
Evidence-Based Treatment of Pathological Gambling

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Pathological Gambling

Persistent and recurrent maladaptive gambling behavior as indicated by five (or more) of the following:

- is preoccupied with gambling
 - needs to gamble with increasing amounts of money in order to achieve the desired excitement
 - has repeated unsuccessful efforts to control, cut back, or stop gambling
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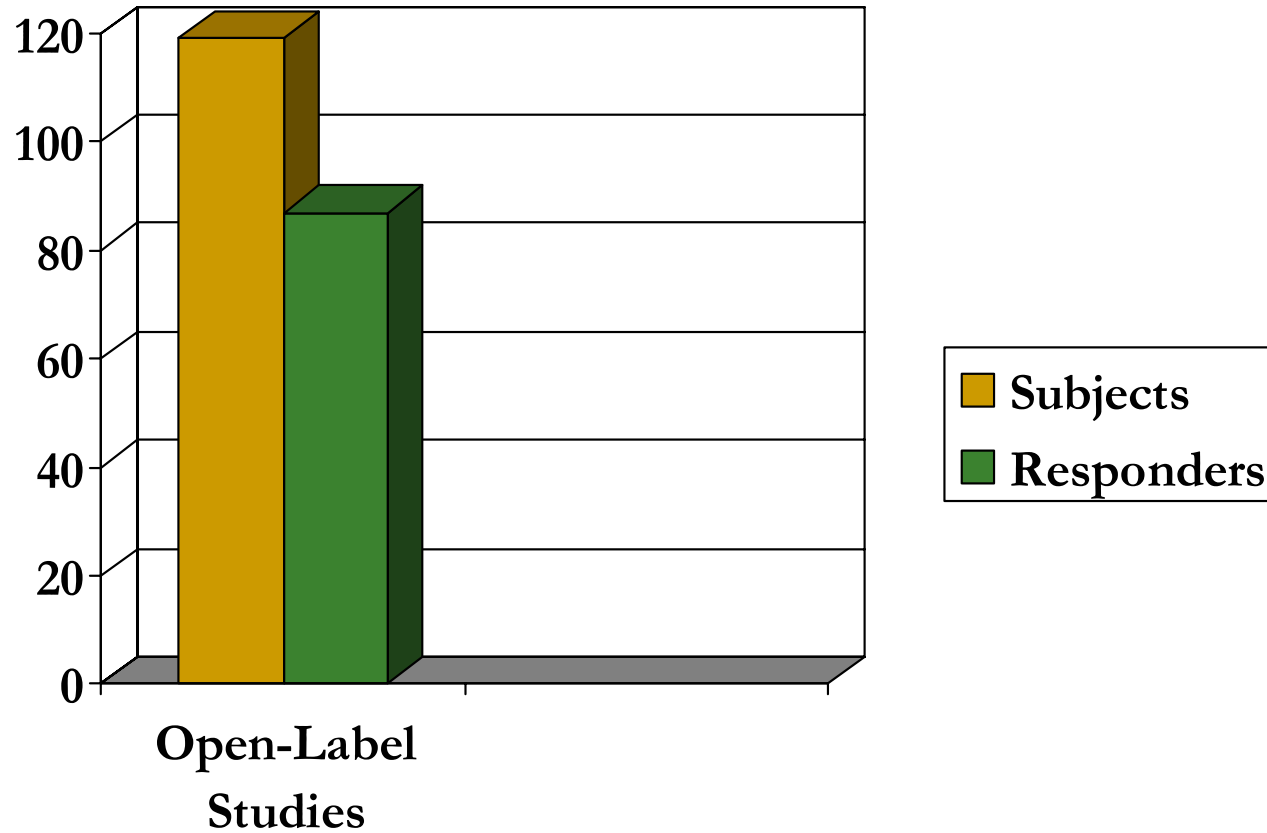
- is restless or irritable when attempting to cut down or stop
- gambles to escape from problems
- “chases” losses
- lies to family members, therapist, or others
- has committed illegal acts
- has jeopardized or lost a significant relationship, job, or educational or career opportunity
- relies on others for money

