

南區頭痛讀書會

*Migraine and Psychiatric
Comorbidity*

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2011-02-19

Migraine and Psychiatric Comorbidity: a review of clinical findings

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J Headache Pain: published online: 06 Jan. 2011

DOI 10.1007/s10194-010-0282-4

Sectional Topics in Review

- Introduction
- Migraine Psychiatric Comorbidity
- General Population studies
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- From Children to Grown-up
- Metanalysis of studies investigating the association of migraine and depression
- Mechanisms of migraine psychiatric comorbidity
- Impact of psychiatric comorbidity on migraine
- Conclusions

Introduction -1

- An Common and Complex disorder
- Heterogeneity (genetic determinants): significant association between other neurological diseases (such as epilepsy, CVD, mitochondrial diseases), cardiovascular disorders (arterial hypertension, mitral valve prolapse), and particularly psychiatric illnesses (anxiety, affective and personality disorders)

-Radat F, Swendsen J (2005) Psychiatric comorbidity in migraine: a review. *Cephalalgia* 25:165-178

Introduction -2

- Heterogeneity (clinical research): phenotypical expression of comorbidity may vary over time.
- Presence of hypertension and psychiatric disorders often facilitates changes in the migraine pattern => daily headache (chronic migraine)

-Lipton RB (2009) Tracing transformation: chronic migraine classification, progression, and epidemiology. Neurology 72(5 suppl): S3-S7

Migraine Psychiatric comorbidity

- Relationship between migraine and certain psychological features, such as a tendency toward perfectionism, neuroticism, repressed aggressivity and melancholic mood, reported for more than a century.
- Earlier than 2004, some nosologic entities, such as chronic migraine (frequently comorbid with psychiatric disorders) were not defined by diagnostic criteria.

Migraine Psychiatric comorbidity

- Psychiatric correlates of migraine is critical for several reasons.
- 1. Depressive disorders: leading causes of disability worldwide and WHO estimates MMD: 2nd leading cause of disease burden by the year 2020.
- 2. Migraine: public health problem, enormous impact on both the individual and society; most burdensome of the primary headache disorders.
- 3. The presence of psychiatric conditions: risk factor for transformation migraine into a chronic form

-Lipton RB (2009) Tracing transformation: chronic migraine classification, progression, and epidemiology.

Neurology 72(5 suppl): S3-S7

Migraine Psychiatric comorbidity

- 4.Migraine and comorbid psychiatric disorders: greater health resources users.
- Recognizing this comorbidity: improved patient management, via first-line treatment targeted at both conditions.
- In this review, mainly considered the studies after the publication of the 1st classification of the IHS [1988], in adults and children, focused on the association between migraine and psychiatric disorders

General population studies

- All cross-sectional investigations of psychiatric disorder prevalence in ‘migraine’ compared with ‘non-migraine’: increased risk of anxiety disorders, particularly panic disorder (PD) and phobias.
- One study found an association between migraine and obsessive-compulsive disorder (OCD) as well as generalized anxiety disorder (GAD).

--Breslau N, Davis GC, Andreski P (1991) Migraine, psychiatric disorders and suicide attempts: an epidemiological study of young adults. Psychiatry Res

Depression

- Previous investigations of mood disorders: highly consistent increased prevalence of major depressive disorder (MDD) in patients with migraine.

--Radat F, Swendsen J (2005) Psychiatric comorbidity in migraine: a review.
Cephalgia 25:165–178

- Increased risk of current depression in migraine
- Migraine and depressive disturbances exert a significant but independent impact on assessment of quality of life (QoL)

Elderly Adult

- Over 65 years: increased risk of current depression
- Headache: independently associated with depression in the elderly.
 - Wang SJ, Liu HC, Fuh JL, Liu CY, Wang PN, Lu SR (1999) **Comorbidity of headaches and depression in the elderly.** *Pain* 82(3):239–243
 - Camarda C, Pipia C, Taglialavori A, Di Fiore P (2008) **Comorbidity between depressive symptoms and migraine: preliminary data from the Zabu´t Aging Project.** *Neurol Sci* 29:S149–S151

Migraine with aura

- Association with suicide attempts, even after adjustment of MD;
- Characterized by psychiatric comorbidity more frequently
- Similar findings in adolescents aged 13–15 years.
- A higher frequency of suicidal ideation in younger adolescents with migraine with aura or with high frequency of attacks; independent of depressive symptoms

--Breslau N, Davis GC, Andreski P (1991) Migraine, psychiatric disorders and suicide attempts: an epidemiological study of young adults.

