

# Anger Attacks in Patients With Depression

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Anger attacks are sudden intense spells of anger that resemble panic attacks but lack the predominant affects of fear and anxiety associated with panic attacks. They typically occur in situations in which an individual feels emotionally trapped and experiences outbursts of anger that are later described by the patient as being uncharacteristic and inappropriate to the situation at hand. Anger attacks consist of both behavioral and autonomic features, and various criteria and an Anger Attacks Questionnaire have been designed to identify the presence of these attacks. The prevalence of anger attacks in depressed patients is approximately 30% to 40%, and the attacks have disappeared in 53% to 71% of depressed patients treated with fluoxetine, sertraline, or imipramine. This article discusses the development of the concept of anger attacks, the presence of anger attacks in depression and other psychiatric disorders, and the current treatment of anger attacks.

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**A**nger attacks are sudden intense spells of anger that resemble panic attacks but lack the predominant affects of fear and anxiety associated with panic attacks. Anger attacks typically occur in situations in which an individual feels emotionally trapped and experiences outbursts of anger. Dysregulated anger is a state in which the behavior must be provoked in order to be observed. Thus, an anger attack is a combination of predisposition—or some enduring state of vulnerability—and provocation. It is possible that dysregulated anger is a response to the fight/flight reaction expressed cognitively and behaviorally as anger and fight instead of fear and flight.<sup>1</sup> On the other hand, anger and irritability may be part of a depressive symptomatology.<sup>2</sup> Irritable mood is a core symptom of major depressive disorder in children and adolescents but is emphasized less as a symptom of depression in adults. Nevertheless, Snaith and Taylor<sup>3</sup> report that 37% of depressed inpatients had moderate-to-severe outwardly directed irritability, and findings from the Epidemiologic Catchment Area surveys indicate that depression is related to violent behavior in samples taken from the community.<sup>4</sup> Moreover, a substantial number of depressed adult patients seek medical treatment because of irritability and/or anger that causes distress and conflict in their lives. This article will discuss

the development of the concept of anger attacks, the presence of anger attacks in depression and other psychiatric disorders, and the current treatment of anger attacks.

In 1990, we<sup>5</sup> reported on a series of patients who experienced sudden outbursts of anger resembling panic attacks. These anger attacks were described by the patients as uncharacteristic behavior that was inappropriate for the situation at hand and was followed by remorse. The outbursts of angry behavior were accompanied by physical features of autonomic activation that included sweating, trembling, tachycardia, and hot flashes. Since the anger attacks improved with antidepressant treatment, they were postulated to be variants of major depression. A self-rating Anger Attacks Questionnaire was subsequently designed as an ad hoc instrument for assessing the presence of anger and was administered to patients already participating in clinical trials. Surprisingly, anger attacks—as defined by the questionnaire—were significantly more common among depressed outpatients than in healthy volunteers with no known psychiatric history.<sup>6</sup>

## ANGER ATTACKS AND DEPRESSION

The prevalence of anger attacks in patients with major depression has been assessed at 44% (56/127) in one sample,<sup>7</sup> 39% (64/164) in a later sample,<sup>8</sup> and 38% (36/94) in patients with atypical major depression, 28% (21/74) in patients with dysthymia, and 0% (0/38) in screened normal controls.<sup>9</sup> Given the presence of mood reactivity in atypical major depression, the prevalence of anger attacks is similar whether patients have typical or atypical major depression. On the basis of these findings, the prevalence of anger attacks in depressed populations is approximately 30% to 40%.<sup>10</sup> While no significant differences in rates of lifetime comorbid anxiety, eating, and substance use disorder

