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REVIEW

Rapid ejaculation: a review of nosology, prevalence and treatment

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Information concerning the epidemiology, etiology and treatment of premature (rapid) ejaculation is reviewed. Evidence concerning the prevalence of premature ejaculation indicates that subjective concern about rapid ejaculation is a common concern worldwide. Hypotheses concerning the pathogenesis of premature ejaculation include: (1) that it is a learned pattern of ejaculation maintained by interpersonal anxiety, (2) that it is the result of dysfunction in central or peripheral mechanisms regulating ejaculatory thresholds and (3) that it is a normal variant in ejaculatory latency. Current evidence based treatment interventions include behavioral psychotherapy and the use of pharmacological agents, including topical anesthetic agents and selective serotonin reuptake inhibitors.
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Premature ejaculation

The conceptualization and treatment of premature ejaculation has evolved considerably in the last five decades. Initially, rapidity of ejaculation was conceptualized as learned behavior, which could best be treated by behavioral therapy. With the recognition that serotonergic drugs could delay ejaculation, clinicians began hypothesizing that physiological rather than psychological mechanisms might be primary in the etiology and maintenance of rapid ejaculation. To date, there is no definitive evidence regarding etiology and there is minimal evidence dictating whether behavioral or pharmacotherapy or their combination should be employed in treatment.

Premature ejaculation is generally regarded as one of the most common male sexual dysfunctions. However, much less is known about this disorder than erectile dysfunction and there is a lack of a commonly accepted definition for this complaint. The officially accepted definitions for premature ejaculation are imprecise. There is lack of consistent agreement concerning operational definitions employed in clinical research and there is also lack of agreement about the threshold cutoff value of ejaculatory latency delineating a pathological condition from normality. Some clinicians have suggested that the term premature ejaculation, which implies pathology be replaced by the term rapid ejaculation which is simply descriptive.

In spite of uncertainty regarding basic conceptualizations concerning premature ejaculation, men continue to seek treatment to delay ejaculation. The purpose of this paper will be to review the existing knowledge base concerning the definition, prevalence, etiology and treatment of rapid ejaculation.

Nomenclature

As mentioned above, there has been a lack of agreement concerning the definition of premature ejaculation. Masters and Johnson defined premature ejaculation as the man's inability to delay ejaculation long enough for his partner to reach orgasm on 50% of coital encounters.[1] This definition has a major flaw in that the definition is based on the partner's orgasmic capacity. For example, if a woman were totally anorgasmic, her male partner would be diagnosed as having premature ejaculation independent of his ejaculatory latency. Helen Singer Kaplan defined premature ejaculation as the absence of voluntary control over when ejaculation occurs.[2] However, many men would not consider their ejaculatory latency as being under voluntary

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control. Other clinicians and clinical investigators have defined premature ejaculation as ejaculation occurring within a certain number of thrusts or varying time periods after penetration.[3–5]

There are only two officially sanctioned definitions of premature ejaculation: the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) and the International Classification of Diseases and Related Health Problems, Tenth Edition (ICD-10). The DSM-IV defined premature ejaculation as persistent or recurrent ejaculation with minimal stimulation before or shortly after perpetration and before the person wishes it. A specific ejaculatory latency was not defined because of the absence of normative data.[6] A second part of the definition requires that the disorder cause marked personal or interpersonal distress. The definition of marked personal or interpersonal distress is problematic. Some clinicians would consider the fact that the patient is seeking treatment to be indicative of personal or interpersonal distress. Other investigators require more formal documentation of distress. The ICD-10 has a similar definition, requiring that there be an inability to delay ejaculation sufficiently to enjoy sexual activity. Occurrence of ejaculation must occur before or very soon after ejaculation.[7]