Characteristics

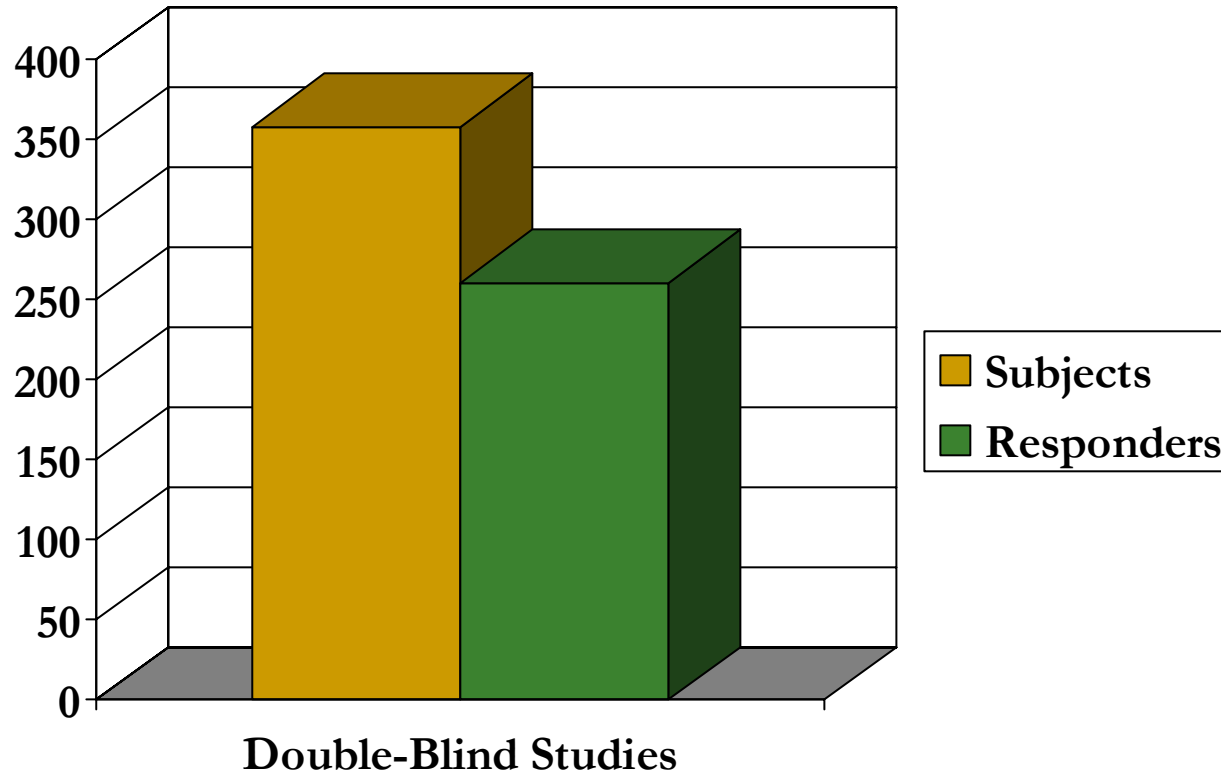
- Age: usually begins in early adulthood
 - Gender: 32% female, 68% male
 - Males tend to start at an earlier age
 - Telescoping phenomenon
 - Mean time: 16 hours per week
 - Amount Lost: 45% of gross annual income
 - Triggers:
 - Advertisements, Boredom, Stress
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Pharmacological Treatment

7 Open-Label Studies



11 Double-Blind Studies



Antidepressant Medication

- Based on the neurobiology of pathological gambling
- Low levels of the serotonin metabolite 5-hydroxyindole acetic acid (5-HIAA) and blunted serotonergic response within the ventromedial prefrontal cortex (vmPFC) have been associated with impulsive behaviors.
- Individuals with PG demonstrate diminished activation of the vmPFC when viewing gambling-related videotapes or when performing the Stroop color-word interference task.
- Individuals with PG also show relatively diminished activation of the vmPFC during a simulated gambling task.
- Findings suggest that decreased serotonin function within vmPFC may engender disinhibition and contribute to PG.

Clomipramine

- SRI that also inhibits norepinephrine reuptake, was the first SRI tested in a controlled fashion in PG.
- Single PG subject using a double-blind, placebo-controlled design.
- After receiving placebo for 10 weeks without response, the woman reported a 90% improvement in gambling symptoms after being treated with 125mg/day of clomipramine.
- No further controlled studies of clomipramine to confirm the limited results on this initial study.
- Side effects: dry mouth, constipation, blurred vision, sexual dysfunction, weight gain, fine tremor, muscle twitching, cardiac conduction problems and has significant drug-drug interactions.