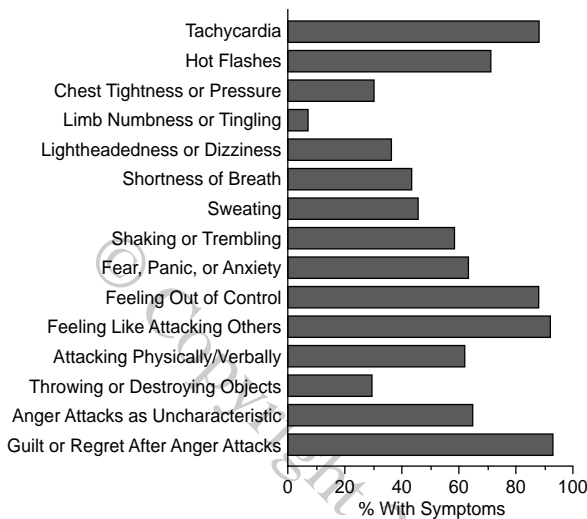
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**Figure 1. Frequency of Autonomic Arousal Symptoms and Behavioral Outbursts During Anger Attacks (N = 56)<sup>a</sup>**



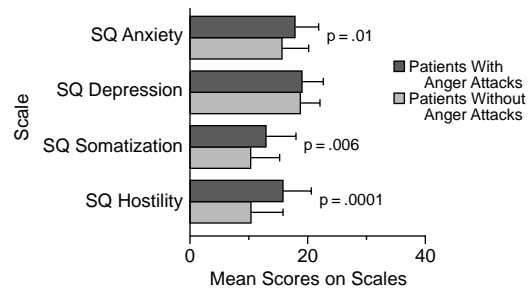
<sup>a</sup>Data adapted from reference 7.

ders were found between depressed patients with and without anger attacks, 8% of depressed patients with anger attacks met criteria for current comorbid panic disorder compared with 3% of depressed patients without anger attacks, with a trend toward a statistically significant difference.<sup>11</sup>

**Criteria and Measurement of Anger Attacks**

The criteria adopted to define anger attacks<sup>6</sup> include (1) irritability during the previous 6 months, (2) overreaction to minor annoyances with anger, (3) occurrence of 1 or more anger attacks during the previous month, and (4) inappropriate anger and rage directed at others during an anger attack. Additional criteria—modeled in part from the DSM-IV criteria for panic attack—include the occurrence of at least 4 of the following autonomic and/or behavioral features in at least 1 of the attacks: heart palpitations, flushing, chest tightness or pressure, paresthesias, light-headedness or dizziness, excessive sweating, shortness of breath, shaking or trembling, intense fear or anxiety, feeling out of control, feeling like attacking others, physically and/or verbally attacking others, and throwing or destroying objects. In 79 consecutive patients (25 men, 54 women) with major depression diagnosed by the Structured Clinical Interview for DSM-III-R (SCID) and assessed with the Anger Attacks Questionnaire, 34 patients (13 men, 21 women) reported having anger attacks according to the criteria.<sup>6</sup> In a sample of 127 depressed outpatients, 56 (44%) reported a mean ± SD of 7.4 ± 13.0 anger attacks per month when assessed with the Anger Attacks Questionnaire.<sup>7</sup> The most frequently reported autonomic arousal symptoms and behavioral features that occurred during the anger attacks were tachycardia, hot flashes, the feeling of being out of control, and the feeling of wanting

**Figure 2. Scores of Depressed Patients With and Without Anger Attacks on Symptom Questionnaire<sup>a</sup>**



<sup>a</sup>Data adapted from reference 7.

to attack others. While 63% of the patients with anger attacks reported physical or verbal attacks directed at others, only 30% actually threw objects or destroyed property. After the attacks, guilt or regret was almost universal (93%) (Figure 1).<sup>7</sup> On the Symptom Questionnaire that measures global psychological distress, depressed patients with anger attacks scored higher on the anxiety, somatization, and hostility scales than depressed patients without anger attacks. No significant difference was noted on the depression scale of the Symptom Questionnaire between patients with and without anger attacks, a finding that corresponded with Hamilton Depression Rating Scale (HAM-D) scores (Figure 2).<sup>7</sup> High scores on the anxiety scale may be a reflection of the autonomic symptoms experienced or a possible link between dysregulated anger and anxiety.