Most modern research uses the intravaginal ejaculatory latency time (IELT) as measured by stopwatch.[8] This technique which was originally used by a psychoanalyst in 1973[9] has become the standard because of work by the Dutch psychiatrist, Waldinger.[10] In a study of Dutch men complaining of lifelong rapid ejaculation, 90% ejaculated within 60 s of penetration. It is unclear how much the direct measurement of ejaculatory latency by stopwatch influences ejaculatory latency. Similarly, this study did not include a group of men without a complaint of premature ejaculation. Other investigators have used 120 s stating that this value results in minimal overlap between men without premature ejaculation and men with premature ejaculation.[11] A recent study of a community sample found that men diagnosed as having premature ejaculation had a median ejaculatory latency of less than 2 min, whereas men without this diagnosis had a median ejaculatory latency of 7.3 min. As this study was not based on a random sample of the population, the results cannot be used to establish normative values.[12] This author is unaware of any normative data on ejaculatory latency in the normal population. One study of ejaculatory latency in healthy Japanese male medical students receiving localized massage by the same woman indicated that ejaculatory times were normally distributed and that the mean ejaculatory latency was 156.5 s.[13] Clearly, comparability between studies requires a consistent definition or at a minimum, a statement indicating the operational definition employed in the study.

The DSM-IV requires that a distinction be made between lifelong and acquired premature ejaculation as well as between global and situational premature ejaculation. There is minimal evidence that such distinctions have clinical correlates or treatment implications. One would expect lifelong rapid ejaculation to reflect a constitutional predisposition to rapid ejaculation and acquired premature ejaculation to reflect the impact of disease processes or stress in late life. However, this is unproven. It is generally assumed that global premature ejaculation (occurring in all sexual situations) would also be likely to reflect a constitutional predisposition to rapid ejaculation, whereas situational premature ejaculation (occurring in one sexual situation and not another) would more likely be related to psychological issues. The DSM-IV also recommends that one distinguish between organic and psychological etiologies. Our current knowledge is so sparse that a distinction is seldom meaningful.

Epidemiology

The largest population study of the epidemiology of sexual disorders in the US was the National Health and Social Life Survey.[14] In this study a representative sample of the US population ages 18–59 years were interviewed. Approximately 28% reported a problem with ejaculating too soon in the past year. This complaint was most common in the oldest age group studied, the never married and in those with least education. A study in the UK utilized anonymous questionnaires sent to a stratified random sample of patients on general practice patient lists.[15] A similar prevalence of premature ejaculation was found. Thirty one percent endorsed this problem. There was a significant association of the presence of premature ejaculation and anxiety as measured by the Hospital Anxiety and Depression Scale.[16] The Global Study of Sexual Attitudes and Behavior provided data on 27 500 subjects ages 40–80 years from 29 countries.[17] A standard questionnaire was used in the study. In some countries, self-completed questionnaires were used. In others, there was either an in person or telephone interview. Sampling methods in North America, Australia, South Africa and New Zealand consisted of random digit dialing telephone interviews. In this population, approximately 28% complained of rapid ejaculation. In all countries, rapid ejaculation was the most common complaint. The prevalence was above 20% in Europe, Asia and South America. In the Middle East by comparison, only approximately 13% had this complaint. A study of sexual behavior in a representative sample of 10 173 Australian men aged 16–59 years found that 24% complained of coming to orgasm too quickly for at least one month of the

preceding year.[18] Other representative population studies using smaller sample sizes indicated a prevalence of premature ejaculation in 10% of married Swedish men[19] and in 14% of 51 year old Danish men.[20] It should be emphasized that none of these epidemiological studies assessed ejaculatory latency or level of interpersonal distress.

The DSM-IV requires the presence of personal or interpersonal distress to make the diagnosis of any sexual disorder. There may be large differences between the prevalence of distress in the male as compared to his partner. Haavio-Mannila and Kontula[21] reported survey data on representative samples of the population in Sweden, Finland, Estonia and St Petersberg, Russia. In all surveys reported, women stated that rapid ejaculation was a problem in her male partner far more often that men reported this problem. In Sweden and Finland, only 2–3% of the men reported than they ejaculated too soon somewhat often as compared to 18–22% of the women who complained that their male partners ejaculated too soon. Of interest is that 2/3 of the men said that their partners took too long to reach orgasm. Later cohorts of females reported this problem in their male partners far more often than earlier cohorts suggesting that societal changes may be raising expectations in women. Again, there was no evidence of a decline in the frequency of premature ejaculation with aging. The highest frequency of this complaint was in the oldest age group.

Neurophysiology

This brief review will focus on basic mechanisms that may be relevant to the understanding of the etiology and treatment of rapid ejaculation. The reader is referred elsewhere for more comprehensive reviews of the neuroanatomy and neurophysiology[22–24] of ejaculation.