Psychiatry Res 37:11–23

--Breslau N, Schultz LR, Stewart WF, Lipton RB, Lucia VC, Welch KMA (2000) Headache and major depression. Is the association specific to migraine? Neurology 54:308–313

--Wang SJ, Fuh JL, Juang KD, Lu SR (2009) Migraine and suicidal ideation in adolescents aged 13 to 15 years. Neurology 72:1148–1152

Other forms of Affective disorder

- Bipolar disorder (BD): only migraine with aura significantly associated;
--Breslau N, et al(1991) Psychiatry Res 37:11–23
- Later observations not confirm this association; not distinguish between migraine subtypes.
--Swartz KL, et al(2000) Mental disorders and the incidence of migraine headaches in a community sample. Arch Gen Psychiatry 57:945–950
- Significant association between migraine and BD; twice as often as without migraine.
--Jette N, et al(2008) Comorbidity of migraine and psychiatric disorders—a National Population-Based Study. Headache 48:501–516
--Ratcliffe GE, et al(2009) The relationship between migraine and mental disorders in a population-based sample. Gen Hosp Psychiatry 31:14–19

Substance-related disorders

- Alcohol and drug abuse: increased risk in migraine (1991, Breslau N), but subsequent studies could not replicate [1993, Merikangas KR]
(BD and substance abuse highly comorbid?).
- No association between migraine and drug, alcohol or substance abuse/dependence in more recent studies.
 - Jette N, et al(2008). Headache 48:501–516
 - Ratcliffe GE, et al(2009). Gen Hosp Psychiatry 31:14–19

Panic disorder and Phobia

- Risk of onset during the follow-up period: greater with migraine
 - Merikangas KR (1994) Psychopathology and headache syndromes in the community. Headache 34:S17–S26
- Following up to 15 years, the presence of phobia predict the subsequent occurrence of migraine
 - Swartz KL, et al(2000) Mental disorders and the incidence of migraine headaches in a community sample. Arch Gen Psychiatry 57:945–950
- Past-year migraine: Associated with depression, dysthymia, bipolar disorder, panic attacks, panic disorder, agoraphobia and simple phobia.
 - Ratcliffe GE, et al(2009) The relationship between migraine and mental disorders in a population-based sample. Gen Hosp Psychiatry 31:14–19

Migraine Familial liability

- Presence of migraine with and without aura, probable migraine and no migraine ? in a large sample of concordantly depressed sibling pairs.
- Findings: migraine with aura representing the extreme end of a continuum of migraine familial liability ⇔ supported two forms of migraine are different
 - Ball H, et al (2009) Depression, migraine with aura and migraine without aura: their familiarity and interrelatedness. *Cephalgia* 29(8): 848-854
- General relationship between recurrent headache and depression, but also specific association between depression and migraine with aura
 - Samaan Z, et al (2009) Migraine in recurrent depression: case-control study. *Br J Psychiatry* 194(4):350-354

Studies on Clinical samples

- None of the studies comparing migraine and tension-type headache could find significant differences in terms of psychiatric comorbidity (1995-1999)
- Risk of psychiatric disorders was found to be increased in chronic headache, and particularly transformed migraine, as compared to episodic migraine.
 - Mitsikostas DD, Thomas AM (1999) Comorbidity of headache and depressive disorders. *Cephalalgia* 19:211–217
 - Verri AP, et al (1998) Psychiatric comorbidity in chronic daily headache. *Cephalalgia* 18:45–49
 - Radat F et al (1999) Psychiatric comorbidity is related to headache induced by chronic substance use in migraineurs. *Headache* 39:477–480
 - Juang KD, Wang SJ, Fuh JL, Lu SR, Su TP (2000) **Comorbidity of depressive and anxiety disorders in chronic daily headache and its subtypes.** *Headache* 40:818–823

Psychiatric Comorbidity vs. Headache Category

- Anxiety and Depression Comorbidity: more pronounced in chronic headache > 5 years
- All psychiatric disorders except for somatoform disorders: associated with headache => psychiatric comorbidity may be confined and specific to headache category
- Migraine with daily headache with chronic substance abuse: MD twice as frequent in analgesic abuse.
- Increased risk of MD, panic disorder and social phobia in transformed migraine and chronic substance use, even after adjustment for age and gender.

