# Migraine Headache and Obsessive-Compulsive Symptoms in a Student Sample

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**ABSTRACT:**

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**Objective:** Converging lines of evidence suggest that serotonergic dysfunction underlies migraine headache. Obsessive-compulsive disorder (OCD) is also associated with serotonergic dysfunction. If migraine headache and OCD are serotonergic disorders, then it is reasonable to assume that migraine headache sufferers will demonstrate a higher incidence of OCD symptoms relative to non-migraine controls.

**Method:** To test this hypothesis, we administered measures of OCD symptoms and general psychopathology to university students who met criteria for migraine headache and non-migraine student controls.

**Results:** We found that migraine headache was associated with elevated scores on measures of obsessive-compulsive (OC) and depressive symptoms. Migraine headache was not associated with social and generalized anxiety, or harm avoidance. Moreover, students with migraine did not demonstrate significantly higher rates of Axis I or Axis II disorders.

**Conclusions:** Serotonergic dysfunction may underlie the observed association between migraine headache, depressive symptoms, and obsessive-compulsive phenomena.

**Key words:** migraine headache, obsessive-compulsive disorder, serotonin, depressive symptoms.

**Klinik Psikofarmakoloji Bülteni 2005;15:174-181**

**ÖZET:**

Bir öğrenci örnekleminde migren başağrısı ve obsessif-kompulsif semptomlar

**Amaç:** Literatürdeki pek çok bulgu, serotonerjik işlev bozukluğunun migrene bağlı başağrısının altında yatan neden olduğunu ileri sürmektedir. Ayrıca obsesif-kompulsif bozukluk da (OKB), serotonerjik işlev bozukluğu ile ilişkilidir. Eğer migren başağrısı ve OKB serotonerjik bozuklukla ilişkili ise, migrene bağlı başağrısı çekenlerin migreni olmayan kontrollere göre, daha yüksek bir sıklıkta OKB semptomları gösterecekleri varsayılabilir.

**Yöntem:** Bu hipotezi test etmek için, migren başağrısı kriterlerini karşılayan üniversite öğrencileri ile migreni olmayan kontrol öğrencilerine, genel psikopatoloji ve OKB semptomlarının ölçüldüğü testler uygulanmıştır.

**Bulgular:** Migren başağrısının, obsesif-kompulsif ve depresif semptomlardaki artışla ilişkili olduğu bulunmuştur. Migren başağrısı, sosyal ve yaygın anksiyete veya zarardan kaçınma ile bağlantılı çıkmamıştır. Ayrıca, migreni olan öğrencilerin Eksen-I veya Eksen-II'de tanı alma oranlarının anlamlı olarak yüksek olmadığı görülmüştür.

**Sonuç:** Serotonerjik aktivitedeki değişiklikler, migren başağrısı, depresif semptomlar ve obsesif-kompulsif drurumlar arasında gözlenen ilişkiyi açıklayan neden olabilir.

**Anahtar sözcükler:** Migren başağrısı, obsesif kompulsif bozukluk, serotonin, depresif semptomlar

**Klinik Psikofarmakoloji Bülteni 2005;15:174-181**

## INTRODUCTION

Several lines of investigation suggest that obsessive-compulsive disorder (OCD) may be associated with serotonergic dysfunction. Researchers have also suggested that serotonin plays an important role in the migraine headache process. However, there are few published reports examining the relation between clinical OCD and migraine headache. Researchers have suggested that the migraine headache syndrome and OCD are "affective spectrum disorders" (1). Indeed, Hudson and colleagues (1) claimed that migraine headache is associated with other psychiatric and medical conditions including major depressive disorder, attention-deficit/hyperactivity disorder, bulimia, cataplexy, dysthymic disorder, generalized anxiety disorder, irritable bowel syndrome, premenstrual dysphoric disorder, social phobia, fibromyalgia, and OCD. Researchers have found that there are increased odds for individuals with migraine to also have OCD. Breslau (2) found that the adjusted (for gender)

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5 Eylül 2005 / September 5, 2005

odds ratio for individuals with migraine without aura and OCD was 4.8. Aura symptoms in addition to migraine increased the adjusted odds ratio to 5.0. There was an increased incidence of co-morbidity with anxiety and mood disorders (including bipolar disorder, panic disorder, and generalized anxiety disorder) in persons with migraine, with and without aura symptoms. Other researchers have found similar results (AOR = 1.3) (3). However, other research utilizing different methodology has found no relationship between OCD symptoms and migraine headache (4). Migraine headache syndrome is also associated with major depressive disorder (5-7). Moreover, a significant number of patients with migraine also meet criteria for panic disorder (7). Radat (8) observed that migraine patients frequently present with co-morbid mood and anxiety disorders. In addition, migraine headache patients presenting with a co-morbid anxiety or depressive disorder are less likely to respond favorably to anti-migraine therapy.