Ejaculation can be understood as a series of spinal cord reflexes that are triggered when erotic stimulation reaches threshold levels. During the emission phase of ejaculation, contractions of the smooth muscle of the vas deferens, seminal vesicles and prostate deposit semen into the posterior urethra and reflex closure of the bladder neck occurs. This phase is mediated by the sympathetic nervous system. Fibers mediating emission arise from the thoracolumbar cord, travel in the hypogastric nerve and synapse with short adrenergic nerves, which appear to be primarily alpha-adrenergic. Electrical stimulation of the hypogastric nerve causes contraction of the vas deferens, prostate and bladder neck. Rhythmic contractions of the perineal musculature result in anterograde expulsion of the ejaculate. These contractions are mediated by motor fibers originating at the S2–S4 area of the cord.

We have minimal information about the neurophysiological mechanisms mediating the sensation of orgasm. Brain areas activated in rats after ejaculation include the posterior medial part of the bed nucleus of the stria terminalis, the lateral subarea of the posterodorsal part of the medial amygdale, the posterodorsal preoptic nucleus, and the medial part of the parvicellular subparafascicular nucleus of the thalamus.[25–27]

There has been minimal study of the brain mechanism involved in the perception of orgasm. Using implanted electrodes, Heath demonstrated that stimulation of the septal area elicited self-report of an orgasm-like experience. He also reported that orgasm produced electrical discharges from the same area.[28–30]

Brain imaging studies during ejaculation are a mechanism to study the brain structrures involved in orgasm in the human. The first positron emission tomography study during ejaculation was reported by Holstege *et al*.[31] Eleven healthy male volunteers were stimulated to orgasm by their female partners. During ejaculation, there was strong activation of the ventral tegmental field and the lateral central tegmental field. Increased activation was also observed in the lateral putamen, claustrum, insula, and parts of the prefrontal, temporal, parietal and insular cortexes. Further study is required to determine if the sensation of orgasm is mediated by these areas.

Supraspinal structures influence the ejaculatory threshold. The major supraspinal structures involved in ejaculation appear to be the medial preoptic area, paraventricular nucleus and the nucleus paragigantocellularis. Microinjection of dopamine D2 agonists into the medial preoptic area and paraventricular area elicit ejaculation.[32] There is reason to believe that the inhibitory effects of serotonin reuptake inhibitors on ejaculation are mediated by inhibitory serotonergic fibers in the nucleus paragigantocellularis in the medulla.[33] Lesions in this area facilitate ejaculation and prevent serotonin reuptake inhibitors from delaying ejaculation. Also, microinjection of serotonin reuptake inhibitors into the anterior lateral hypothalamus delays ejaculation.[34] It has been suggested that serotonin release in this area may be responsible for the refractory period. Gabaergic, cholinergic, adrenergic neurotransmission as well as nitric oxide may play secondary roles in modulating the ejaculatory response.[11]

From this brief sketch of the neurophysiology of ejaculation, one can understand the logic behind various strategies to delay ejaculation. Topical anesthetic agents are employed to decrease sensory input. Serotonergic agents are hypothesized to work by modifying the threshold value that elicits the ejaculatory response although these agents may also raise sensory thresholds in the genitalia. Alpha-blockers may exert their primary influence on the postsynaptic short adrenergic nerves.

It is important to remember that most of the information concerning the neurophysiology of ejaculation has been obtained from studies in lower animals and then extrapolated to the human. It is assumed but not proven that this information can be applied to the human.

Etiology

Given the absence of agreement concerning definition, it is not surprising that there are disparate theories concerning etiology. These theoretical positions are all connected to differing treatment approaches and there is minimal evidence to support one theory over the others. These theories fall into two major classes: psychological and biological. The psychological theories then mainly fall into two groups: psychodynamic and learning theory based. Psychodynamic concepts are rarely embraced by contemporary clinicians posit unconscious anger toward the partner as the major etiological factor. The man with premature ejaculation is hypothesized to have intense unconscious sadistic feelings toward women, an emotional immaturity preventing successful coping with his ambivalence, and with these ambivalent feelings finding symbolic expression in rapid ejaculation which denies pleasure to women.[35] Treatment consists of insight-oriented individual psychotherapy.[36] Given the complexity of psychodynamic theory construction, there is minimal evidence either supporting or disproving such formulations. Similarly, there are no controlled studies investigating the efficacy of psychoanalytically oriented psychotherapy in patients with rapid ejaculation.