Sertraline

- Double-blind placebo-controlled study with 60 subjects with PG were treated for 6 months (mean dose = 95mg/day)
 - 23 sertraline-treated subjects (74%) and 21 placebo-treated subjects (72%) were rated as responders based on the primary outcome measure (Criteria for Control of Pathological Gambling Questionnaire).
 - Sertraline did not demonstrate superiority to placebo.
 - Well tolerated, but may cause sedation, constipation, weight gain, headache, sexual dysfunction and dry mouth.
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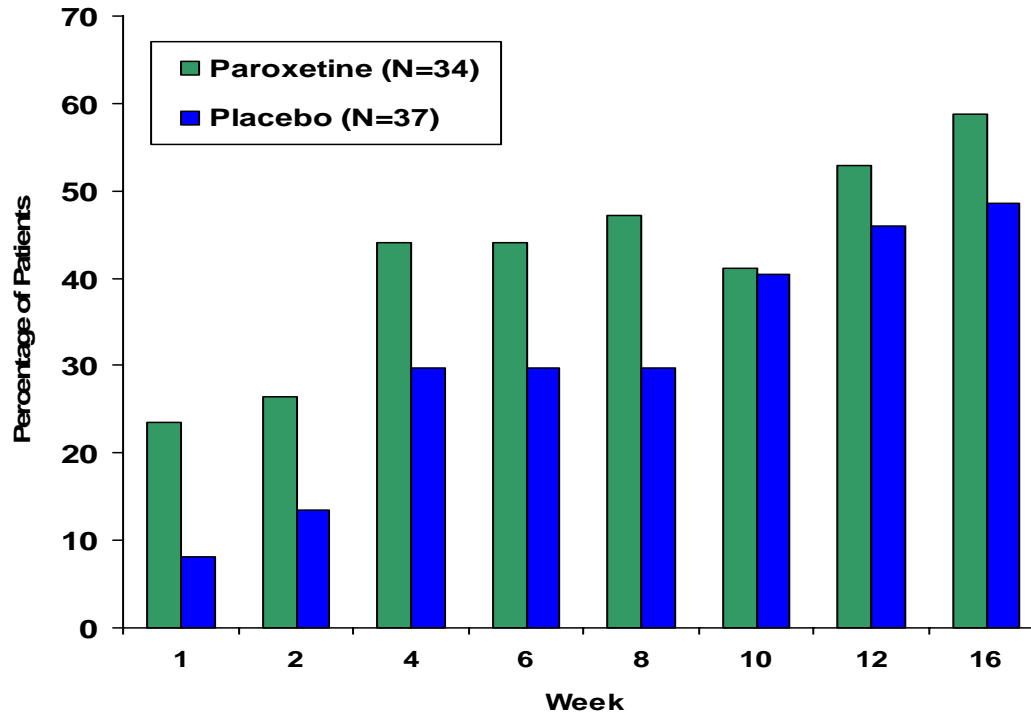
Fluvoxamine

- Double-blind, 16-week crossover study in 15 PG subjects demonstrated a significant difference compared to placebo.
- Phase order treatment interaction (i.e., the medication did not separate from placebo during the first phase but did in the second phase).
- 6-month double-blind placebo-controlled trial in 32 gamblers failed to show statistical significance compared to placebo.
- First study - used the PG-YBOCS as the primary outcome measure. Second study used amount of money spent weekly.
- Gastrointestinal distress, sedation, mild anxiety, headache, and sexual dysfunction. Drug-drug interactions should be considered.
- One randomized, blind-rater study of fluvoxamine and topiramate found a greater percentage of responders in the group treated with topiramate.