Converging lines of research suggest that serotonergic dysfunction underlies migraine headache. Obsessive-compulsive disorder (OCD) is also associated with serotonergic dysfunction. If migraine headache and OCD are serotonergic disorders, then it is reasonable to assume that migraine headache sufferers will demonstrate a higher incidence of OCD symptoms relative to non-migraine controls. Therefore, we predicted that individuals meeting criteria for migraine headache would obtain significantly higher scores on measures of OCD symptoms. To determine whether migraine symptoms are selectively associated with OCD symptoms or are associated with a broad range of anxiety and mood disorders, we administered measures of OCD symptoms, social and generalized anxiety, harm avoidance, depressive symptoms, and general psychopathology (Axis I and II disorders) to university students who met criteria for migraine headache and non-migraine student controls.

## METHODS

Participants were 89 undergraduate students recruited from introductory psychology courses at Boston University. The sample comprised 56 female and 33 male students, a proportion that reflects the gender ratio in the College of Arts and Sciences at Boston University. Written informed consent was obtained from all subjects. Participants completed the following questionnaire:

*Have you experienced headache episodes that last at least 4 hours?*

*If yes: Are these headache episodes associated with three or more of the following characteristics?*

- *Pulsating pain;*
- *Moderate or severe pain intensity;*
- *Aggravation by walking up stairs or similar routine physical activity;*
- *Nausea or vomiting;*
- *Excessive sensitivity to light or sound;*
- *Pain usually starts on one side of your head.*

Eleven students (10 female students and 1 male student) met criteria for migraine headache. Their ages ranged from 17 to 21 years (mean±SD= 19.2±1.4) and their mean educational level was 14.1 years (SD= 1.4). The non-migraine comparison group comprised 46 female and 32 male students. Their ages ranged from 17 to 21 years (mean±SD= 18.5±0.9) and their mean educational level was 13.4 years (SD= 0.8). We administered a battery of personality questionnaires and clinical scales including the Mini International Neuropsychiatric Interview (MINI) (9), Personality Diagnostic Questionnaire-4 (PDQ-4) (10), Beck Depression Inventory (BDI) (11), Liebowitz Social Anxiety Scale (12), Tridimensional Personality Questionnaire (TPQ) (13), and the Obsessive-Compulsive Inventory (OCI) (14).

### Clinical/Personality Measures

***Obsessive–Compulsive Inventory (14).*** The OCI is a self-report measure of obsessive-compulsive symptoms. This psychometrically sound instrument yields a total score and seven subscale scores reflecting the following OC-symptom subtypes: compulsive checking; obsessional ideation; compulsive doubting; washing rituals; compulsive hoarding; ordering; and mental neurtralizing.

***Beck Depression Inventory (11).*** The BDI is a psychometrically sound, self-report instrument and

was employed to measure the strength of depressive symptoms.

***Liebowitz Social Anxiety Scale (12).*** The Liebowitz scale is a 24-item questionnaire that yields two subscale scores reflecting symptom severity and avoidance behavior. Participants are instructed to indicate the degree of anxiety they experience during specific social situations. Participants also indicate how frequently they avoid these situations.

***Mini International Neuropsychiatric Interview (MINI) (9).*** The MINI is a structured psychiatric interview reflecting DSM-IV and ICD-10 diagnostic criteria. Diagnostic algorithms are provided. The second author administered the following diagnostic modules:

- Major Depressive Episode (current and lifetime)
- Dysthymia (current)
- Panic Disorder (past month)
- Social Anxiety Disorder (past month)
- Alcohol Abuse/Dependence (past 12 months)
- Substance (non-alcohol) Abuse/Dependence (past 12 months)
- Generalized Anxiety Disorder (past 6 months)

***Personality Diagnostic Questionnaire (10).*** The Personality Diagnostic Questionnaire (PDQ-4) is a forced-choice, self-report instrument. The PDQ-4 consists of ten subscales based on DSM-IV criteria for Axis-II disorders (10) (see Table 2).