--Mitsikostas DD (1999). Cephalalgia 19:211–217

--Verri AP, et al (1998). Cephalalgia 18:45–49

--Radat F et al (1999). Headache 39:477–480

Headache category Comparison-1

- Compared transformed migraine with chronic tension-type headache: higher frequency of anxiety in transformed migraine after adjustment for age and gender.
--Juang KD, Wang SJ, Fuh JL, Lu SR, Su TP (2000) Comorbidity of depressive and anxiety disorders in chronic daily headache and its subtypes. *Headache* 40:818–823
- Migraine: higher severity of somatic, depressive and anxiety complaints; strongest independent factor in predicting somatic severity of MDD, even after controlling for anxiety and demography
--Hung CI, Liu CY, Cheng YT, Wang SJ (2009) Migraine: a missing link between somatic symptoms and major depressive disorder. *J Affect Disord* 117(1-2):108–115

Headache category Comparison-2

- Panic disorder: prevail in migraine compared with tension-type headache or migraine plus tension-type headache; association stronger when migraine compared to pure tension-type headache;
- OCD: more associated with migraine than to tension-type headache.
- Impact of psychiatric comorbidity on chronicity and impaired quality of life in chronic daily headache.
- Complex interplay of factors underlying relationship between migraine, suicide risk and mood disorders deserve scientific interest and better methodologically based investigation
 - Beghi E, et al(2010) Headache, anxiety and depressive disorders: the HADAS study. *J Headache Pain* 11:141–150
 - Pompili M, et al(2009) Psychiatric comorbidity in patients with chronic daily headache and migraine: a selective overview including personality traits and suicide risk. *J Headache pain* 10:283–2890
 - Pompili M, et al(2010) Psychiatric comorbidity and suicide risk in patients with chronic migraine. *Neuropsychiatr Dis Treat* 6:81–91

From Children to grown-up -1

- Hypothesis: relationship between migraine and psychiatric disorders beginning with anxiety in childhood and adolescence, followed by migraine and later depression =>attention on pediatric age.
- Psychiatric disorders: more related to severity and frequency of non-migrainous headache than to migraine
- Higher prevalence of comorbid psychiatric disorders in chronic daily headache than other headache subtypes both in children/ adolescents and adults
- Burden of childhood adversities on chronic daily headache did not differ between chronic migraine and chronic tension-type headache in a population study

From children to grown-up -2

- Hypothesis: chronic illness in general, rather than a specific disorder, explains variations in psychological functioning
- Psychiatric disorders may not specifically relate to migraine, but as a kind of disabling and recurrent pain.
- Comparing migraine and chronic non-headache pain: No difference in anxiety and depression levels.
- Not find specific psychological characteristics between migraineurs and tension-type headache

From children to grown-up -3

- Comparing headache and recurrent abdominal pain: not differences by psychological point of view (internalizing vs. externalizing disorders)
- In pediatric age: psychological factors more related to frequency and severity of headaches, than to sole migraine.
- Increased risk of suicidal ideation among migraine with aura and high frequency non-migrainous headache; the risk increased with increasing frequency of attacks

--Wang SJ,.., Lu SR (2009) Migraine and suicidal ideation in adolescents aged 13 to 15 years. Neurology 72:1148–1152

From children to grown-up -4

- 25 ~ 30% of psychiatry-admitted children had physical symptoms(headache, food intolerance, abdominal pain, nausea and dizziness).
- greater somatic complaints in migraineurs and higher ratings of depression and anxiety among migraineous adolescents, compared to headache-free subjects.
- Hypothesis: “frequent, unexplainable and intense head pain would likely lead to heightened levels of depression and anxiety”.

From children to grown-up -5

- Subclinical conditions: psychological distress following life-events (e.g. parental divorce) or personality characteristics (e.g. tendency to perfectionism), contribute to trigger headache.
- Diagnostic workup of headache in children and adolescents should always include clinical psychological assessment.
- Connection between childhood maltreatments, adult chronic and/or severe migraine and MD: migraineurs with current depression reported more frequent physical and sexual abuse
- Women with migraine and depression: 4 times more have a history of some childhood maltreatment.
- Interface existing between neurology and psychiatry, organic and psychological, and likely genetic and environmental factors linked to migraine.

Gender differences

- Headache: most frequent somatic symptom in children and adolescents referred for emotional and behavioural disorders, as well as depression and/or anxiety.
- : females more affected.
- Boys: comorbid associations with allergy, bronchial asthma, DM and stomach-ache
- Girls: psychiatric symptoms and sleep disturbances.
- Longitudinal adolescent headache occurrence: associated to depression, insomnia and low self-esteem, and a likely temporal trend (preceding headache onset), even only in girls.