Paroxetine

- One double-blind, placebo-controlled study of paroxetine showed significant improvement in subjects randomized to 8 weeks of treatment.
 - A larger multi-center double-blind placebo controlled trial in PG, however, failed to reproduce the results.
 - A high placebo response rate (“very much improved” or “much improved” based on the Clinical Global Improvement scale) was observed.
 - 48% of those assigned to placebo and 59% of those taking paroxetine were considered responders.
 - Further study appears warranted to determine whether specific subgroups of individuals with PG (e.g., those with specific genetic characteristics) will respond preferentially to treatment with paroxetine or other SRIs.
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Percentage of Patients Achieving Response (PG-CGI-I Score of 1 or 2) During Treatment with Paroxetine or Placebo



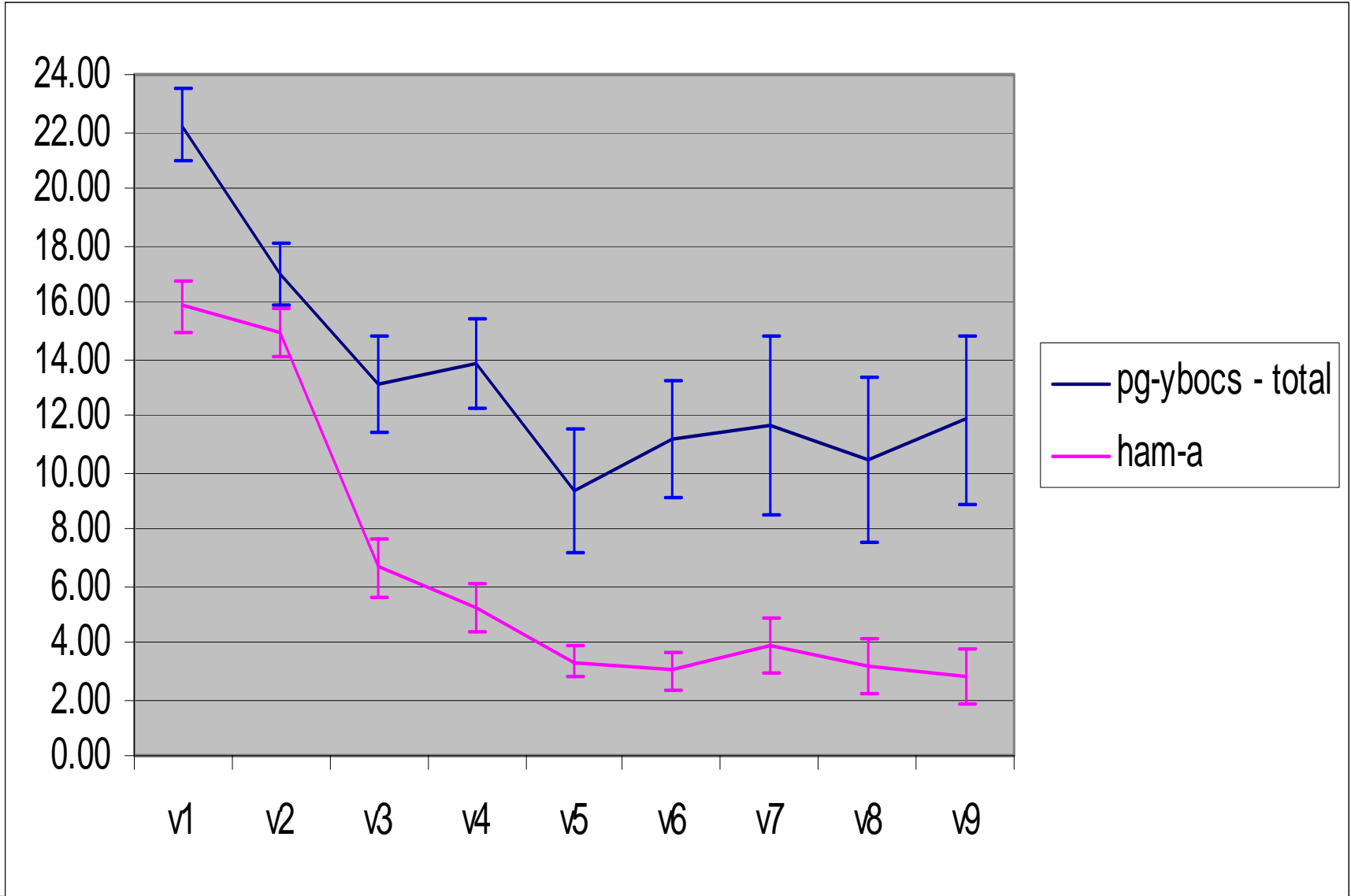
59% response rate in the paroxetine group

