Approach to treating depersonalization/derealization disorder

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Literature review current through: **Oct 2023.**
This topic last updated: **Mar 10, 2021.**

INTRODUCTION

Depersonalization/derealization disorder (DDD) is characterized by persistent or recurrent depersonalization and/or derealization that causes clinically significant distress. Reality testing remains intact, and no medical causes can be identified [1]. Depersonalization and/or derealization can be precipitated by acute and chronic traumatic experiences.

DDD has a prevalence of approximately 1 to 2 percent and is associated with significant morbidity, yet often goes undetected or misdiagnosed, leading to delays in treatment. DDD has high rates of comorbidity with depression and anxiety disorders, as well as avoidant and borderline personality disorders.

This topic discusses our approach to selecting treatments for DDD (algorithm 1). The epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis of DDD are discussed separately. Information on the components, efficacy, and administration of individual psychotherapies for DDD are also described separately. Information on the efficacy, dosing, and side effects of individual medications for DDD are also described separately. (See "Depersonalization/derealization disorder: Epidemiology, clinical features, assessment, and diagnosis" and "Depersonalization/derealization disorder: Psychotherapy" and "Pharmacotherapy of depersonalization/derealization disorder".)

DEFINITIONS

Depersonalization — Depersonalization is a persistent or recurrent feeling of detachment or estrangement from one's self. An individual experiencing depersonalization may report feeling like an automaton, as if in a dream, or as if watching themself in a movie. Depersonalized individuals may report the sense of being an outside observer of their mental processes or their body, or at its extreme, lacking a sense of self. Another common feature is hypoemotionality (emotional numbing or blunting), specifically detachment from feelings that an individual knows they have. They often report feeling a loss of agency over their thoughts, perceptions, and actions.

Derealization — Derealization is a subjective sense of detachment or unreality regarding the world around them (eg, individuals or objects are experienced as unreal, dreamlike, foggy, lifeless, seen through a glass, bubble, or veil, or visually distorted).

GENERAL PRINCIPLES

Treatment of all patients with depersonalization/derealization disorder (DDD) should incorporate elements of psychoeducation and supportive psychotherapy [2], including:

- **Education** – Giving the condition a name and providing information about the nature and course of the disorder can help patients significantly, particularly since many may have struggled for years with misdiagnosis or inaccurate labeling of their symptoms. (See "Depersonalization/derealization disorder: Epidemiology, clinical features, assessment, and diagnosis".)
- **Reassurance** – Common fears about the disorder lack foundation:
  - The condition will not evolve into a psychotic disorder.
  - There is no evidence linking the disorder to permanent brain damage.
- **Alleviating potential sources of guilt or shame** – In the case of chronic depersonalization triggered by use of an illicit drug, it can be useful to explain to the patient that, while we do not know to a scientific certainty, we assume that the individual had an underlying diathesis to depersonalize, which could have been triggered at any point in his or her life by a variety of chemical or psychosocial stressors. (See "Depersonalization/derealization disorder: Epidemiology, clinical features, assessment, and diagnosis", section on 'Pathogenesis'.)

- **Substance use** – Most patients with symptom onset triggered by substance abuse become "drug phobic" after onset and stop using the substance. The small minority who continue use should be counseled that they must stop or risk an intensification of symptoms. (See "Depersonalization/derealization disorder: Epidemiology, clinical features, assessment, and diagnosis", section on 'Organic precursors'.)

- **Providing hope for the future** – Although accurate prognostic statistics based on prospective studies are not available, it is clear that at least a portion of those affected, whether with the assistance of treatment or spontaneously, experience improvement or remissions over time. (See "Depersonalization/derealization disorder: Epidemiology, clinical features, assessment, and diagnosis", section on 'Course'.)

- **Heritability** — Reassuring women who are considering pregnancy that the heritability of DDD, while not well studied, appears to be limited. (See "Depersonalization/derealization disorder: Epidemiology, clinical features, assessment, and diagnosis", section on 'Pathogenesis'.)

- **Challenging the "physicality" of the experience** – This is a common patient experience, and thus it is important to emphasize that as physical as the symptoms may feel, the disorder is psychological. This understanding can provide the patient with a sense of control over the symptoms that may otherwise be perceived as physically imposed rather than mentally maintained.

INITIAL TREATMENT

Choosing between psychotherapy and medication — For patients with a new diagnosis of depersonalization/derealization disorder (DDD) in the absence of significant comorbid symptoms such as depression or anxiety, we suggest first-line treatment with psychotherapy rather than medication or other interventions. These modalities have not been compared in randomized clinical trials of DDD patients. In our clinical experience, psychotherapy can reduce depersonalization and derealization associated with DDD, while medication has only been found efficacious for selected target symptoms [3]. (See "Pharmacotherapy of depersonalization/derealization disorder" and "Depersonalization/derealization disorder: Psychotherapy".)

