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BRIEF REVIEW

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Relationship of anger and anger attacks with depression

A brief review

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Abstract Anger is a common and potentially destructive emotion that has considerable social and public health importance. The occurrence of anger, irritability and hostility in depression have been known for many years, but the prevalence, significance for treatment and prognosis and the mechanisms involved remain poorly understood. More recently, anger attacks have been proposed as a specific form of anger in depression. They are characterized by a rapid onset of intense anger and a crescendo of autonomic arousal occurring in response to trivial provocations. Though the presence or absence of hostility, anger and aggression in depression has been a matter of controversy, anger attacks have been found to occur more often in depressed patients in comparison to healthy controls. Some studies have reported that depressed patients with anger attacks differ from those without such attacks in terms of clinical profile, comorbid personality disorders and certain biological variables. Serotonergic dysfunction may characterize this distinct subtype of depression – depression with anger attacks.

Key words anger · anger attacks · depression

Introduction

Depression is an illness of major public health importance, in terms of its prevalence and consequent suffering, dysfunction, morbidity, mortality and economic losses. It has been shown that the presence of anxiety in depression adds to the suffering, dysfunction, and health care utilization (van Valkenburg et al. 1984). It can, thus, be expected that as the third dimension of depression, dysphoria (anger-irritability) may similarly influence the outcome of depression and affect the lives of depressed patients and their care-givers.

Although anger has been described as an important dimension in psychoactive substance intoxication and withdrawal, hypochondriasis, personality disorders, paranoia, delusional disorder and schizophrenia (Kretschmer 1927; Berner and Kufferle 1982; Kennedy 1992; Craig et al. 1985; Fava et al. 1990, Muscatello and Scudellari 2000), most theoretical, clinical and research interest has been devoted to the link between anger and depression. Perhaps this is because the concept of dysphoria implies a connection between anger, irritability and depressive illness (Muscatello and Scudellari 2000).

Anger in depression may lead to a variety of negative outcomes such as poor evaluation by others, lowered self-esteem, interpersonal conflicts and occupational maladjustment (Deffenbacher 1992). In particular, anger-irritability may be associated with impulsive suicides (Brown et al. 1982; Coccaro et al. 1989). Anger attacks among pregnant and 18-months postpartum women have been reported to be more often associated with depression, often directed at their spouse and/or children and being related to lower satisfaction with social support (Mammen et al. 1999).

The emerging evidence linking anger and related emotions with depression has helped to bring anger into psychiatric nosology; for example, agitated depression in Research Diagnostic Criteria (Spitzer et al. 1978) and sensitivity to interpersonal rejection as one of the criteria for atypical features in depression in DSM-IV (American Psychiatric Association 1994).

The present review focuses attention on anger as an important area for research for depressive disorders.

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Anger and related phenomena: basic concepts

Phenomenology

Kennedy (1992) aptly states that, despite a long history of interest in the psychopathology of anger and its obvious social relevance, it is a 'forgotten emotion' as reflected in the absence of the very efforts to have consensual definition of terms related to it. Anger, irritability, aggression, hostility, agitation, and dysphoria are related terms, with certain distinctions and overlaps, as reflected in Table 1.

While the Schedule for Affective Disorder and Schizophrenia (SADS) restricted the term irritability for overt behaviour (Spitzer and Endicott 1979), the Present State Examination (PSE) (Wing et al. 1974) and, later, Snaith and Taylor (1985) consider irritability as present even without observed manifestation and rate it even if it is subjective and never expressed.

Anger episodes that are grossly disproportionate to any provocation or precipitating psychosocial stressors have been described under various labels, e. g. episodic dyscontrol syndrome. This syndrome has been reported to occur in many psychiatric and medical conditions, e. g. mental retardation, personality disorders, head injury, epilepsy, brain tumour, cerebro-vascular disease, and other neurological, endocrine and metabolic disorders (Elliott 1984). When such episodes occur in the absence of other disorders, notably substance use disorders and organic disorders, they are diagnosed as intermittent explosive disorder in current classificatory systems, i. e. ICD-10 (World Health Organization 1992) and DSM-IV (American Psychiatric Association 1994).

Fava et al. (1990) reported a series of cases that presented with sudden episodes of anger accompanied by physiological features resembling panic attacks in the background of depression or anxiety. These attacks occurred spontaneously or in response to a provocation, were experienced by the subjects as uncharacteristic of themselves and inappropriate to the situation, and were followed by profound feelings of guilt. Since these patients did not meet the criteria for other psychiatric disorders (including personality disorders) and these episodes responded well to antidepressants, the authors hypothesized that these attacks were variants of panic or depressive disorders and comprised a distinct syndrome, which if not recognized and treated, may lead to secondary anxiety or depression (Fava et al. 1993a) (Table 2).

