

Addiction

ROLE OF METHYL
FOLATE

Presenter

Dr. Muhammad Haris Khan

M.B.B.S., Ph.D.

Elected Mem: World association of Sexology.

European Association of Psychiatrists

International Association of Pain and
Chemical Dependency

Senior Member,

Education Liaison Network, WPA.

Member

Psychiatry & Sexual Health section
of WPA.

International Early Psychosis
Association.

WPA Section on Developing
Countries.

CO AUTHORS

- DR ROZINA WAHEED research officer
Genetic pharma
- Muhammad Zubair Mukhhtar MSc clinical
diploma psychology

Definition

- Dorland dictionary:

"A state of being given up to some habit, especially strong dependence on a drug"

Types

- It can be chemical and nonchemical
- - Chemical includes addiction of alcohol, heroin etc
- Non chemical- it include pathological gambling, workaholic, sex addiction and etc

Different phases of consumption

- Social drinkers
- Habitual drinker
- Heavy drinker
- Addict

Who is an Addict?

Criterion from DSM-IV

- 1) Dependence is defined as cluster of three or more symptoms.

Tolerance : Requiring greater amount of substance to have same effect or markedly diminished effect with continued use of same dose of substance.

Criterion contd...

Withdrawal: Unpleasant effects and feelings when drug level falls beyond certain level.

Withdrawals are the compensatory opposite effects working unabated.

- Two are not necessary for the diagnosis as in case of cannabis individual show pattern of compulsive use without signs of tolerance or withdrawals

Criterion contd...

- 2) Loss of control of amount consumed ,time and place where drug is consumed.
- 3) Failed attempt to quit.
- 4) Greater time is spent on the activities necessary to obtain substance, use the substance or recover from its effects.

Criterion contd...

5) Important social ,occupational ,and recreational activities are given up or reduced because of substance use.

6) Continue despite deleterious consequence.

Neurobiology of Addiction

- Our understanding is improving owe to progress in neuroimaging ,gene targeting and availability of specific agonists and antagonists of receptors.

Reward

- Most of the drugs of abuse increases dopamine in nucleus accumbens which play key role in mediating reward effects of abused substance.

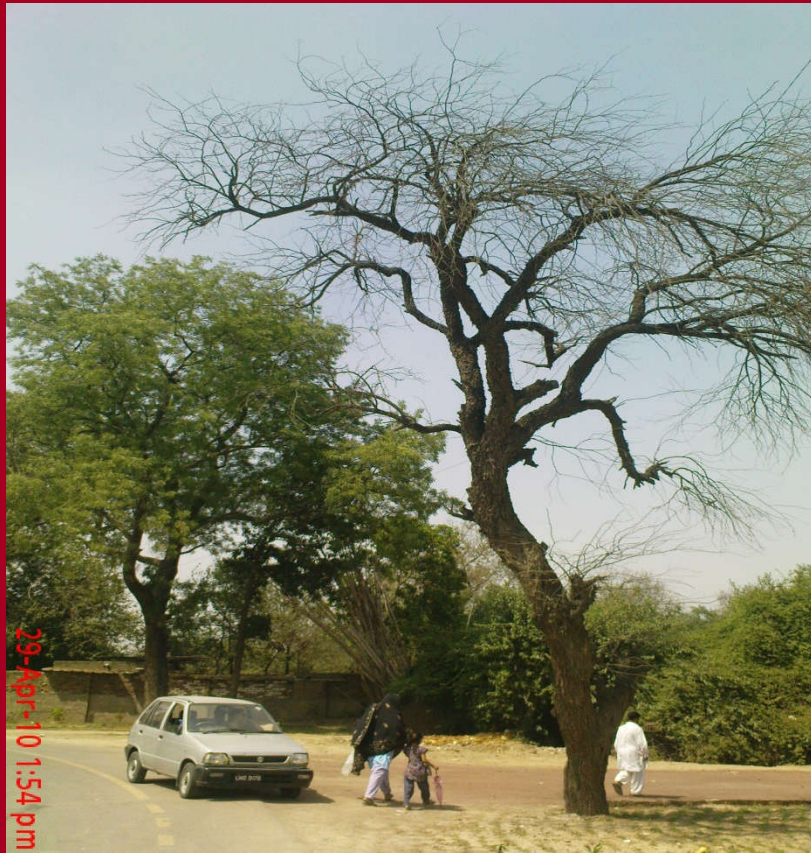
Anticipation

- Cue of drug availability activate dopamine in anticipation ,giving feelings of euphoria.
- Dysphoria follow when drug is not actually there.

Withdrawal

- During early abstinence phase reduced levels of dopamine are found which produces feelings lack of enjoyment.
- D2 Receptors get down regulated diminish effect of available dopamine.
- During active addiction serotonin is also get depleted.

UNTREATED ADDICTION



Models of Addiction

Dopamine Depletion Theory

- According to this theory nerve terminals get depleted of dopamine due to repeated use of addictive substance or behavior.

Down Regulation of D2 Receptor

- It puts the individual at the risk of addiction and addictive behaviors as both temporary stimulate the reward center, regulated by D2 receptor.

Role of frontal cortex

- Neuroimaging studies reveals morphological changes in frontal cortex in different forms of addiction like alcohol, cocaine and heroin. Supervisory and social motivational function of frontal cortex is impaired, resulting in unleashing of stimulus driven behavior.

