NPA -	47	1.04	1.06		
Hot Flushes	NPA +	51	1.71	1.24	1.59	0.12
	NPA -	47	1.32	1.16		
Weakness in legs	NPA +	51	1.73	1.15	1.70	0.09
	NPA -	47	1.32	1.22		
Inability to relax	NPA +	51	1.57	1.27	1.10	0.27
	NPA -	47	1.30	1.16		
Fear of "bad things will happen"	NPA +	51	1.82	1.18	2.64	<0.01
	NPA -	47	1.17	1.27		
Dizziness	NPA +	51	1.61	1.22	1.96	0.05
	NPA -	47	1.15	1.05		
Palpitations	NPA +	51	2.33	1.05	3.25	<0.01
	NPA -	47	1.62	1.13		
Sensations of loosing balance	NPA +	51	1.47	1.36	2.10	0.04
	NPA -	47	0.94	1.13		
Horror	NPA +	51	1.49	1.27	1.24	0.22
	NPA -	47	1.17	1.27		
Nervousness	NPA +	51	1.63	1.25	1.01	0.31
	NPA -	47	1.38	1.13		
Sensations of smothering	NPA +	51	2.10	1.22	3.32	<0.01
	NPA -	47	1.26	1.29		
Tremors at hands	NPA +	51	1.33	1.23	1.33	0.19
	NPA -	47	1.02	1.09		
Shaking	NPA +	51	1.57	3.13	2.05	0.04
	NPA -	47	0.60	0.95		
Loosing control	NPA +	51	1.10	1.17	0.99	0.32
	NPA -	47	0.87	1.08		
Shortness of breath	NPA +	51	1.98	1.29	1.34	0.18
	NPA -	47	1.55	1.84		
Fear of death	NPA +	51	2.59	2.89	2.33	0.02
	NPA -	47	1.51	1.36		
Fright	NPA +	51	2.18	1.14	3.07	<0.01
	NPA -	47	1.45	1.21		
Gastric discomfort	NPA +	51	1.43	1.31	1.79	0.08
	NPA -	47	0.98	1.19		
Blackout	NPA +	51	0.49	0.93	1.11	0.27
	NPA -	47	0.30	0.78		
Facial flushes	NPA +	51	0.78	1.06	1.04	0.30
	NPA -	47	0.57	0.93		
Sweating	NPA +	51	1.51	1.28	0.43	0.67
	NPA -	47	1.40	1.16		

t: Student t test, NPA: Nocturnal Panic Attack, S.D.: Standart deviation

Table 2 : Behaviors of Avoidance-Prevention

		NPA		Non-NPA-2		DF	p
		n	%n	%			
Worrying for having a serious somatic disease	a	14	27.5	16	34.0	4.99	3 0.17
	b	1	2.0	0	0		
	c	4	7.8	0	0		
	d	32	62.7	31	66.0		
Inability to stay alone and need of an Accompanier most of the time	a	15	29.4	28	59.6	10.04	3 0.02
	b	2	3.9	1	2.1		
	c	2	3.9	0	0		
	d	32	62.7	18	38.3		
Always carrying some pills (in your car, Wallet or pocket) when you are out	a	18	35.3	31	66.0	9.73	3 0.02
	b	2	3.9	2	4.3		
	c	2	3.9	1	2.1		
	d	29	56.9	13	27.7		
Carrying some stuff in the amounts of Your lucky number	a	41	80.4	41	37.2	2.76	3 0.43
	b	0	0	1	2.1		
	c	1	2.0	1	2.1		
	d	9	17.6	4	8.5		
Carrying home address or phone Number of your spouse	a	29	56.9	33	70.2	9.37	3 0.03
	b	1	2.0	5	10.6		
	c	1	2.0	2	4.3		
	d	20	39.2	7	14.9		
Leaving bedroom lights on when you Are sleeping	a	28	54.9	26	55.3	1.67	3 0.64
	b	3	5.9	5	10.6		
	c	1	2.0	0	0		
	d	19	37.3	16	34.0		
Leaving door of the bedroom open When you are sleeping	a	23	45.1	23	48.9	2.94	3 0.40
	b	6	11.8	2	4.3		
	c	1	2.0	3	6.4		
	d	21	41.2	19	40.4		
Need of someone nearby when you Are sleeping	a	13	25.5	28	59.6	12.21	3 <0.01
	b	1	2.0	0	0		
	c	3	5.9	2	4.3		
	d	34	66.7	17	36.2		
Paying attention to choose a seat close To the exit in places like movie theaters	a	24	47.1	34	72.3	6.47	2 0.04
	b	0	0	0	0		
	c	2	3.9	1	2.1		
	d	25	49.0	12	25.5		
Always eating something when going out	a	37	72.5	39	83.0	2.21	3 0.53
	b	1	2.0	1	2.1		
	c	1	2.0	0	0		
	d	12	23.5	7	14.9		
Avoidance in wearing valuable jewelry Due to worry about fainting or loosing Consciousness and be robbed afterwards	a	41	80.4	38	80.9	2.49	3 0.48
	b	0	0	1	2.1		
	c	0	0	1	2.1		
	d	10	19.6	7	14.9		