The most widely accepted psychological hypotheses concerning the etiology of rapid ejaculation resemble the original Masters and Johnson formulation that it is a learned pattern of rapid ejaculation maintained primarily by performance anxiety.[37] Anxiety about sexual failure might interfere with a man's ability to monitor his level of sexual arousal and sensations indicating he is approaching ejaculatory inevitability.[38] This hypothesis has an appealing common sense simplicity to it although there is minimal evidence either supporting or rejecting this viewpoint. Other clinicians have stressed relationship factors such as the female partner not fostering or even sabotaging her mate's learning control and situations in which the couple may 'need the symptom' in order to divert attention from other issues. This viewpoint is promoted by a limited number of clinician whose practices may be limited primarily to couples for whom simpler treatment approaches have failed.[39,40] Laboratory studies have failed to demonstrate differences between men with premature ejaculation and normals in sexual arousal or sensory awareness.[41–43] However, it is unclear how closely behavior in laboratory setting approximates behavior in private sexual activity with a partner. Although there is minimal evidence to support a relationship between laboratory measures of performance anxiety and rapid ejaculation, there is some evidence supporting a relationship between premature ejaculation and anxiety as a general trait or psychiatric disorder. As mentioned previously, Dunn *et al*. found that a highly significant relationship ($P<0.0004$) between scores on the Hospital Anxiety and Depression Scale and the complaint of premature ejaculation. Figueira *et al*.[44] examined sexual function in patients with panic disorder and social anxiety. Premature ejaculation was found to be a problem in 47% of the patients diagnosed with social phobia. Studies reporting shorter ejaculatory latency in coital than masturbatory activities in men with premature ejaculation as compared to men with better ejaculatory control might be construed as supportive of the proposition that cognitive as well as biological factors play a role in the genesis and maintenance of rapid ejaculation.

Biological theories concerning the etiology of premature ejaculation can be separated into two major groups: those that emphasize peripheral or spinal mechanisms as opposed to those which posit cerebral mechanisms. Clearly, it is likely that the two may be related in that brain mechanisms may influence peripheral ejaculatory thresholds and sensory sensitivity. To date, studies of differences in penile sensitivity between men with premature ejaculation and thus without have been inconsistent.[45,46] Similarly, studies of the bulbocavernous reflex and evoked cortical sensory potentials have not consistently found differences between the two groups of men.[47,48] The major theoretical formulation concerning cerebral mechanisms underlying lifelong premature ejaculation has been formulated by the Dutch psychiatrist, Waldinger.[49] He postulates that lifelong patterns of rapid ejaculation are genetically determined and that men with hyposensitivity of the 5HT2c receptor and hypersensitivity of the 5HT1a receptor have their ejaculatory thresholds set at a lower point. The hypothesis of different effects on ejaculation by stimulation of serotonergic receptors is based primarily on data that serotonergic drugs which activate the 5HT2c receptor (ex paroxetine) delay ejaculation and that this can be reversed by drugs which stimulate the 5HT1a receptor (ex buspirone).[50,51] Although this hypothesis is appealing, there is little direct evidence to support it. Waldinger has reported a higher familial incidence of premature ejaculation based on a very small sample of men with rapid ejaculation. Intrinsic to Waldinger's formulation is that rapid ejaculation represents a normal variation in ejaculatory speed and as such is not a psychiatric disorder. This is similar to the hypothesis that rapid ejaculation probably may have had adaptive value.[52] It is worth noting that the hypothesis of genetic

differences in ejaculatory thresholds does not preclude men with a tendency toward rapid ejaculation being able to learn ways to compensate for their hereditary tendencies.

In summary, there is minimal evidence to support any of the current theories concerning the etiology of lifelong premature ejaculation. It would appear reasonable to assume that there are inherited differences in ejaculatory threshold that the tendency to rapid ejaculation may be offset to a certain extent by social learning and that interpersonal anxiety might interfere with such learning. Although this statement is consistent with available data, there is minimal evidence to support it.