Negative effect

- Increased risk for females of higher depression (and anxiety), and an elevated risk of developing chronic daily headache and medication overuse when psychiatric disorders
- Negative effect of psychiatric disorders in general and depression in particular on the outcome
 - Pakalnis A, et al (2007) Emotional problems and prevalence of medication overuse in pediatric chronic daily headache.
J Child Neurol 22:1356–1360
 - Galli F, et al(2004) Chronic daily headache in childhood and adolescence: clinical aspects and a 4-year follow-up.
Cephalalgia 24(10):850–858
 - Wang SJ, Fuh JL, Lu SR, Juang KD (2007) Outcomes and predictors of CDH in adolescents: a 2-year longitudinal study.
Neurology 68(8):591–596

Headache Familial recurrence -1

- Anxiety and mood disorders: frequent in migraineurs and their relatives
- Psychiatric disorders are equally in migraine and other headache subtypes.
- Parents of migraine children: significant higher comorbidity with psychiatric disorders than other headache subtypes. => 1st point clearly differentiating migraineurs from other headache.
- Migraine children: higher headache familial recurrence and psychiatric disorders in parents, than other headache subtypes.
- Both psychiatric comorbidity and headache familial recurrence: also very frequent in children with other headaches

Headache familial recurrence -2

- Anxiety/depression and headache familial recurrence act as additive factors in non-migrainous headaches, while in migraine together with psychiatric disorders in parents
- Only in migraine: higher the weight of headache familial recurrence the higher psychiatric comorbidity.
- Children and adolescents with migraine: association with anxiety (and mood) disorders an important topic, even recent systematic review suggested overall inconclusive evidence .
- Depression: associated with a poor outcome for any headache subtype.
- Females: increased risk

Prospect in Further studies

- Aetiology of the comorbid association is also unclear;
- No studies on treatment of the comorbid disorders due to the young age.
- Further studies based on proper assessment tools and fulfilling the international systems of classification of both headache and mood disorders are required.

Metanalysis of studies investigating the association of Migraine and Depression

- Most investigated psychiatric comorbidity, i.e. depression, the crucial issue:
- Whether depression is more frequent in individuals with headache and particularly with migraine and vice versa ?
- Cohort study: occurrence during time of depression in headache without depression and in normal non-depressed; reversed looking for the occurrence of headache in depression without headache.
- Cross-section and Case-Control studies

Table 1 Prevalences and odds ratios of depression in migraineurs with respect to subjects without migraine for each one of the 12 considered studies

Study	Subject age range (years)	Diagnostic tool	Without migraine Depression		With migraine Depression		OR (95% CI)
			No	Yes (%)	No	Yes (%)	
Ratcliffe et al. [19]	18–65	CIDI	3,762	305 (7.5)	455	79 (14.8)	2.1 (2.1–1.7)
Hung et al. [37]	ND	HAMD-S DSSS	62	20 (24.4)	38	35 (47.9)	2.8 (2.9–1.5)
Jette et al. [18]	15–over 65	CIDI	31,772	1,122 (3.4)	3,641	343 (8.6)	1.8 (1.8–1.6)
Camarda et al. [23]	ND	CES-D	1,043	242 (18.8)	80	71 (47.0)	3.8 (3.8–2.7)
Merikangas et al. [27]	27–28	SPIKE	367	29 (7.3)	52	9 (14.7)	2.2 (1.0–4.8)
Breslau et al. [56]	25–55	CIDI	453	86 (16.0)	287	209 (42.1)	3.8 (2.9–5.1)
Samaan et al. [30]	19–85	SCAN, BDI	808	1,070 (57.0)	43	189 (81.5)	3.3 (2.4–4.6)
Lipton et al. [21]	18–65	PRIME-MD	315	64 (16.9)	206	183 (47)	4.4 (3.2–6.0)
Lanteri-Minet et al. [58]	ND	HADS	6,651	1,264 (15.7)	1,465	442 (23.2)	1.6 (1.4–1.8)
Breslau et al. [24]	25–55	CIDI	492	94 (16.0)	318	218 (40.7)	3.6 (2.7–4.7)
Kececi et al. [59]	Over 18	DSM-IV	682	102 (13.0)	110	53 (32.5)	3.2 (2.2–4.7)
McWilliams et al. [60]	25–74	CIDI-SF	1,319	185 (13.5)	243	97 (28.5)	2.8 (2.2–3.7)
							2.2 (2.0–2.3)