Psychotherapy for DDD should be provided weekly for a minimum of three months, but is often a longer-term therapy in those with major character pathology. (See 'General principles' above.)

Selecting a psychotherapy — Several psychotherapies are used to treat DDD, including psychodynamic, cognitive-behavioral, hypnotherapeutic, and supportive therapies. None of these psychotherapies have been tested in randomized clinical trials in comparison with placebo or compared with one another.

For most patients newly diagnosed with acute DDD, we suggest first-line treatment with cognitive-behavioral therapy (CBT) over other psychotherapies. The focus of CBT for DDD is on normalizing the symptoms and their interpretation; blocking of ruminative thoughts surrounding the condition; resisting checking behaviors; and grounding exercises. Our clinical experience and an uncontrolled, prospective trial suggested CBT can reduce DDD symptoms [4]. Treatment of DDD with CBT is reviewed in greater detail separately. (See "Depersonalization/derealization disorder: Psychotherapy", section on 'Cognitive-behavioral therapy'.)

Patient subgroups

Affect intolerance — For psychologically minded patients with DDD in whom the fluctuation of symptoms is linked to affect intolerance, identity confusion, separation fears, or various traumas, we suggest psychodynamic psychotherapy focused on affect processing rather than CBT.

No clinical trials have been conducted on psychodynamic psychotherapy for DDD. In our clinical experience, psychodynamic psychotherapy can be very helpful for the suggested subgroup. A case report illustrates such an approach [5]. Treatment of DDD with psychodynamic psychotherapy is reviewed in greater detail separately. (See "Depersonalization/derealization disorder: Psychotherapy", section on 'Psychodynamic therapy'.)

In our experience, psychodynamic psychotherapy needs to be conducted at a minimum of once weekly, and often more frequently, to facilitate working through the dissociation and processing the underlying affects and dynamics, leading to structural change.

Co-occurring depression or anxiety — For most DDD patients with co-occurring depression or an anxiety disorder, we suggest first-line treatment with CBT in combination with a selective serotonin reuptake inhibitor (SSRI). CBT should target symptoms of both co-occurring disorders. SSRIs and CBT are effective treatments for depression and anxiety disorders. (See "Depersonalization/derealization disorder: Epidemiology, clinical features, assessment, and diagnosis", section on 'Comorbid conditions' and "Depersonalization/derealization disorder: Psychotherapy" and "Pharmacotherapy of depersonalization/derealization disorder" and "Unipolar major depression in adults: Choosing initial treatment" and "Generalized anxiety disorder in adults: Management".)

Although the only randomized trial of an SSRI for DDD did not find the SSRI to be efficacious compared with placebo [6], in our clinical experience, DDD will often lessen as the co-occurring disorder is treated, especially in the acute phase of the illness. Although head-to-head comparisons between psychotherapy alone and combined therapy and medication have not been made, it could reasonably argued that for any DDD patient with depression, medication is better started sooner rather than later.

As an example in treating depression concurrent with DDD, paroxetine can be used at an initial therapeutic dose of 20 mg/day. If the response is insufficient after a trial of four to six weeks, trials at higher doses to a maximum of 40 mg/day can be tried. When treating anxiety, the SSRI is started at a low dose (eg, 10 mg/day) to minimize the risk of feeling “drugged,” which is a common trigger that leads DDD patients to stop medications.

Common side effects of SSRIs include sexual dysfunction, nausea, diarrhea, insomnia, and withdrawal on discontinuation. SSRIs can also cause drug interactions, weight gain, and agitation and/or hyperactivation. (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects".)

Intense, disabling anxiety — If anxiety is intense and disabling, a benzodiazepine can be added for the first few weeks when the SSRI is not yet effective. As an example, clonazepam can be used, starting at an initial dose of 0.5 mg/day two times daily and increased to reasonable symptom control. (See "Pharmacotherapy of depersonalization/derealization disorder", section on 'Benzodiazepines'.)

TREATMENT RESPONSE

Poor or partial response — Treatment options for depersonalization/derealization disorder (DDD) patients who experience an inadequate response to a trial of education, psychotherapy, and support include longer-term psychotherapy, medication, and (for those potentially responsive) hypnosis. In the absence of data comparing the efficacy of these interventions, the selection among them can be made on the basis of patient preference and treatment availability. Specific medications are suggested for patient subgroups with certain clinical features.