Assessment of anger

Given that anger is related to many negative outcomes, it is important to measure it reliably and validly. Early efforts in this direction were based on simple observation of behaviour, clinical interviews, projective tests, and physiological assessments such as galvanic skin response and heart rate, and self-reported psychometric

Table 2 Criteria for anger attacks (Fava et al. 1990)

A. Sudden spells of anger, at least one in the last month, accompanied by intense autonomic activation, experienced by patients as uncharacteristic of them, inappropriate to the situations in which they occurred and leading to guilt or regret afterwards.

B. At least one attack is accompanied by four or more of the following autonomic and behavioural symptoms:
   1. Palpitations
   2. Flushing
   3. Chest tightness or pressure
   4. Parasthesias
   5. Lightheadedness or dizziness
   6. Excessive sweating
   7. Shortness of breath
   8. Shaking or trembling
   9. Intense fear or anxiety
   10. Feeling out of control
   11. Feeling like attacking others
   12. Physically and/or verbally attacking others
   13. Throwing or destroying objects

Table 1 Anger and related phenomena

Anger	An affect with physiological concomitants which is experienced as the motivation to act in ways that warn, intimidate or attack those who are perceived as challenging or threatening (Gottschalk et al. 1963; Kennedy 1992).
Irritability	A feeling state characterized by reduced control over temper, which usually results in irascible verbal or behavioural outbursts (Snaith and Taylor 1985).
Aggression	A deliberate verbal or physical act, which is interpreted by others as destructive (Gottschalk et al. 1963).
Hostility	A self-reported attitude of dislike, resentment or suspicion towards the world or the objects in it (Gottschalk et al. 1963).
Agitation	Motor restlessness such as fidgeting and pacing associated with inner tension (Schatzberg and deBattista 1999).
Dysphoria	Dysphoria refers both to depressive mood as well as irritability and may also be used specifically to refer to a pathological mood state 'irritable mood' (Musalek et al. 2000).
Episodic dyscontrol	Violent outbursts with loss of control over aggressive behaviour upon minor provocation (Campbell 1996).
Intermittant explosive disorder	Discrete episodes of failure to resist aggressive impulses, which result in serious assaults or destruction of property (DSM-IV) (American Psychiatric Association 1994).
Anger attacks	Sudden spells of anger, surge of autonomic arousal, and symptoms like tachycardia, sweating, flushing and a feeling of being out of control. These attacks occur spontaneously or in response to a provocation, and are experienced by the subjects as uncharacteristic of themselves and inappropriate to the situation (Fava et al. 1990).

scales. However, due to a historical lack of differentiation among the constructs of anger, hostility and aggression, there were many ambiguities about what was actually being measured (Kassinove et al. 1997).

Of late, anger is increasingly being seen as a feeling state which can be linked to other variables of interest such as aggressive motor patterns or physiological reactions and can be assessed by reliable self-report measures (Kassinove et al. 1997). In this tradition, State-Trait Anger Expression Inventory (Spielberger and Sydeman 1994) represents an important tool in anger assessment and has become a standard in the field. It measures anger under the following dimensions: state anger, trait anger and anger expression. Other self-report scales developed to measure anger include Cook-Medley Inventory (Cook and Medley 1954), Buss-Durkee Hostility Inventory (Buss and Durkee 1957), Harburg Anger-in/Anger-out scale (Harburg et al. 1973), Novaco Anger Inventory (Novaco 1975), Multidimensional Anger Inventory (Seigel 1986) and Anger Response Inventory (Tangney et al. 1991).

Relationship between anger and depression

Prevalence

Psychoanalysts understood depressive reactions to result from the turning of original object directed aggression inwards onto the incorporated loved and hated object while there was denial, suppression or repression of hostile feelings toward significant others (Freud 1917; Abraham 1927). Studies have shown a relationship between inwardly directed hostility and depression (Kendell 1970; Schless et al. 1974; Biaggio and Godwin 1987).

Though a causal link between repressed anger and depression is generally acknowledged (White 1977), research has resulted in conflicting findings. Lower 'expressed outward' hostility was reported in depressed patients compared to normal subjects (Friedman 1970). As against the finding of less expressed anger in depressed patients, Snaith and Taylor (1985) reported that 37 % of depressed inpatients had moderate or severe outwardly directed irritability, the proportion being significantly greater than the proportion of irritable subjects among the normal controls. Similar findings were reported by Goldman and Hagga (1995). Some (Weissman et al. 1971; Biglan et al. 1985; Feldman and Gotlib 1993), but not all (Goldman and Hagga 1995), studies have reported that depressed subjects express more anger towards close family members including their spouses and children in comparison to non-depressed subjects.

To explain the inconsistency of findings, Goldman and Hagga (1995) gave an alternative hypothesis for the lower expressed hostility in depressed patients observed in some studies. They suggested that these patients inhibit anger expression because of the fear of the consequences of such expression. Consistent with this hypothesis, they showed that depressed outpatients had higher levels of fear of anger expression than the non-depressed subjects, and the fear of expressing anger was highly correlated with anger suppression (Goldman and Hagga 1995).