***Tridimensional Personality Questionnaire (TPQ) (13).*** The TPQ is a self-report measure of three personality dimensions based on Cloninger's tridimensional model of personality including: 1) harm avoidance; 2) novelty seeking; and 3) reward dependence.

Independent-samples t-tests were performed to assess between-group differences. Fisher's Exact Test was used to assess between-group differences on categorical variables (i.e., the presence or absence of diagnoses based on the MINI). Given the exploratory nature of the study, we did not employ a Bonferroni-corrected significance level. Rather, a p-value of .05 was used.

## RESULTS

As shown in Table 1, migraine headache sufferers

**Table 1: Clinical Measures:  Mean (SD)**

|  | Migraine (n=11) x±SD | Control (n=78) x±SD | t | p |
|---|---|---|---|---|
| **Obsessive-Compulsive Inventory (OCI)-Frequency** |  |  |  |  |
| Checking | 12.5  (5.8) | 7.8  (5.4) | 2.66 | .009 |
| Doubting | 5.0  (2.3) | 2.9  (2.4) | 2.75 | .007 |
| Hoarding | 5.7  (3.3) | 4.5  (2.8) | 1.24 | .21 |
| Neutralizing | 8.8  (5.1) | 4.3  (3.2) | 3.87 | .0001 |
| Obsess. Ideation | 9.2  (5.3) | 5.8  (4.8) | 2.16 | .04 |
| Ordering | 9.2  (5.2) | 6.4  (4.3) | 1.99 | .05 |
| Washing | 10.2  (6.4) | 8.2  (5.2) | 1.13 | .26 |
| OCI-Total Frequency | 61.0  (26.3) | 40.2  (22.0) | 2.85 | .005 |
| **Obsessive-Compulsive Inventory (OCI)-Distress** |  |  |  |  |
| Checking | 9.8  (4.6) | 5.2  (4.8) | 2.89 | .005 |
| Doubting | 4.1  (2.0) | 2.5  (2.8) | 1.85 | .07 |
| Hoarding | 3.9  (2.8) | 2.4  (2.3) | 1.86 | .07 |
| Neutralizing | 5.7  (3.7) | 2.9  (3.1) | 2.72 | .008 |
| Obsess. Ideation | 9.0  (5.7) | 5.5  (5.3) | 2.01 | .05 |
| Ordering | 7.0  (5.0) | 4.6  (4.1) | 1.69 | .09 |
| Washing | 8.1  (4.4) | 6.2  (4.9) | 1.19 | .23 |
| OCI-Total Distress | 47.7  (20.8) | 29.5  (22.8) | 2.5 | .015 |
| **OCI-Total Score** | 108.7  (45.2) | 69.7  (43.4) | 2.76 | .007 |
| **Beck Depression Inventory** | 13.5  (10.6) | 6.6  (6.9) | 2.88 | .005 |
| **Liebowitz Social Anxiety Scale** |  |  |  |  |
| Anxiety | 22.0  (9.2) | 17.9  (11.1) | 1.16 | .24 |
| Avoidance | 19.8  (10.5) | 15.9  (9.9) | 1.2 | .23 |
| Total | 41.9  (18.6) | 33.8  (20.1) | 1.24 | .21 |

Note.  One control participant did not complete the OCI and the Liebowitz Social Anxiety Scale, x±SD= mean±standart deviation