HAMDS Somatic items of the Hamilton Depression Rating Scale, *DSSS* Depression and Somatic Symptoms Scale, *CES-D* Center for Epidemiologic Studies Depression Scale, *HADS* Hospital Anxiety and Depression Scale, *SCAN* Schedule for Clinical Assessment in Neuropsychiatry, *BDI* Beck Depression Inventory, *CIDI (SF)* Composite International Diagnostic Interview (Short Form), *SPIKE* Structured Psychopathological Interview and Rating of the Social Consequences for Epidemiology, *PRIME-MD* Primary Care Evaluation of Mental Disorders

Results & Conclusion

- Prevalence estimates of depression were highly variable, whereas the ratio of depression prevalence between subjects with and without migraine was more consistent.
- The prevalence estimates: 3.4 ~ 24.4% without migraine; migraineurs: 8.6 ~ 47.9%.
- Individual Odd ratios (OR): **1.6 ~ 4.4**;
Overall OR (95% CI): **2.2 (2.0-2.3)**.
- 2 largest studies [Jette-18, Lanteri-Minet-58] reported the lowest odd ratios (1.8, 1.6, respectively).
- Depression is almost **2** time more frequent in migraine

Mechanisms of migraine psychiatric comorbidity

- 3 main potential mechanisms, as follows:
- 1. psychiatric disorders are causal factors in the development of migraine.
- 2. migraine is a causal factor in the development of psychiatric disorders.
- 3. shared aetiological factors and common determinants explain the co-occurrence of both entities: no clear causal association, and a common substrate (e.g., deranged activity of neurotransmitters or receptors)

--Lipton RB, et al(1994), Neurology 44:S4-S5; McWilliams LA, et al(2004), Pain 111:77-83; Radat F, et al(2005), Cephalgia 25:165-178

Psychiatric disorders as Risk factors for migraine ? -1

- Relationship between the frequency of psychiatric comorbidity and the severity of migraine: significant association between frequency and duration of the attacks, but not with the intensity of pain.
- Correlation between evolution of headache and the presence of anxiety or depression: anxiety precede migraine in most patients => preceded depression.
- Ages of onset of each disorder were significantly correlated.

Psychiatric disorders as Risk factors for migraine ? -2

- Only the an-amnestic presence of phobic disorder was predictive of the onset of migraine, at variance with that of affective disorders.
- Depression and Dysthymia are Not risk factors for the onset of migraine.

--Swartz KL, et al(2000) Mental disorders and the incidence of migraine headaches in a community sample. Arch Gen Psychiatry 57:945–950

--Merikangas KR, et al(1990) Migraine and psychopathology: results of the Zurich cohort study of young adults. Arch Gen Psychiatry 47:849–853

--Breslau N, et al(1993) Migraine, physical health and psychiatric disorder: a prospective epidemiologic study in young adults. J Psychiatr Res 27:211–221

Migraine as Risk of Depression or Panic disorder

- During F/U > 1 year : slightly greater in history of migraine (15.5%) than current migraine (13%)[Breslau 1993].
- Complex statistical hazard model: No preferential order of onset for depression or panic relative to migraine, although a trend towards an order of major depressive episodes in relation to severe non-migraine headache.

--Breslau N, et al(2000) Headache and major depression. Is the association specific to migraine? Neurology 54:308–313

--Sheftell FD, et al(2002) Migraine and psychiatric comorbidity: from theory and hypotheses to clinical application. Headache 42:934–944

Bidirection vs. Predictor !?

- Comorbid disorders are bidirectionally linked
- Anxiety predicted the persistence of headache in both migraine and tension-type headache children.

--Guidetti V, et al (1998) Headache and psychiatric comorbidity: clinical aspects and outcome in a 8-year follow-up study.

Cephalgia 18:455–462

- Only **phobic disorders** predict the migraine
- Clear bidirectional relationship exists between migraine and depression or panic disorder
↔ Risk factor of the other.

Common Genetic and/or Environmental Risk factors ?

- No familial crosstransmission between migraine and affective or anxiety disorders [Merikangas 1993].
- Risk of bipolar disorder was not increased in the relatives of non-bipolar migraine patients [Merikangas 1998].
- Not support depressive and bipolar disorders share common genetic determinants with migraine.
- Both migraine and affective disorders, the frequency of episodes can increase with time, and progress to more chronic states with poor recovery between episodes and development of drug resistance
↔ Sensitization phenomena may underlie both disorders.

