TREATING CO-OCCURRING DISORDERS IN THE SUBSTANCE USE DISORDER PATIENT: DEPRESSION, ANXIETY, AND SOMETIMES PAIN

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QUESTIONS
RESEARCHERS ARE ASKING

What is the “psychic structure” of opioid-addicted patients? Or stated another way, what are some of the “characteristics of psychopathology” of opioid-addicted patients?

Are psychosocial treatments, such as psychotherapeutic approaches, useful in patients with OUDs? And if so, does it matter whether or not those psychosocial treatments are integrated into the OUD treatment program?

More specifically, what do we know about the efficacy of various treatments for co-occurring depressive and anxiety disorders in patients with OUDs?
Dr. Pier Pani and his group applied a “Principal Component Analysis” (“PCA”) to the items on the Symptom Checklist (SCL)-90, which is a 90-item, 5-point, self-report rating scale that takes about 15 minutes to complete. The SCL-90 allows patients to report obsessive-compulsive symptoms, depressive symptoms, anxiety symptoms, somatic symptoms, psychotic symptoms, and others. It is considered to be well-suited for measuring general mental health and changes in symptoms over time.

They found a 5-factor aggregation of psychological/psychiatric symptoms when they applied their analysis (their “PCA”) to a cohort of patients with heroin addiction.
CHARACTERISTICS OF PSYCHOPATHOLOGY

The Five Factors:
- “Worthlessness and Being Trapped”
- “Somatic Symptoms”
- “Sensitivity-Psychoticism”
- “Panic-Anxiety”
- “Violence-Suicide”

Their study, which they published in 2016 in the journal, Addictive Disorders & Their Treatment, looked at whether there is any difference in these 5 dimensions between heroin-addicted patients with lifetime psychiatric problems and those heroin-addicted patients who do NOT have lifetime psychiatric problems.

They found that while all the SCL-90 factor scores were higher in those heroin-addicted patients with lifetime psychiatric illness than in those without, the only statistically significant differences occurred in the case of “Panic-Anxiety,” which was higher in those heroin-addicted patients who did have a history of psychiatric illness at some point in their lives.

They then performed a “stepwise discriminant analysis,” which showed that the severity of “Somatic Symptoms” and “Panic-Anxiety” made those two factors the only ones that successfully discriminated between those heroin-addicted patients who had a lifetime history of psychiatric illness and those who did not.
Another study, this one out of China, also used the SCL-90 – in this case, a Chinese version – to look at the characteristics of comorbid psychiatric symptoms in over 500 heroin-addicted patients and see if there was any relationship between different routes of drug administration and psychiatric problems. They looked at three different routes of administration: injecting heroin, snorting heroin, and “chasing the dragon” (“chasing the dragon” is a slang phrase of Cantonese origin from Hong Kong referring to inhaling the vapor from a heated solution of morphine, heroin, oxycodone, opium, or ya ba [which is a pill containing caffeine and methamphetamine]). They found that comorbid psychopathology conditions were more severe among these heroin-addicted patients on all dimensions of the SCL-90 compared to adult controls, and the average score of depression was highest among the 9 dimensions in heroin-addicted patients.

Psychiatric symptoms were generally more severe in the heroin-injecting group than in the “chasing the dragon” group, but only the difference in “Obsessive-Compulsive” symptoms was statistically significant between these two groups.

More significant differences were found between those patients who snorted heroin and the other two groups – those who injected heroin or “chased the dragon” – and the average score of each dimension of the SCL-90 was higher in the snorting group.

So this study seems to suggest that the heroin-addicted population has more severe psychiatric pathology than do non-addicted controls, and that there may be some interesting correlations between the routes of administration of heroin and the types and severity of psychiatric symptomatology.
ARE PSYCHOSOCIAL TREATMENTS USEFUL? IS INTEGRATION IMPORTANT?

- A study published in 1983 in *Archives of General Psychiatry* looked at 110 patients with heroin addiction and randomized them into 3 groups:
  - “drug counseling” alone;
  - counseling plus 6 months of supportive-expressive psychotherapy;
  - counseling plus 6 months of cognitive-behavioral psychotherapy.
- All three groups showed significant improvement.
- Patients receiving the additional psychotherapies showed improvement in more areas and to a greater degree than those who received counseling alone – and with less use of medication.

Woody GE; Luborsky L; McLellan AT; et. al. *Arch Gen Psychiatry.* 1983; 40 (6): 639-645
More recently (2011), Laura Amato and her colleagues in Italy published a meta-analysis of 34 controlled trials (31 of which were in the USA) involving 3,777 opioid-addicted patients treated in a methadone maintenance program, to compare psychosocial intervention + agonist treatment for opioid dependence to agonist treatment alone. They found no benefit of psychosocial intervention + agonist treatment vs. agonist treatment alone for:

- Retention in treatment
- Abstinence from opioids during treatment
- Compliance with treatment
- Psychiatric symptoms

The “control” intervention of “agonist treatment alone” was a program that routinely offered counseling sessions in addition to methadone. Duration of the studies was too short to analyze relevant outcomes such as mortality. So, this study did not answer the question of whether any psychosocial intervention is needed when patients are treated with methadone maintenance, but rather, the narrower question of whether a specific, more structured intervention provides any additional benefit over standard psychosocial support.