**Table 2: Personality Measures: Mean (SD)**

| | Migraine (n=11) x±SD | Control (n=78) x±SD | t | p |
|---|---|---|---|---|
| **Personality Diagnostic Questionnaire (PDQ-4)** | | | | |
| Paranoid Personality Disorder | 4.1 (1.6) | 2.7 (1.7) | 2.55 | .012 |
| Schizoid Personality Disorder | 1.1 (1.1) | 1.1 (1.3) | 0.06 | .94 |
| Schizotypal Personality Disorder | 3.1 (1.1) | 2.2 (1.7) | 1.63 | .10 |
| Histrionic Personality Disorder | 2.5 (1.0) | 2.3 (1.7) | 0.46 | .64 |
| Narcissistic Personality Disorder | 3.1 (1.0) | 3.2 (1.8) | -0.15 | .88 |
| Borderline Personality Disorder | 2.0 (1.1) | 1.8 (1.8) | 0.22 | .82 |
| Antisocial Personality Disorder | 1.0 (0.8) | 1.2 (1.2) | -0.72 | .46 |
| Avoidant Personality Disorder | 2.4 (2.1) | 2.4 (2.0) | 0.06 | .94 |
| Dependent Personality Disorder | 1.8 (1.9) | 1.3 (1.5) | 0.83 | .40 |
| Obsessive-Compulsive Personality Disorder | 4.3 (1.2) | 3.8 (1.7) | 1.01 | .31 |
| **Tridimensional Personality Questionnaire** | | | | |
| Harm Avoidance | 98.0 (19.5) | 92.1 (21.6) | 0.84 | .40 |
| Reward Dependence | 106.1 (11.7) | 103.8 (15.5) | 0.46 | .64 |
| Novelty Seeking | 99.2 (16.0) | 97.6 (15.7) | 0.31 | .75 |

obtained significantly higher scores, relative to non-migraine controls, on the OCI subscales measuring the frequency of compulsive checking (t(86)= 2.66, p< .009), doubting (t(86)= 2.75, p<.007), obsessional ideation (t(86)= 2.16, p< .04), ordering (t(86)= 1.99, p< .05), and mental neutralizing (t(86)= 3.87, p< .0001), and obtained significantly higher total OCI-frequency scores (t(86)= 2.85, p< .005). Students meeting criteria for migraine obtained significantly higher scores on the OCI subscales assessing the degree of distress associated with compulsive checking (t(86)= 2.89, p<.005), mental neutralizing (t(86)= 2.72, p< .008), and obsessional ideation (t(86)= 2.01, p< .05), and obtained higher total OCI-distress scores (t(86)= 2.50, p< .015) relative to non-migraine controls. Group differences on the compulsive doubting (t(86)= 1.85, p< .07), and hoarding (t(86)= 1.86, p< .07) subscales approached significance. Students with migraine obtained higher scores on the washing subscales; however, group differences did not approach significance (ps> .23). Groups differed significantly on the OCI (total score), with migraine headache participants obtaining a mean score of 108.7 (SD = 45.2) and controls obtaining a mean score of 69.7 (SD = 43.4), with t(86) = 2.76, p < .007. Note that one control participant did not complete the OCI and the Liebowitz scale. Students meeting criteria for migraine also obtained significantly higher BDI scores (t(87)= 2.88, p< .005) relative to non-migraine controls.

Group differences on the Liebowitz Social Anxiety Scales (ps> .21) and TPQ subscales (ps> .40) were not significant. As shown in Table 2, groups did not differ significantly on 9 of 10 PDQ-4 subscales (ps> .10). However, participants with migraine obtained higher scores on the Paranoid Personality Disorder subscale (t(87)= 2.55, p< .012). Fisher's Exact Test was used assess group differences on the Mini International Neuropsychiatric Interview (MINI). Analysis revealed that the migraine group did not demonstrate significantly higher rates of Axis I disorders including major depressive episode, dysthymia, social anxiety disorder, alcohol abuse/dependence, substance (non-alcohol) abuse/dependence, and generalized anxiety disorder (Fisher's Exact Test, all ps> .19). However, group differences on the panic disorder module approached significance (p= .053, Fisher's Exact Test).