--Scher AI, et al(2008) Risk factors for headache chronification. Headache 48:16–25

Biologically based studies

- Association between a particular dopamine D₂ receptor genotype and comorbid migraine with aura, MD and generalized anxiety disorder.
 - Peroutka SJ, et al(1998) Comorbid migraine with aura, anxiety, and depression is associated with dopamine D₂ receptor (DRD₂) NcoI alleles. Mol Med 4:14–21
- A lifetime history of MD was reported to be associated with reduced tyramine conjugation (a marker of endogenous depression) in migraine
 - Jarman J, et al (1990) High incidence of endogenous depression in migraine: confirmation by tyramine test. J Neurol Neurosurg Psychiatry 53:573–575

Neurobiological mechanisms

- Serotonin receptors and transporters, and catecholamines: implicated in migraine and various psychiatric disorders
- effectiveness of several antidepressants (including SSRI abd SNRI) in the prevention or treatment of migraine.
- Female migraineurs often experience attacks associated with falling estrogen levels around menses;
Mood disturbances often coincide with menses, as well as the postpartum period and the perimenopausal period.
- Ovarian hormones, modulating numerous neurotransmitters: important role in migraine and depression.

Impact of psychiatric comorbidity on migraine

- Comorbidity with psychiatric disorders raises the global burden of migraine.
- Associated with poorer health-related outcomes (disability, restriction of activity, quality-of-life(QoL) or mental health care utilization)
- Restricted to migraine, without taking into consideration psychiatric comorbidities.

Comorbid Bipolar disorder and Migraine

- Male: more likely to utilize mental health care services.
- Females: more likely to require assistance in their daily routine

--McIntyre RS, et al(2006) The prevalence and impact of migraine headache in bipolar disorder: results from the Canadian Community Health Survey. Headache 46:973–982

Migraine /c various Psychiatric disorders

- Concomitantly to report job absenteeism, to rate their general health as fair or poor, and to use mental health services
- Migraine and One Mental health disorder: Health-related QoL generally lower
- MDD & migraine: predict a significant negative impact on all physical subscales and vitality in the assessment of quality of life.
- Migraine, Anxiety, or Chronic Depression: higher depression scores and poor quality of life;
- Migraine, specific Phobia, and Panic disorder: important and independent comorbidities predicting QoL.

--Hung CI, Wang SJ, et al(2005) Risk factors associated with migraine or chronic daily headache in outpatients with major depressive disorder.

Acta Psychiatr Scand 111(4):310–315

--Hung CI, Wang SJ, et al(2008) The impacts of migraine, anxiety disorders, and chronic depression on quality of life in psychiatric outpatients with major depressive disorder.

J Psychosom Res 65(2):135–142

Prospect

- Migraine should be considered as an important clinical symptom in all clinic-based Depression.
- Currently available studies do not elucidate whether health-related outcome variables are specific to migraine or to mental disorders.
- Impairment in QoL may mirror a real ill condition, or an altered perception of life circumstances, or both ?.
- Prospective studies will probably help to clarify these important points

Conclusions -1

- Population based studies generally indicate an increased risk of affective and anxiety disorders in migraine
- A trend towards an association of migraine with bipolar disorder.
- Definitely no comorbidity with substance abuse/dependence.
- Migraine subtypes, comorbidity (e.g. suicide attempts, bipolar disorder) mainly involves migraine with aura

Conclusions -2

- Limitations:
- 1. Lack of diagnostic recognition of certain forms of migraine (chronic migraine), due to 1st version of IHS criteria, may have significantly affected the results of several studies.
- 2. Some studies were carried over within psychiatric research protocols, not originally investigate the comorbidity between migraine and psychiatric disorders.

Conclusions -3

- No significant difference between migraine and tension-type headache in prevalence of psychiatric comorbidity.
- Migraine: decreased risk of affective and anxiety disorders compared to chronic daily headache
- Affective and anxiety disorders prevail in chronic forms of headache and substance use than migraine alone.
- “Transformed” (or chronic) migraine: increased prevalence of affective and anxiety disorders compared to simple migraine or chronic tension-type headache.
- Early studies: Correlation between Frequency of headache and Frequency of anxiety or depressive disorders
- Little evidence: Correlation between the Severity of migraine and anxious or depressive symptoms.

Conclusions -4

- Mechanisms underlying migraine psychiatric comorbidity : presently poorly understood => remain a priority for future research.
- Psychiatric comorbidity indeed affects migraine evolution => chronic substance use and change treatment strategies => modifying the outcome



Thanks For Your Attention !!