There is isolated evidence concerning possible factors contributing to acquired premature ejaculation. Several clinical series[53,54] have reported a high prevalence of premature ejaculation in men with chronic prostatitis and there is a case report of ejaculatory time normalizing with treatment of the prostatitis.[55] There are also reports of a high incidence of premature ejaculation after traumatic brain injury,[56] after spinal cord injury,[57] in men with noninsulin-dependent diabetes,[58] in men with idiopathic hypogonadism[59] and in male hemodialysis patients.[60] None of these studies had a comparison group. Given the high incidence of rapid ejaculation in the general population, the absence of a uniform definition, and the small sample size in most of these studies, these findings should be regarded as hypothesis generating.

Treatment

Three major approaches to the treatment of rapid ejaculation have been advocated: behavioral therapy procedures, topical anesthetic ointments and central oral agents, particularly those with serotonergic effects. There is reason to believe that all three approaches are effective.

Semans[61] described a behavioral technique involving manual stimulation of the penis by the partner which was momentarily stopped when the male signaled impeding orgasm. Repetition of this sequence several times at least twice a week for 5–6 weeks while abstaining from coitus was reported to result in greater ejaculatory control presumably because the male became more aware of his level of sexual arousal. This technique was modified by the addition of the frenulum squeeze when the male signaled to his partner that ejaculation was imminent.[62] Numerous clinicians have reported high success rates utilizing both procedures, either alone or in combination with couple psychotherapy.[63–67] Although initial success rates were often in the 80% range, follow-up studies demonstrated that most of this gain in ejaculatory control was not sustained 3 years later.[68,69] Although it is commonly assumed by most clinicians to be an effective intervention, it should be noted that most of these studies did not use a waiting list control group, a common definition of premature ejaculation, nor direct measurement of ejaculatory latency. One study reported that behavioral techniques were superior to a waiting list control in increasing ejaculatory latency[70] and one study found that behavior therapy was equivalent to sertraline in its efficacy.[71] The absence of sustained efficacy would appear to be of minor consequence for a procedure which only involved 5–6 outpatient visits. In other words, recurrence of the problem could be treated by the same brief intervention. Another form of psychological intervention has been described by de Carufel.[72] This approach has been described as functional-sexological treatment and consists of teaching the male to recognize signals which indicate various levels of sexual excitement and then to learn ways to keep excitement at high levels of intensity yet below the ejaculatory threshold. One controlled study indicated that this approach has comparable efficacy to standard behavioral treatment (frenulum squeeze and start stop) and that both methods are superior to a waiting list control.[70]

The use of topical local anesthetic creams or sprays have been reported to be effective in delaying ejaculation. The major side effect is penile hypoanesthesia. Vaginal absorption may also occur unless a condom is utilized. Although one investigator reported that ethyl aminibenzoate[73] could be used, most have studied the use of prilocaine-lidocaine mixture either in cream[74–76] or aerosol formulations.[77] IELT has been reported to increase by 7–11 min. Studies have demonstrated the efficacy of such mixtures as compared to inert creams. Another approach has been the use of SS-cream, which is made with extracts from nine natural herbs, some of which have local anesthetic properties. This cream is applied 1 h before coitus and washed off immediately before coitus.[78] Double-blind, placebo-controlled randomized studies have demonstrated efficacy of this approach, with intravaginal ejaculatory latency increasing from an average of 1.37 min to an average of 10.92 min.[79] Another randomized, double-blind, placebo-controlled study found a dose–response relationship between dose of SS-cream and increase in vibratory thresholds.[80] A study in rabbits have demonstrated that SS-cream increase the latency of spinal somatosensory potentials evoked by stimulation of the glans penis.[81] The necessity of application before coitus combined with removal of the ointment or use of a condom to prevent transfer to the female partner before intromission limits the attractiveness of this approach for many men.