Longer-term psychotherapy — DDD patients with a partial response may, in our experience, benefit from longer-term psychotherapy addressing underlying conflicts and traumas for continued symptomatic improvement. After experiencing some benefit, the patient may actively seek out extended therapy or may be more open to considering it. As with any other condition,

resistances to cognitive-behavioral or dynamic approaches may be more prominent in certain patients, and some become convinced they cannot function in the world, leading to gradual steady decompensation. It is important to help patients see the value of maximizing functioning despite distressing symptoms.

Hypnotizable patients — In our experience, hypnosis can be a useful tool for treating patients with DDD who have not adequately responded to cognitive-behavioral therapy. One way in which hypnosis works to modulate symptoms is by helping the patient imagine being in those situations that reduce their symptoms. Hypnosis can be used to induce physical comfort and better manage stressors by dissociating them from their customary somatic responses (eg, picturing the stressor while imagining being in a physically comfortable situation) [7,8]. Alternatively, patients may imagine being in a situation that exacerbates their symptoms and learn to avoid struggling against depersonalization and/or derealization which may exacerbate it. Under hypnosis patients can also imagine and evoke memories of when they were not in a depersonalized state. There are no clinical trials testing the efficacy of hypnosis in patients with DDD.

Hypnosis for patients with DDD is typically provided in 10 60-minute sessions occurring weekly. A brief clinical test of hypnotizability such as the Hypnotic Induction Profile [9,10] provides information about whether or not the patient is sufficiently hypnotizable to potentially benefit from the technique [7,8]. Treatment of DDD with hypnosis is reviewed in greater detail separately. (See "Depersonalization/derealization disorder: Psychotherapy", section on 'Hypnosis'.)

Medication strategies

Noncomorbid patients — For noncomorbid DDD patients with a poor or partial response to initial psychotherapy, we suggest a trial of lamotrigine. Lamotrigine has been found to be efficacious in DDD in a randomized clinical trial [11]. Lamotrigine can be started at 25 mg daily for the first two weeks of treatment, then increased to 50 mg daily for weeks 3 and 4. The dose is thereafter titrated to effect and tolerance. After week 4, the daily dose can be increased by 50 mg every one to two weeks. A common maintenance dose is 200 mg daily given in two divided doses, but total daily doses up to 400 mg given in two divided doses have been used. (See "Pharmacotherapy of depersonalization/derealization disorder", section on 'Lamotrigine'.)

Data are inadequate to guide the duration of medication treatment for DDD, but in our clinical experience, DDD patients who respond to medication should continue it for a minimum of 6 to 12 months.

Emotional numbing — Some DDD patients may experience worsened hypoemotionality (emotional numbing or blunting) with selective serotonin reuptake inhibitors (SSRIs) and respond better to an alternative medication. For DDD patients with pronounced hypoemotionality that does not respond adequately to psychotherapy or SSRIs, we suggest a trial of clomipramine to target depression, anxiety, and obsessional ruminations based on our clinical experience. There are no clinical trials of clomipramine for DDD.

Treatment with naltrexone, a nonselective opioid antagonist, would be a reasonable alternative. Naltrexone has not been studied in randomized clinical trials for DDD; a small uncontrolled trial reported an average 30 percent improvement [3]. In our clinical experience, DDD patients with pronounced hypoemotionality that does not respond to psychotherapy may benefit from naltrexone. Naltrexone is given orally at a starting dose of 50 mg/day, and gradually increased up to 250 mg/day if tolerated. Treatment of DDD with naltrexone is reviewed in greater detail separately. (See "Pharmacotherapy of depersonalization/derealization disorder", section on 'Naltrexone'.)

Common side effects of oral naltrexone are nausea, headache, and dizziness, which subside with continued use. Higher doses of naltrexone are associated with an increased risk of hepatotoxicity. Use of naltrexone, like any medication, should be preceded by a discussion of potential risks and benefits. Use of the drug should be accompanied by monitoring with liver function tests every two weeks while starting and increasing doses, followed by every six weeks during acute treatment and at three-month intervals thereafter.

TREATMENT RESISTANCE

Patients who do not experience adequate remission of depersonalization/derealization disorder (DDD) following the interventions above can be offered a trial of transcranial magnetic stimulation (TMS). Two small, uncontrolled trials found TMS to be associated with reduced DDD symptoms in some patients [12], one trial using a posterior cortical target and the other a prefrontal one. (See "Pharmacotherapy of depersonalization/derealization disorder", section on 'Other interventions'.)