2: Ki square test, NPA: Nocturnal Panic Attack, D.F.: Degree of Freedom

Seeking Reassurance: The patients were assessed according to the responses to 18 questions in seeking reassurance part of Panic Disorder Behavioral Changes Form. NPA patients needed more reassurance ($x^2=9.9$, $p=0.02$) from their friends and families for "nothing bad will happen to them" and more frequently they try to find out a doctor, hospital or a pharmacy nearby when they are out ($x^2=9.7$, $p=0.02$).

VII. DISCUSSION

Nocturnal panic attack is a very common clinical situation among patients with panic disorder nevertheless it is not well appreciated. Some studies report that nocturnal panic attacks indicate a more severe prognosis. It is considered that nocturnal panic attack is a separate syndrome or disorder which has unique etiological, psychopathological and biological pathways (24). Norton et al. (3) observed no difference in terms of age and age of onset when they compared the patients with and without nocturnal panic attacks. These findings are parallel to the outcomes of our study.

When gender is taken into consideration, panic disorder is much more frequent in women than men (2). In our study, the number of women patients dominated both NPA (84.3%) and non-NPA (70.2%) groups. The ratio of female and male patients in our study is consistent with the same ratio (62%/38%) in the study of Briggs et al (25). Out of their study of 1168 multinational patients, 62% were women and 38% were men (25). In our study, level of education was significantly different across the groups. The level of education of patients with NPA was found to be lower. In two studies, conducted in 2007 and 2008, no difference emerged in terms of the level of education (11,13).

There were more unemployed patients in NPA group. Besides, most of the patients included in our study were housewives of low socioeconomic class. This may be caused by the fact that patients who administer to our hospital are mostly from low socioeconomic class. It was declared that low socioeconomic level causes a tendency to panic disorder and patients from low socioeconomic class were exposed to more traumatic life events that were supposed to have an important role in the etiology of panic disorder (26). The sociodemographic data in our study supports the hypothesis of that panic disorder is more common among people from low socioeconomic class. However more extensive research is needed to prove this.

The data about the prevalence of NPA from other studies shows a wide range from 18% to 69% (5,27-30). In our study, we found a prevalence of 47.9% which is consistent with a wide range found in other studies.

On the other hand, it was asserted that separation anxiety in childhood, experienced loss and

separations might have contributed to the etiology. In their studies Tweed et al. (31) showed that the risk of panic disorder was increased in people who have lost their mothers or separated from their families below the age of 10. Different researchers reported that separation from mother or father due to death or other reasons was significantly associated with bad prognosis (32). However in our study, no difference emerged across the groups in terms of loss of parents, divorce of parents, school phobia, separation anxiety and suicide attempt. Also some studies revealed that patients with nocturnal panic attack history have anxiety difficulties in their childhood and were less healthy compared to patients with panic attack of daytime only (33). However, contrary results in our study may be due to the acquirement of childhood experiences via self-report and to the difficulties in recall. Also patients may not have shared childhood difficulties since researchers were not patients' regular physicians. In order to get more precise results, follow-up studies should be done.

It was suggested that panic disorder usually occurs after a loss and a trauma and these life events may trigger the onset of disorder (34). Moreover, 64% of patients with panic disorder have experienced unfavorable life events in preceding year of onset of the disorder while in control group this ratio was 35%. It was reported that people from low socioeconomic class were exposed to more severe stress in longer durations (35,36). In our study we found no significant difference between groups in terms of stressful life events in the preceding year, which was not consistent with the literature. However, the observation of more frequent stressful life events only within the last month supports the literature.

In NPA group it was observed that the attacks occurred mostly at 03:00 AM (28%), less frequently at 02:00 AM (10%) and 04:00 AM (5%). Therefore, one can say that nocturnal panic attack is more frequent in the first hours of night. As a matter of fact, this result of our study is parallel to the reports of 18% of panic attacks occurring during sleep between 01:30-03:00 AM in literature (37). In their studies, Craske et al. (38) showed that panic disorder patients with regular nocturnal panic attacks represent the severe side of the scale and sleep disturbances are at higher rates compared to patients not having nocturnal panic attacks. Similarly, in this study it was observed that compared to non-NPA group, NPA group had more problems in initiating and maintaining sleep and more complaints of morning fatigue. Also it was found that NPA group more frequently avoided going to bed and sleeping alone. The decrease in sleep quality may cause negative effects on the clinical presentation (38-40). It was asserted that just similar to the patient with daytime panic attack who develop agoraphobia, patients with NPA might have developed secondary early anxiety and avoidance (41).