49% rate in the placebo group

45 completers (Grant et al. 2003)

Limitations

- Despite the high rates of co-occurring psychiatric disorders in PG, most pharmacotherapy studies performed to date have excluded people with co-occurring psychiatric conditions.
 - An open-label 12-week trial of escitalopram with an 8-week double-blind discontinuation period for responders was recently performed.
 - Of 13 subjects treated with a mean dose of 25.4mg/day, 62% were considered responders in terms of both PG and anxiety symptoms.
 - Other antidepressants with different mechanisms of action have been tested in open-label designs. Bupropion, a dopaminergic medication, and serzone, a mixed serotonin/norepinephrine reuptake inhibitor, have shown initial promise in treating PG in small samples (10 and 12 subjects, respectively).
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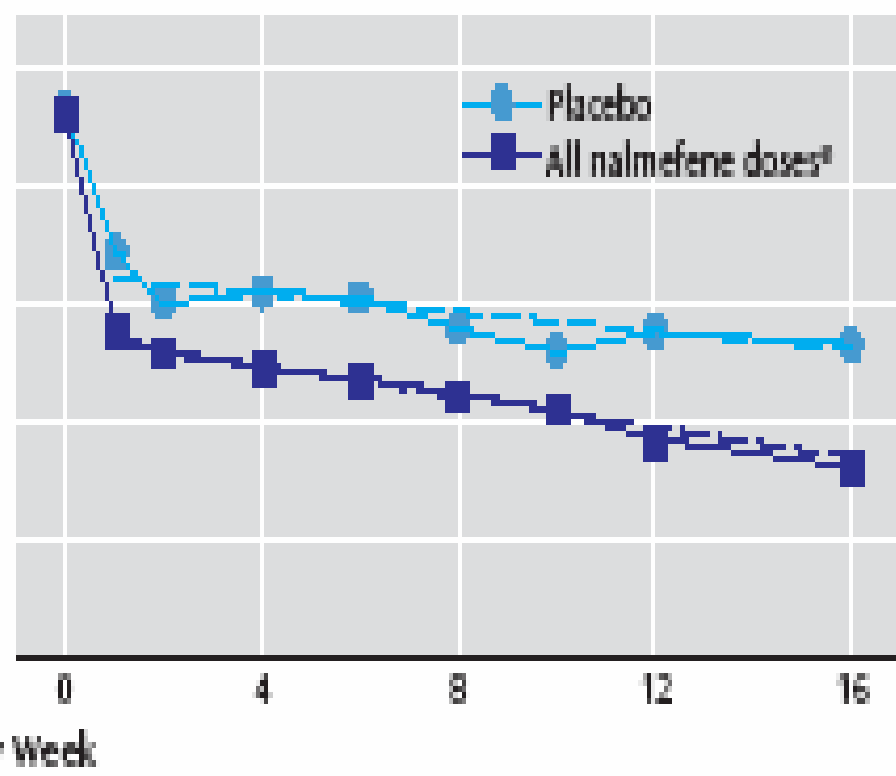
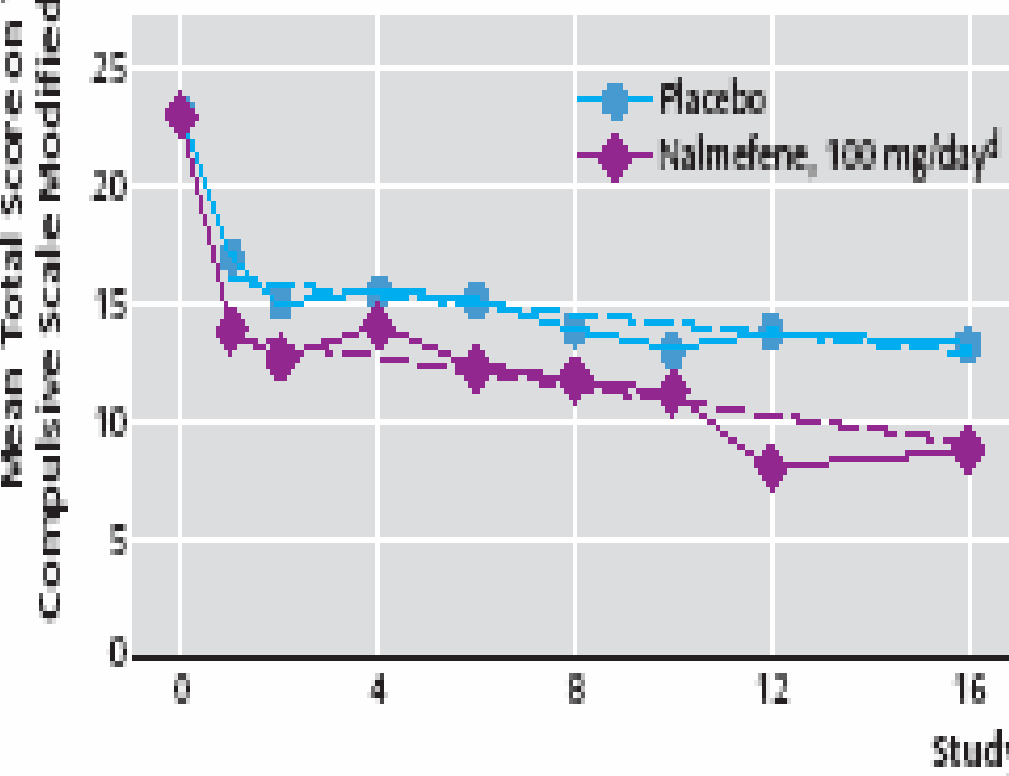
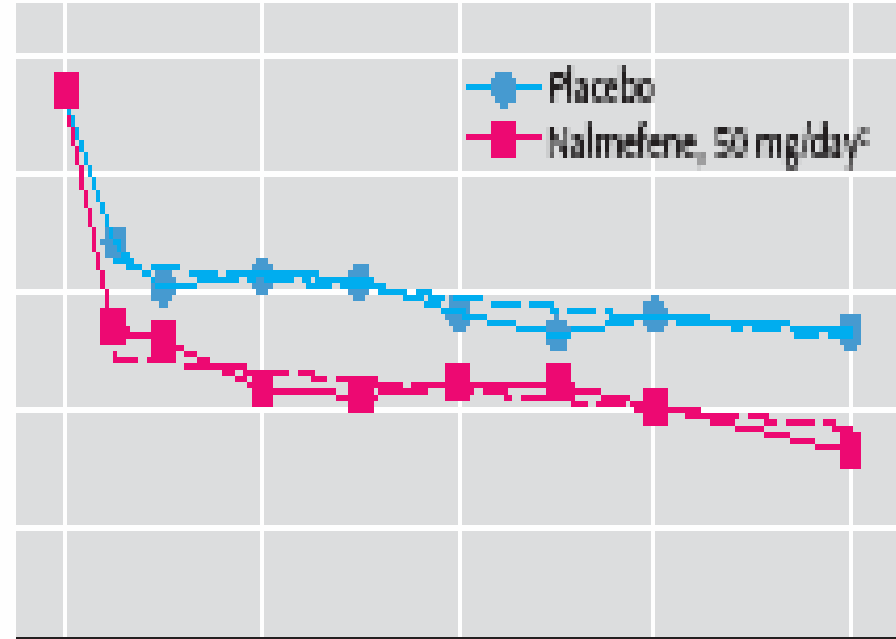
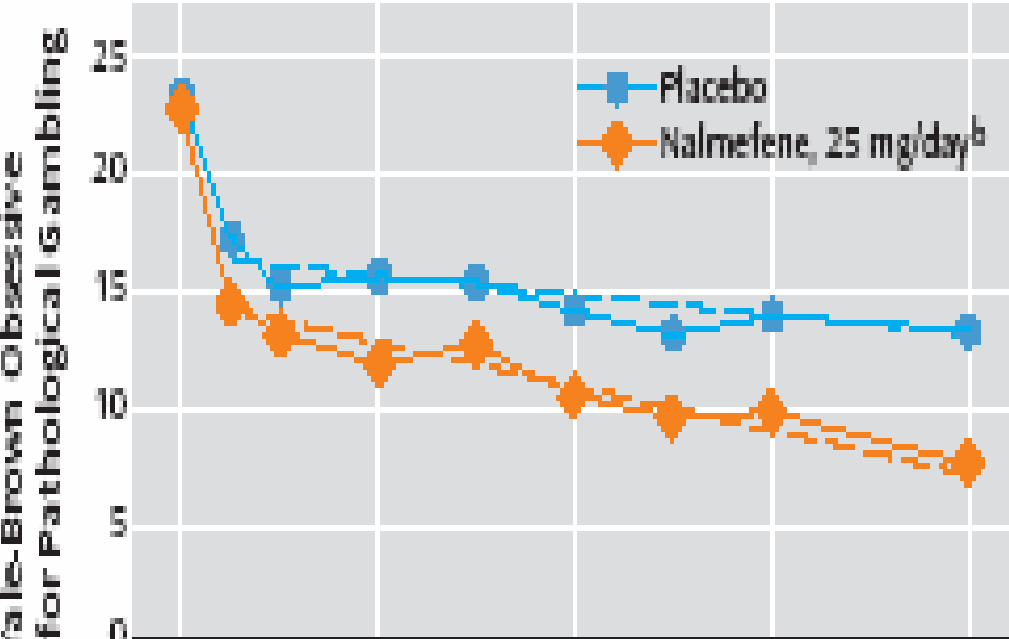