Neurochemical studies

- Advance phase of addiction is due to cellular adaptation in anterior cingulate and orbitofrontal glutamatergic projections to nucleus accumbens. This glutamatergic transmission diminishes prefrontal cortex ability to initiate behavior in response to limbic reward and provide executive control over drug seeking.

Neurochemical studies

- It become more sensitive to cues of availability of drug resulting in increase firing in nucleus accumben manifesting as compulsive drug seeking. It has been demonstrated that NMDA receptors antagonists block development of tolerance.

RELAPSE

- Relapse is very common in addiction patients.
- Relapse occurs due to highly unpleasant post acute withdrawals.
- By controlling PAW we can prevent relapse.
- For that anticraving strategies including medicines are required.

ROLE OF HOMOCYSTEINE

- . Homocysteine level which are increased in addiction stimulates NMDA receptors and thus leads to an increased glutamatergic neurotransmission. Therefore it has been assumed that the extent of craving during withdrawal assessed with the Obsessive Compulsive Drinking Scale (OCDS) is influenced by plasma homocysteine levels.

HOMOCYSTEINE AND ALTERATIONS OF THE DOPAMINERGIC SYSTEM

It has been demonstrated in vivo and in vitro studies that homocysteine has toxic effects especially on dopaminergic neurons. As the rewarding effects of alcohol are mediated by the dopaminergic system, a homocysteine-dependent impairment of the reward system possibly leads to an altered drinking behaviour according to the deficit hypothesis of addiction.

- Any strategy which can restore reservoirs of neurotransmitter can be helpful in treatment of addiction.
- IS THERE ANY?

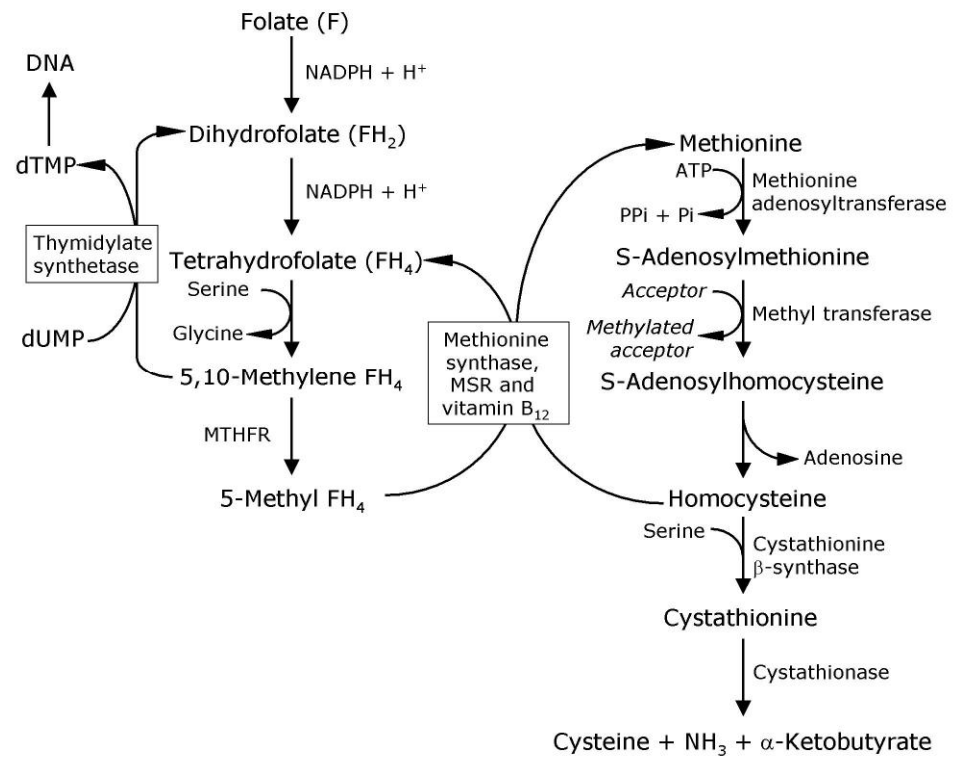
RAY OF HOPE



ROLE OF FOLATE

- Studies demonstrate low levels of folate among patient of addiction.
- There is bilateral relation between addiction and depression high homocysteine level and low folate level are found in both disorders

- L methyle folate is important coenzyme for production of neurotransmitters
- Folic acid requires a 4 step transformation process to be converted to the active form of folate, L-methylfolate. Dietary folate requires 3-steps
- L-methylfolate is the active form that can immediately get absorbed and can cross the blood brain barrier .



- Homocysteine can be remethylated to methionine via folate-dependent or folate independent mechanisms.
- The folate-dependent remethylation is catalyzed by the vitamin B12-dependent enzyme methionine synthase (MS) utilizing a methyl group from 5-methyltetrahydrofolate (5-CH₃-THF).

CONCLUSION

- Methyl folate along with B6 and B12 can be used for elimination of homocysteine .
- It can help replenish depleted reservoir of neurotransmitters in case of addiction.
- Greater amount of serotonin would help provide improvement of mood, lowering of anxiety greater self control and increased supply of dopamine would provide necessary motivation for life in post addictive phase.
- This would mitigate PAW and thus would act as anticraving agent.

Thank you