Irritability and anger in depressed patients is sometimes viewed as evidence for a personality disorder, and the self-rated Personality Diagnostic Questionnaire-Revised (PDQ-R) was used to assess comorbid personality disorders in depressed patients with and without anger attacks. Depressed patients with anger attacks were more likely to meet criteria for histrionic, narcissistic, borderline, and antisocial personality disorders than depressed patients without anger attacks.<sup>7</sup> In another sample of 333 depressed outpatients (148 men, 185 women, mean ± SD age = 40.0 ± 10.4 years), the clinician-rated SCID-II (Structured Clinical Interview for Personality Disorders), the SCID, and the Anger Attacks Questionnaire were used for evaluation, and depressed patients with anger attacks were significantly more likely to meet criteria for dependent, avoidant, narcissistic, borderline, and antisocial personality disorder than depressed patients without anger attacks.<sup>10</sup>

**Serotonergic Function and Anger Attacks**

Derangements in serotonergic function have been reported in both depression and aggressive behavior.<sup>12,13</sup> Coccaro et al.<sup>12</sup> evaluated central serotonergic function in 45 male patients with clearly defined major affective disorder (N = 25) and/or personality disorder (N = 20), and in 18 control patients. A single dose of 60 mg p.o. fenflura-

mine hydrochloride, a serotonin-releasing/uptake-inhibiting agent, resulted in a reduced prolactin response in both groups of patients compared with the response in controls. Additionally, reduced prolactin response was also correlated with high ratings of impulsive aggression in patients with personality disorder.<sup>12</sup>

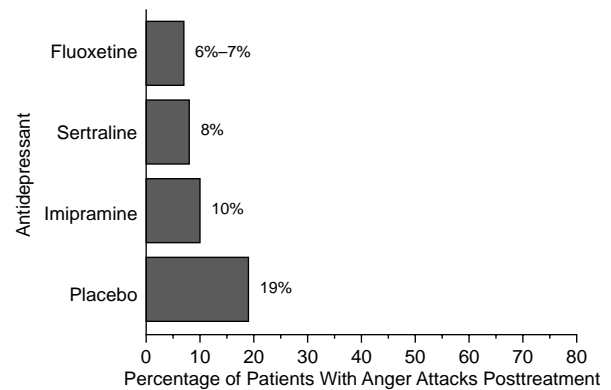
We<sup>13</sup> conducted a study to determine whether a subset of depressed patients with anger attacks had a different prolactin response to thyrotropin-releasing hormone (TRH) stimulation from that of depressed patients without anger attacks. TRH infusion was administered to 25 patients with major depression, 12 of whom reported having anger attacks; the depressed patients with anger attacks had a blunted prolactin response to TRH stimulation compared with depressed patients without anger attacks. Twenty-two subjects participated in the TRH test again after 8 weeks of fluoxetine (20 mg/day) treatment, and the drug significantly increased prolactin response to TRH in patients with anger attacks. These results suggest that patients with major depression and anger attacks may have a relatively greater serotonergic dysregulation than depressed patients without such attacks.

#### ANGER ATTACKS AND OTHER PSYCHIATRIC DISORDERS

Anger attacks and irritability have been suggested as indicators of a bipolar depressive episode in adults.<sup>10</sup> Jain et al.<sup>14</sup> explored anger attacks in a longitudinal population of 100 depressed (50 unipolar, 50 bipolar) patients and found that 17 (34%) of the unipolar depressed patients reported anger attacks while none (0%) of the bipolar depressed patients experienced these attacks ( $p < .05$ ). Tedlow et al.<sup>11</sup> reported that switches into mania or hypomania are no more frequent in unipolar patients with anger attacks as in unipolar patients without anger attacks.