Pharmacological treatments for rapid ejaculation had their origin in the clinical observation that many drugs, especially psychiatric drugs, had side effects of delaying ejaculation. There were case

reports of various agents including monoamine oxidase inhibitors, tricyclic antidepressants and antipsychotics being used to treat rapid ejaculation.[82] Controlled trials with serotonergic drugs began relatively recently These drugs were in clinical usage for almost a decade before their sexual side effects were generally recognized by clinicians.[83,84] For example, a placebo-controlled trail of clomipramine for the treatment of obsessive-compulsive disorder in 1987 found that 96% of patients had inability to ejaculate or severely delayed ejaculation as a side effect.[85] The severity and frequency of side effect lead to serious treatment noncompliance. However, it was not until 1993 and 1995 that there were published controlled trials of the use of clomipramine for the treatment of rapid ejaculation.[86,87] The selective serotonin reuptake inhibitors (SSRIs) were next noted to cause ejaculatory delay as a side effect. The presence or absence of sexual side effects was then used as a marketing strategy by some companies.

Subsequently, numerous clinical trials have assessed whether the sexual side effects of serotonergic drugs might have some benefit in treating rapid ejaculation. There have been controlled trials indicating that chronic dosing with clomipramine, paroxetine, sertraline, fluoxetine and citalopram all delay ejaculation in men with rapid ejaculation.[88–100] The few trials comparing clomipramine (a serotonergic tricyclic antidepressant) with the SSRIs, have found a tendency for clomipramine to cause more ejaculatory delay than serotonin reuptake inhibitors.[11,90] Studies comparing chronic dosing of various serotonin reuptake inhibitors with each other have consistently found more ejaculatory delay with paroxetine.[95,96] The studies of the efficacy of various agents for the treatment of rapid ejaculation are consistent with results from studies of the sexual side effects of these drugs when used to treat psychiatric patients. In those studies, clomipramine has a very high incidence of ejaculatory disturbance[85] and paroxetine usually is found to have a higher incidence of sexual side effects than other SSRIs.[101–104] There have been two studies evaluating serotonergic agents used on a PRN basis. Both paroxetine taken 3–4 h before coitus and clomipramine taken 6 h before coitus have been shown to be effective if taken on a PRN basis.[87,93] There have not been studies to determine the optimal time interval between drug ingestion and beginning of sexual activity. There is suggestive evidence that as needed dosing of paroxetine may be more effective after several weeks of steady dosing.

There have also been several reports that sildenafil in addition to serotonergic drugs may help in the treatment of rapid ejaculation.[105,106] To date, there have no large multicenter trials indicating that sildenafil affects ejaculatory latency. A recent double-blind, placebo-controlled study of sildenafil in the treatment of men with premature ejaculation did not find any effect of sildenafil on ejaculatory latency.[107]

It has long been recognized that drugs that block alpha-adrenergic receptors have side effects of retarding ejaculation. This has been recognized both with traditional antipsychotics, certain antihypertensives, and in alpha-adrenergic blockers used to treat the symptoms of prostatic hypertrophy. One controlled crossover study found that both alphuzosine and terazosine delayed ejaculation more than vitamin C.[108]

Conclusions

The absence of a commonly accepted and precise definition of premature ejaculation limits the conclusions one can make concerning the epidemiology of this disorder. It is clear that subjective complaints of rapid ejaculation are quite common in most cultures studied. There is limited evidence suggesting that the frequency of this subjective complaint may be related to changes in societal norms regarding female expectations of pleasure in sexual activity.

To date, there is no evidence regarding the etiology of premature ejaculation, which has been consistently replicated by other investigators. There is suggestive evidence that men with premature ejaculation are more likely to endorse questionnaire items indicating anxiety. Research concerning etiological factors may be difficult to replicate because of the varying and often imprecise definitions of premature ejaculation employed by different investigators. Most of the research concerning etiology has proceeded on the assumption that men with and without premature ejaculation represent dichotomous populations. An alternative strategy is to assume that ejaculatory latency is a normally distributed variable. This assumption would redirect research to finding variables, which co-vary with ejaculatory latency.

The available data suggests that both behavioral therapy and pharmacotherapy may be effective. There is more evidence supporting the efficacy of pharmacotherapy but the minimal evidence available suggests that both are effective in delaying ejaculation. Among pharmacotherapeutic approaches, evidence supports the efficacy of serotonergic antidepressants and the use of topical anesthetic agents. Of the currently available serotonergic drugs, paroxetine and clomipramine appear most effective. There is no evidence concerning when psychotherapy as opposed to pharmacotherapy should be employed or when both should be used concurrently.

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