A disproportionate number of female students met criteria for migraine headache. Is it possible that group differences (migraine vs. migraine-free) on the OCI reflect gender differences rather than clinical status per se? (Note that we did not expect to observe gender differences on the OCI.) To address this concern, we compared the OCI profiles of male students to the profiles of female participants (total sample). We performed independent-samples t-tests with gender as the grouping variable. Male and female groups did not significantly differ on OCI subscales assessing the frequency of compulsive checking (p> .85), doubting (p> .41), hoarding (p> .09), obsessional ideation (p> .67), ordering (p> .16), and washing (p> .98). However,

female participants scored significantly higher on the mental neutralizing subscale (t(86)= 2.63, p< .01). To further address this issue, we compared the OCI profiles of female students meeting criteria for migraine headache (n = 10) to the profiles of non-migraine female controls (n = 45). Migraine headache sufferers obtained significantly higher scores on the OCI subscales measuring the frequency of compulsive checking (t(53)= 3.18, p< .002), doubting (t(53)= 2.55, p< .013), mental neutralizing (t(53)= 4.0, p< .001), obsessional ideation (t(53)= 2.31, p< .025), ordering (t(53)= 2.16, p< .035), and total OCI score (t(53)= 3.01, p<.004). Group differences on the hoarding and washing subscales did not achieve statistical significance (ps> .09). Increased scores among migraine sufferers on measures of OC symptoms do not reflect gender differences.

## DISCUSSION

Migraine headache was associated with elevated scores on a self-report measure of OC symptoms. Students with migraine headache did not obtain significantly higher scores on measures of social anxiety, harm avoidance, and general psychopathology suggesting a specific relation between OCD symptoms and migraine headache. Since we carried out a substantial number of comparisons and the target group was relatively small, we must be cautious and not over-interpret findings. Migraine sufferers also obtained higher scores on the BDI. This finding is consistent with prior reports demonstrating an association between depressive disorders and migraine headache (e.g., 5–7,15,16). Depressive symptoms may also be associated with serotonergic dysfunction. The migraine group did not demonstrate significantly higher rates of Axis I disorders including major depression, dysthymia, panic disorder, social anxiety disorder, alcohol abuse/dependence, substance (non-alcohol) abuse/dependence, and generalized anxiety disorder (as determined by performance on the MINI). However, it is important to bear in mind that participants in the present study were relatively young, high-functioning adults (i.e., university students). Therefore, subjects may still go on to develop major psychopathology. Unexpectedly,

migraine sufferers obtained higher scores on the Paranoid Personality Disorder subscale from the PDQ-4. The meaning of this finding is uncertain.

Serotonergic dysfunction may underlie the observed association between obsessive-compulsive symptoms and migraine headache. There are growing, but separate, bodies of research examining the role of serotonergic dysfunction in migraine headache and OCD. These are discussed in the following subsections.

### Serotonin and the vasoconstriction/vasodilation model of migraine

Early investigators (e.g., Wolff) suggested that the vascular system played a crucial role in the migraine headache syndrome (17). Wolff went on to describe several phases of a migraine attack (18). According to Wolff and colleagues, there is an initial cerebral vasoconstriction phase (17). During this initial phase, blood vessel constriction may be occurring near the retinal or ophthalmic artery or the occipital lobes generating the visual distortions associated with classic migraine headache. Early investigators claimed that prodromal migraine symptoms (e.g., visual disturbances and the migraine aura) reflect the constriction of intracranial arteries (19). This is followed by extracranial or intracranial vasodilation as well as an increase in the concentration of substances that lower the pain threshold. These events generate the severe head pain associated with the migraine syndrome. Wolff and colleagues measured the extracranial (temporal) arteries of patients with migraine during the acute headache phase and found that they were dilated (17). Early workers concluded that acute head pain is generated by arterial dilation (e.g., distension of the external carotid artery) (19). The vasoconstriction/vasodilation model of migraine is supported by the fact that vasoconstrictors (e.g., sumatriptan) alleviate migraine pain (17), while vasodilators (e.g., nitroglycerin) increase migraine pain. When patients received vasoconstrictors, arterial dilation as well as pain decreased.

Researchers have also suggested that serotonin plays an important role in the migraine headache process (20). Several researchers have concluded that prodromal symptoms are associated with

hyperserotonergia (vasoconstriction phase), while the acute pain phase emerges after a reduction in serotonergic function and "rebound dilation" of cranial arteries. Theisler (21) noted that "(s)erotonergic nerves innervate and control cerebral blood vessels, so that a significant drop in serotonin would be expected to cause a rebound dilation of the large branches of the extracranial arteries..." (pp. 31-32). Indeed, serotonergic neurons in raphe nuclei project to cerebral blood vessels (19,22) and agents that deplete serotonin (5-HT) may trigger a migraine episode (19). Researchers have also reported that the administration of 5-HT agonists such as meta-chlorophenylpiperazine (mCPP) may trigger a migraine-like headache (23-25). The administration of agents that deplete serotonin and serotonin agonists may generate migraine-like episodes. Drugs that enhance serotonergic activity may initiate the vasoconstriction phase, while agents that deplete serotonin may trigger the "rebound dilation" of extracranial arteries and the acute pain phase.