Anger attacks have been rarely studied in psychiatric disorders other than depression. In a 2-site study by Gould et al.,<sup>15</sup> the prevalence of anger attacks in patients with panic disorder was approximately 33% at both sites. Anger attacks were not unique to panic disorder, and similar rates emerged for patients with other anxiety disorders. Depressed patients were twice as likely to report anger attacks as patients with anxiety disorder. Additionally, anxiety disorder patients with anger attacks were significantly more depressed than anxiety disorder patients without anger attacks. Anger attacks have also been reported in women with eating disorders.<sup>16</sup> Of 132 female patients with anorexia nervosa and/or bulimia nervosa and 39 normal female volunteers, 41 (31%) of eating disorder women met the criteria for anger attacks compared with 4 (10%) of the control subjects. Severely bulimic patients reported the highest prevalence of anger attacks, and women with eating disorders with anger attacks had more depressive symptoms than women with eating disorders

Figure 3. Effect of Antidepressant Treatment on Emergence of Anger Attacks<sup>a</sup>



<sup>a</sup>Data from reference 9. In patients without anger attacks pretreatment.

without anger attacks. These studies suggest that the severity of depressive symptoms may be a significant predictor of the presence of anger attacks among patients with eating and anxiety disorders.<sup>10</sup>

#### TREATMENT OF ANGER ATTACKS

A number of studies<sup>7-9</sup> have evaluated the treatment of anger attacks with antidepressants, and anger attacks have disappeared in 53% to 71% of depressed outpatients treated with the selective serotonin reuptake inhibitors (SSRIs) fluoxetine or sertraline or the tricyclic antidepressant imipramine. In an open-label study,<sup>7</sup> 44% of depressed outpatients reported anger attacks at baseline and demonstrated significantly higher scores on measures of anxiety, somatization, and state and trait hostility than did the subjects without anger attacks. After 8 weeks of treatment with a fixed dose (20 mg/day) of fluoxetine, significant reductions in these measures occurred and the anger attacks disappeared in 71% (24/34) of patients who previously reported them. In a subsequent open-label study,<sup>8</sup> 64% (41/64) of the depressed patients who reported anger attacks at baseline reported no attacks after fluoxetine treatment. The change in the severity of depression after fluoxetine treatment in patients both with and without anger attacks was comparable whether measured by the 17-item HAM-D, the 8-item HAM-D, or the Clinical Global Impression-Severity of Illness (CGI-S) scale. In a double-blind, placebo-controlled study,<sup>9</sup> the efficacy of sertraline (up to 200 mg/day) versus imipramine (up to 300 mg/day) treatment of anger attacks was compared in 168 outpatients with diagnoses of atypical depression or primary dysthymia. Anger attacks ceased in 53% (9/17) of patients taking sertraline, 57% (12/21) of patients taking imipramine, and 37% (7/19) of the placebo group. These treatment studies suggest that antidepressants are effective treatment for anger attacks.

Patients who fail to meet the full criteria for anger attacks before antidepressant treatment occasionally do so after antidepressant treatment. The emergence of anger attacks in depressed patients after fluoxetine treatment has been reported to be 6% to 7%, after sertraline treatment as 8%, after imipramine treatment as 10%, and after placebo as 20% (Figure 5).<sup>9</sup> Large placebo-controlled studies comparing SSRIs with relatively noradrenergic tricyclic antidepressants may help to determine whether depressed patients with anger attacks show a distinct response to specific drug treatment.

### CONCLUSION

Depression with anger attacks appears to be a distinct subtype of depression that is associated with increased serotonergic dysfunction. The presence of anger attacks in patients with depression predicts a good response to antidepressant treatment, particularly treatment with SSRIs. Finally, the assumption that antidepressant treatment may mobilize anger attacks in depressed patients is challenged and calls for additional studies.

*Drug names:* fenfluramine (Pondimin), fluoxetine (Prozac), imipramine (Tofranil and others), sertraline (Zoloft).

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### DISCLOSURE OF OFF-LABEL USAGE

The authors of this article have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented herein that is outside Food and Drug Administration-approved labeling.