Chronic DDD with severe impairment — Some severely impaired patients with chronic DDD and extreme distress may require long-term supportive psychotherapy. These are patients whose educational, occupational, or social lives have been significantly impaired by the disorder, but whose course has been continuous with unrelenting intensity and minimal fluctuations, which limit the therapist's ability to apply psychodynamic or cognitive-behavioral therapy techniques.

Supportive psychotherapy for DDD has not been tested formally, but in our clinical experience, it can be helpful in maintaining or improving occupational and social functioning, and in lessening the severe distress often associated with the disorder by cultivating an attitude of acceptance within the context of striving for change. Participation in supportive psychotherapy by family members and significant others (who may have a limited understanding of DDD or may misunderstand the disorder) can at times be very helpful. (See "Depersonalization/derealization disorder: Psychotherapy", section on 'Supportive psychotherapy'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Dissociative disorders".)

SUMMARY AND RECOMMENDATIONS

- An algorithm depicts our approach to treating depersonalization/derealization disorder (DDD) (algorithm 1). The treatment recommendations are based on clinical experience and very limited published data.

- For most patients with DDD, we suggest first-line treatment with cognitive-behavioral therapy (CBT) rather than other interventions (**Grade 2C**). Treatment should include education about the disorder and components of supportive psychotherapy such as reassurance and maintaining hope for the future. (See 'Initial treatment' above and 'General principles' above and "Depersonalization/derealization disorder: Psychotherapy", section on 'Cognitive-behavioral therapy'.)

  - For patients with DDD in whom the fluctuation of symptoms is linked to affect intolerance and identifiable underlying conflicts, we suggest psychodynamic psychotherapy focused on affect processing to treat the disorder rather than CBT (**Grade 2C**). (See 'Affect intolerance' above and "Depersonalization/derealization disorder: Psychotherapy", section on 'Psychodynamic therapy'.)

  - For DDD patients with co-occurring depression or an anxiety disorder, we suggest first-line treatment with CBT in combination with a selective serotonin reuptake inhibitor (SSRI) rather than CBT alone (**Grade 2C**). CBT should target symptoms of both co-occurring disorders. For anxiety that is intense and disabling, a benzodiazepine may be

added to the SSRI during the initial weeks of treatment before the serotonergic drug can take effect. (See 'Co-occurring depression or anxiety' above.)

- Treatment options for DDD patients who experience an inadequate response to a psychotherapy trial include longer-term psychotherapy, medication, and (for those potentially responsive) hypnosis. In the absence of data comparing the efficacy of these interventions, the selection between them can be made on the basis of patient preference and treatment availability. (See 'Poor or partial response' above.)

  - DDD patients with a partial response to psychotherapy may, in our experience, benefit from longer-term psychotherapy addressing underlying conflicts and traumas for continued symptomatic improvement. (See 'Longer-term psychotherapy' above.)

  - Hypnosis can be a useful tool for teaching patients with DDD who have not adequately responded to CBT in our clinical experience. Hypnosis aims to modulate symptoms by helping the patient to imagine being in situations that usually reduce or even exacerbate them. Hypnosis can also be used to induce physical comfort and better manage stressors by dissociating them from their customary somatic responses. (See 'Hypnotizable patients' above.)

  - For many noncomorbid DDD patients with a poor or partial response to initial psychotherapy, we suggest a trial of lamotrigine rather than other medications (**Grade 2C**). Data are inadequate to guide the duration of medication treatment for DDD, but based on our experience, DDD patients who respond to medication should continue it for a minimum of 6 to 12 months. (See 'Medication strategies' above and "Pharmacotherapy of depersonalization/derealization disorder", section on 'Lamotrigine'.)

  - For DDD patients with pronounced hypoemotionality that does not respond adequately to psychotherapy or SSRIs, we suggest a trial of clomipramine rather than other medications (**Grade 2C**). Treatment with naltrexone would be a reasonable alternative. (See 'Emotional numbing' above and "Pharmacotherapy of depersonalization/derealization disorder".)

- Patients with chronic, treatment-refractory DDD can benefit from supportive psychotherapy that addresses occupational and social functioning, and alleviating to the degree possible the severe distress often associated with the disorder. Transcranial magnetic stimulation can also be considered in patients with treatment-refractory DDD. (See 'Chronic DDD with severe impairment' above and "Depersonalization/derealization

disorder: Psychotherapy", section on 'Supportive psychotherapy' and "Pharmacotherapy of depersonalization/derealization disorder", section on 'Other interventions'.)

Topic 108150 Version 10.0

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