Also it was suggested that once the patient had experienced NPA, s/he might develop conditioned fear to sleep and this might cause worse daytime and nocturnal panic attacks which intensifies behaviors of fear and avoidance (41). Besides, low quality in sleep, shorter sleep duration in total, lack of sleep in middle and late phases and poor quality in subjective sleep and waking were reported in NPA patients (42). In one of the studies conducted in our country, it was declared that recurrent NPA caused lack of sleep in patients with PD (4). These findings are consistent with our study. Same researchers found that compared with non-NPA patients, PD patients with NPA had higher frequency of major depression and they suggested that NPA might have contributed to the risk of suicidality by altering severity of the disease (4). This situation is consistent with the findings of other studies showing that patients with NPA have worse prognosis compared with patients without NPA (4,5,13,14). In our study, compared with non-NPA patients, patients with NPA have higher scores on PAS and HAM-D. In literature, there are many studies that have similar results (4,5,13,14). Although no significant difference emerged in terms of total scores on Beck Anxiety Score, numbness, feelings of bad thing will happen, palpitation, loss of balance, trembling, fear of death, fright and sensations of choking or smothering were significantly different as anxiety symptoms are separately assessed. These symptoms are more severe in NPA group. Same findings were reported in the studies of Craske and Barlow (15). Craske and Barlow found out that patients with NPA history had declared two folds increase in diurnal attacks as compared with non-NPA patients and attacks were worse in terms of chest pain or tightness and nausea. Moreover, the greater part of NPA patients reported sensations of smothering and choking. It was observed that the greater part of NPA group had palpitations, irregular pulse, loss of pulse, chest tightness and flatus. Norton et al. (3) too found that NPA patients had more symptoms than non-NPA patients and NPA patients had more complaints of chest pain during daytime attacks as compared with non-NPA patients.

Other important findings in our study are discussed in the subtitles of avoidance, seeking reassurance and prevention which are under behavioral changes. Patients with nocturnal panic attacks more frequently report that when they are out they always carry some pills, telephone number or address of their homes or spouses in their bags, pockets, wallets or cars.

In literature it was reported that PD cases had complaints of carrying "objects of security" in order to deal with anticipatory anxiety (8). These "objects" which are never used and which make patients feel more secure may have symbolic meanings. The similarity between this situation and little children who always

carry their favorite toys or blankets and feel insecure when they are lost is remarkable (8).

In our research, as compared to non-NPA patients, NPA patients more frequently reported that they needed their friends and families to reassure them that "nothing bad will happen to them" and they tried hard to find a doctor, hospital or a pharmacy nearby when they were out. This finding is consistent with the reports in literature that patients with panic disorder may exaggerate their symptoms, display tricky behaviors and pretend in order to have reassurance they need (30). It may be observed that these patients seek reassurance by frequently administering to emergency departments, running medical tests and establishing "friendship relationships" with physicians (30, 43). Many patients with panic disorder ask for help from their friends, families, neighbors and physicians in order to deal with the feelings of insecurity. In NPA group the higher frequency of these findings, compared with non-NPA group, represent more severe disease.

One of the most important limitations in this study was assessing NPA by self-reports of patients and not assessing the sleep by polysomnography. The other weaknesses might be exaggeration and difficulties in recalling the symptoms, superficial discussion about separation anxiety, life events and triggering stressors which are all due to retrospective questioning.

VIII. CONCLUSION

The group of patients with nocturnal panic attack (NPA), compared with the group of without nocturnal panic attacks, experience more difficulties in falling asleep and maintaining sleep, more fatigue in the mornings and decreased quality of sleep which cause negative effects on clinical presentations. Therefore, in clinical practice, considering these factors in the treatments of NPA patients is crucial for prognosis. Besides, higher frequency of prevention behavior in NPA patients and more severe symptoms, as compared with patients with daytime panic attacks only, suggest that this phenomenon might be a separate subgroup of panic disorder. A follow-up study focused on this subject will help to clarify whether NPA patients are a subgroup of panic disorder.

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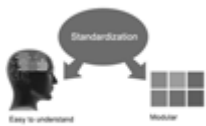
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- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
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- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
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- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
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References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring



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