Mood Stabilizers

- Although a case report and an open-label study, respectively, suggest that carbamazepine and valproate may be efficacious in the treatment of PG
- Only 1 randomized, placebo-controlled trial of a mood stabilizer tested in PG.
- In a double-blind, placebo-controlled study of forty PG subjects with bipolar spectrum disorders (bipolar type II, bipolar not otherwise specified, or cyclothymia), sustained release lithium carbonate (mean lithium level 0.87 meq/liter) was shown to be superior to placebo in reducing PG symptoms during 10 weeks of treatment.
- Majority (83%) of subjects in the treatment group displayed significant decreases in gambling urges, thoughts and behaviors as measured by the PG-YBOCS
- No differences were found in amount of money lost, episodes of gambling per week or time spent per gambling episode.
- Lithium may cause fine tremor, nausea, diarrhea, and nephrotoxicity is possible when used chronically.

Opioid Antagonists

- Opioid antagonists are thought to decrease dopamine neurotransmission in the NA and linked motivational neurocircuitry, thus dampening gambling-related excitement and cravings.
- In 12-week double-blind placebo-controlled trial of naltrexone in 45 subjects with PG, naltrexone (mean dose of 188mg/day) was effective in reducing the frequency and intensity of gambling urges, as well gambling behavior.
- Liver enzyme elevations are possible
- Opioid antagonist, nalmefene, studied in 207 subjects
- Nalmefene demonstrated statistically significant improvement in gambling symptoms compared to placebo in a 16-week double-blind trial
- High rates of treatment discontinuation (63%).
- Side effect of opioid antagonists: nausea, dizziness, insomnia, headaches, and loose stool.



Psychosocial Treatment

Cognitive Behavioral Therapy

- Cognitive aspect includes psychoeducation, increased awareness of irrational cognitions, and cognitive restructuring.
- Behavioral techniques include identification of gambling triggers and the development of non-gambling sources to compete with the reinforcers associated with gambling.
- 9 published randomized trials of CBT for PG.
- Motivational enhancement therapy in combination with CBT in 1 randomized study.
- Gamblers Anonymous and self-exclusion programs have been examined, but not in controlled studies.

CBT

- One study of 40 subjects, individual cognitive therapy plus relapse prevention resulted in reduced gambling frequency and increased perceived self-control over gambling at 12 months when compared with a wait list control group.
- Another study of cognitive therapy plus relapse prevention in 88 subjects also produced improvement in gambling symptoms compared to a wait-list group at 3 months which was maintained for 12 months.
- Treatment discontinuation was high in both studies (37% and 47%, respectively)
- Outcome analyses included only those subjects who completed the studies.
- Although the treatment was manualized, no measures of therapist competence and adherence were reported.