The action of anti-migraine medications (e.g., tricyclic antidepressants and serotonin agonists) lends further support to the contention that serotonin plays a crucial role in the migraine headache syndrome (26). There are two dominant classes of medication used to treat migraine headaches: prophylactic and acute (abortive) agents. Many anti-migraine medications, both prophylactic and abortive agents, modify serotonergic activity (19). Prophylactic medications include beta-blockers (such as propranolol), calcium-channel blockers (such as verapamil), tricyclic antidepressants (such as amitriptyline), and antiepileptics (such as gabapentin) (27) and abortive agents include triptans (such as sumatriptan) (28). The action of anti-migraine agents and drugs used in challenge studies (e.g., mCPP) may be best understood in relation to the two-phase model described above (serotonin-mediated vasoconstriction / vasodilation sequence). During the acute headache phase, abortive agents (e.g., sumatriptan) are used to alleviate the severe head pain. Abortive agents such as dihydroergotamine and sumatriptan are serotonin receptor agonists and constrict blood vessels (19,29). Double-blind, placebo-controlled studies have established the anti-migraine efficacy of sumatriptan (a serotonin mimetic) (30,31).

In contrast, prophylactic agents diminish serotonergic activity (e.g., 5-HT receptor antagonists) and a wide range of medications have been used to prevent the onset of migraine episodes including beta-blockers, calcium-channel blockers, tricyclics, and anticonvulsants (19,27). Many of these agents influence other transmitter systems; however, they also influence serotonergic function (19). Effective prophylactic pharmacotherapy may be associated with the inhibition of serotonergic activity. One possibility is that decreased serotonergic activity prevents the initial vasoconstriction phase that underlies the migraine process.

### Serotonin and OCD

Converging lines of evidence (e.g., treatment and challenge studies) suggest that obsessive-compulsive disorder (OCD) may be associated with serotonergic dysfunction. Medications affecting serotonin receptors are primarily used as treatments for OCD; antidepressants that do not influence serotonergic function are ineffective at reducing the symptoms of OCD (32). Moreover, the administration of 5-HT agonists such as mCPP (meta-chlorophenylpiperazine) (a 5-HT receptor agonist) may increase the frequency and intensity of OCD symptoms (33-35). This effect seems counterintuitive when one considers the fact that selective serotonin reuptake inhibitors (SSRIs) are highly efficacious anti-obsessional agents. SSRIs obstruct the reuptake of serotonin, thereby augmenting the amount of 5-HT available and enhancing serotonergic function. An understanding of the short-term and long-term effects of SSRI pharmacotherapy may help us resolve this apparent contradiction. During SSRI pharmacotherapy, many patients with OCD demonstrate a therapeutic lag (i.e., a delayed clinical response). Moreover, patients may initially report an increase in the intensity of OC symptoms; however, extended SSRI pharmacotherapy is associated with symptom reduction. One possibility that researchers are exploring is that extended SSRI treatment is associated with a reduction in serotonergic activity and decreased activity in the orbitofrontal-striatal system among OCD patients demonstrating a favorable clinical outcome. However,

other researchers maintain that SSRI therapy actually enhances serotonergic function after an extended period of treatment (36). The administration of mCPP (5-HT receptor agonist) may increase the frequency and intensity of OCD symptoms. As noted previously, researchers have reported that mCPP also triggers migraine episodes (23-25). It is also interesting to note that investigators have suggested that hyperserotonergia may be associated with harm avoidance and punishment sensitivity. In the present study, migraine sufferers did not obtain significantly higher scores on measures of harm avoidance and social anxiety; however, group differences were in the expected direction.

Our findings support the contention that migraine headache phenomena are associated with obsessive-compulsive and depressive symptoms. Clinicians may consider screening patients with migraine for OC and depressive symptoms, since treatment of co-morbid psychiatric conditions may enhance outcome.

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