Amato L, Minozzi S, Davoli M, Vecchi S. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD004147. DOI: 10.1002/14651858.CD004147.pub4
Robert Brooner and his colleagues at Johns Hopkins School of Medicine studied a group of 316 methadone-maintained opioid-addicted patients who had at least one comorbid psychiatric disorder.

They compared the outcomes for those 160 patients who received psychiatric care on-site, as an integrated part of the substance abuse treatment program vs. the 156 patients who received the same type and schedule of psychiatric care, but off-site in a non-integrated way, at a community psychiatry program.

Onsite participants were significantly more likely to initiate psychiatric care, remain in treatment longer, attend more psychiatrist appointments, and have greater reductions in GSI (Hopkins Symptom Checklist Global Severity Index) scores.

No differences were observed for drug use.

The authors concluded that onsite integrated psychiatric and substance misuse treatment services in a methadone treatment setting might improve psychiatric outcomes compared with patients treated in an off-site and non-integrated psychiatric setting, but the improvement might not translate into improved substance misuse outcomes.

Brooner RK; Kidorf MS; King V; Peirce J; Neufeld K; Stoller K; Kolodner K. Managing psychiatric comorbidity within versus outside of methadone treatment settings: a randomized and controlled evaluation. Addiction. 2013; 108: 1942-51
EFICACY OF TREATMENTS FOR CO-OCCURRING DEPRESSIVE & ANXIETY DISORDERS IN OUD PATIENTS

- McRae et. al. published a study in the *American Journal on Addictions (2004)*, which was a randomized, placebo-controlled trial of buspirone for the treatment of anxiety in opioid-dependent patients.
- It was a 12-week study of 36 methadone-maintained, opioid-addicted patients who presented with anxiety symptoms.
- Buspirone treatment did not significantly reduce anxiety symptoms in these patients.
- However, buspirone treatment was associated with trends toward reduction in depression scale scores and a slower return to substance use.
Pani et al. (2010) conducted a meta-analysis of 7 RCTs, examining the efficacy of antidepressant medication in 482 depressed opioid-addicted patients who were in treatment with opioid agonist medication.

No difference was observed among those patients who dropped out of the program between those patients receiving antidepressant therapy and those receiving placebo.

In two of the studies the severity of depression was reduced with antidepressant treatment, while another showed no difference between antidepressant medications and placebo.

No differences were observed in the drug use between the group treated with antidepressant medication and the group treated with placebo.

The authors concluded that there was “little evidence to support the use of” antidepressant medications for treating depressed opioid-addicted patients, but they noted that differences between the studies in clinical and methodological characteristics made it difficult to draw “confident conclusions” about the efficacy and safety of antidepressants for the treatment of depression in opioid-addicted patients.
In a paper published in 2017 in the *American Journal on Addictions*, Ahmed Hassan et. al. in Toronto published a meta-analysis of 8 RCTs of patients receiving opioid agonist treatment (OAT) who were treated with antidepressants compared to patients receiving (OAT) treated with placebo.

Two of the seven studies that initiated antidepressant treatment in patients receiving OAT showed significant results for antidepressant effects vs. placebo.

Tricyclic antidepressants (TCAs, n = 235) significantly improved mean depression scores, but Selective Serotonin Reuptake Inhibitors (SSRIs, n = 311) were not significantly different from placebo.

4 out of 5 studies that implemented psychotherapeutic approaches reported a greater reduction of depressive symptoms than the comparison group.

The authors concluded that “to date, psychotherapy has the most documented evidence for efficacy,” and that TCAs appear more effective than SSRIs, but with more adverse side effects.
WHAT HAVE WE LEARNED?

- Patients with OUDs have higher prevalence of psychiatric disorders than the general population.
  - Somatic symptoms and panic/anxiety may be among the more prevalent conditions
  - Among patients with heroin addictions, those who snort heroin may be more severely psychiatrically ill than patients who use heroin via other routes of administration.
- Although the evidence available in the extant literature seems to suggest that patients with OUDs who receive drug counseling may be likely to show improvement, recent studies in particular (unlike older studies) have not shown that particular forms of psychotherapeutic approaches provide any advantages over “drug counseling” alone, with respect to OUD treatment outcomes.
- Providing psychiatric care to patients with OUDs in the same setting, and in an integrated program along with their OUD treatment program may improve the access to, utilization of, and benefits from psychiatric treatment experienced by the OUD patient population, but it is not entirely clear that this will improve substance use outcomes.
- Recent reviews and meta-analyses of the available methodologically sound RCTs in populations of OUD patients do not seem to support the efficacy of buspirone for treatment of anxiety disorders or antidepressants* for depressive disorders or anxiety disorders, with the possible exception of TCAs for depression.
- Psychotherapeutic approaches seem to have the most documented evidence supporting their efficacy in treating co-occurring psychiatric conditions in patients with OUDs.