CBT

- A randomized study of CBT in PG compared four groups: (1) individual stimulus control and in vivo exposure with response prevention, (2) group cognitive restructuring, (3) a combination of 1 and 2, and (4) a wait list control.
- At 12 months, rates of abstinence or minimal gambling were higher in the individual treatment (69%) compared with group cognitive restructuring (38%) and the combined treatment (38%).
- The same investigators further assessed individual and group relapse prevention for completers of a 6-week individual treatment program.
- At 12 months, 86% of those receiving individual relapse prevention and 78% of those in group relapse prevention had not relapsed, compared to 52% with no follow-up.

CBT

- 8-session manualized form of CBT with 231 subjects randomized to weekly sessions with an individual counselor, the therapy in the form of a workbook, or referral to Gamblers Anonymous.
- Using an intent-to-treat analysis, the individual therapy and workbook reduced gambling behaviors to a greater degree than referral to Gamblers Anonymous.
- This study has been summarized by the author in various review articles but the actual study methodology and results have not yet been published.

Group CBT

- Group cognitive therapy was tested against a wait-list control condition in 71 subjects with PG.
- Groups met weekly for 10 weeks and each session was 2 hours.
- After 10 sessions, 65% of those in group CBT no longer met criteria for PG, compared to 20% in the wait-list condition.
- At 24-month follow-up, 33% of the original sample still did not meet criteria for PG.

Brief Interventions

- One study randomly assigned 29 subjects to either workbook or to workbook plus a single in-depth interview.
- Workbook included cognitive-behavioral and motivational enhancement techniques.
- Both groups reported significant reductions in gambling at 6-months.
- A separate study assigned gamblers to a CBT workbook, a workbook plus a telephone motivational enhancement intervention, or a wait list.
- Abstinence at 6 months did not differ between groups although frequency of gambling and money lost were lower in the motivational intervention group.
- Compared to the workbook alone, those gamblers assigned to the motivational intervention and workbook reduced gambling throughout a 2-year follow-up period.

Imaginal Desensitization

- Used in conjunction with CBT.
- Taught relaxation and then instructed to imagine experiencing and resisting triggers to gambling.
- One study reported significant reduction in gambling behaviors in a comparison of imaginal desensitization to traditional aversion therapy in the randomized treatment of 20 compulsive gamblers.
- In a large study of 120 subjects randomly assigned to aversion therapy, imaginal desensitization, in vivo desensitization, or imaginal relaxation, subjects assigned to imaginal desensitization reported better outcomes at 1 month and up to 9 years later.
- This latter study, however, failed to follow-up on approximately half of the subjects.

Conclusions

- All studies have generally lacked a large enough sample for adequate statistical power. One exception is the multi-center nalmefene study that was adequately powered at the time of enrollment. The nalmefene study, however, suffered from a large treatment discontinuation rate which complicates the findings.
- Although several different classes of medication have shown efficacy in treating PG in individual studies, no positive, randomized, placebo-controlled study of medication in PG has been successfully reproduced.
- CBT has shown efficacy for PG, but no manualized CBT treatment has been examined in a confirmatory study by another independent investigator and most published studies have relatively small sample sizes.
- Manualized treatments of CBT have generally lacked published therapist adherence and competence measures.

More Conclusions

- Different classes of medication seem equally effective in PG. No comparison studies of medications have been performed in a randomized, placebo-controlled design.
- Both drug and behavioral treatments appear effective for PG.
- Few studies have systematically compared interventions or examined whether combinations of treatments are more beneficial.
- No study has examined whether certain individuals with PG would benefit differentially from specific pharmacotherapies or behavioral treatments.
- Comparisons of treatment studies have generally been problematic due to the lack of consensus on appropriate outcome measure or measures.
- With one exception, there have been no systematic dose-response studies for medication. The exception showed that 25mg/day and 50mg/day, but not 100mg/day was more effective than placebo

Even More Conclusions

- CBT studies have shown that both brief interventions and longer term therapy are potentially effective, but no study has yet examined the optimal duration of CBT.
- The long-term effects of medication for PG remain largely untested.
- Only two studies have examined pharmacological effects for 6 months, but these studies experienced drop-out rates of 59% and 44%.
- No study has examined pharmacological treatment effects for longer than 6 months or whether the effects of acute treatment last beyond the 8-16 weeks.
- Predictors of a positive response to pharmacotherapy and CBT have largely yet to be identified.
- There are limited data concerning the effectiveness of pharmacotherapy or CBT for PG subjects with co-occurring psychiatric conditions.