Other researchers have suggested that a positive correlation between hostility and depression exists mainly in some subtypes of depression such as nonendogenous depression (Pilowsky and Spence 1975) or some subgroups of depressed patients, e. g. those who had not suffered interpersonal losses (Fava et al. 1982) or younger depressed patients (Paykel 1971; Perris et al. 1983). The findings in depressed gender-subgroups are inconsistent. While Sethi et al. (1980) reported greater hostility in depressed men and greater guilt in depressed women, Perris et al. (1983) failed to find any gender-specific differences.

Anger has been found to be more likely in bipolar depression than in unipolar depression (Akiskal and Benazzi 2003). Assessing hypomanic symptoms during major depressive episode led to the finding of a high frequency (more than 20 %) of bipolar II depressive mixed state (defined as major depressive episode plus some concurrent hypomanic symptoms) in which anger was very common (Akiskal and Benazzi 2003; Benazzi and Akiskal 2001). Recognizing anger in a depressive episode could also be a cross-sectional clinical marker of bipolar II depression as Benazzi (2003) showed that sensitivity and specificity of anger for predicting bipolar II disorder were 61.2 % and 64.3 %, respectively. This fact can have an important impact on the treatment of depression, because misdiagnosis of bipolar depression as unipolar depression is high, and treatment of bipolar depression with antidepressants without concurrent mood stabilizers can induce mania/hypomania, mixed states, and rapid cycling (Benazzi 2003).

Relationship between anger and severity and course of depressive disorders

A positive correlation between degree of depression and inwardly directed hostility has been reported (Friedman 1970; Schless et al. 1974). Riley et al. (1989) found that the severity of depression was associated with the level of hostility and anger experience, and partly with anger suppression. However, others have reported no difference in hostility in moderately versus severely depressed patients (Trivedi et al. 1981; Gupta 1987). This apparent contradiction may be explained by the fact that studies that found a relationship between anger and severity of depression evaluated depression as a dimension, while the studies with negative findings examined depressive categories and were expected to be less sensitive for finding any relationship. Severity of expressed anger has been found to be correlated with severity of depression in some studies (Schless et al. 1974; Pilowsky and Spence 1975; Fava et al. 1982), but not all (Snaith and Taylor 1985; Riley et al. 1989).

Improvement in all domains of inwardly directed hostility including general punitiveness and intropunitiveness has been reported with the improvement of depression (Friedman 1970; Blackburn et al. 1979; Mayo 1978). Similarly, Fava et al. (1986) found that there was no significant difference in hostility between recovered depressed patients and control subjects, while this difference was striking during the illness. As against this set of findings, Blackburn et al. (1979) observed that though inwardly directed hostility decreased with the improvement of depression in nurses' rating of mood (depression), this association was not evident in self-report or interviewer's rating of depression. Similarly, Brody et al. (1999) found that in comparison to the never-depressed control group, recovered depressed patients reported holding anger in and being afraid of expressing it. In fact, these authors hypothesized that anger inhibition may play a causal role in the recurrence of depression.

With regard to outwardly directed anger, studies have found that symptomatic improvement in depression was not correlated with the expression of 'anger outwards' (Friedman 1970; Klerman and Gershon 1970).

Anger as a principle for classification of depression

In depressed patients, a cluster analysis based on the Brief Psychiatric Rating Scale led to three subgroups – anxious, retarded and (manifestly) hostile (Hollister et al. 1967). Similarly, a cluster analysis based on clinical symptoms, previous history, life stress, and pre-morbid neuroticism led to the identification of four subgroups (Paykel 1971). The first group had good premorbid adjustment, a severe illness, sometimes with delusions, and corresponded to 'psychotic depression'. The second group had moderate depression with strong admixture of anxiety, higher incidence of previous illness and higher neuroticism scores. The third group comprised depression with a considerable amount of (manifest) hostility. The last group contained young patients whose relatively mild depression developed on a background of personality disorder. This classification was consistent with psychotic-neurotic dichotomy, but suggested that non-psychotic depressives are diverse and comprise groups associated with high neuroticism, high hostility and personality disorder. The association of hostility with 'non-psychotic depression' was consistent with the findings of Pilowsky and Spence (1975). The finding of greater inwardly directed hostility (as against outwardly expressed anger) in manic-depressive patients in comparison to neurotically depressed patients (Trivedi et al. 1981) also agrees with this scheme.

Bagby et al. (1997a, b) suggested that the category of hostile depression might have some validity. They used a trait measure of anger and hostility to divide depressives into high and low angry hostile groups. The high angry hostile group was less conscientious, less agreeable and interpersonally more sensitive. However, the two groups were found to have a similar symptom profile and treatment response.

Anger and related phenomena have been recognized as a basis for classification in formal classificatory approaches, but only to a limited degree. Agitated depression was posited as a subtype of major depressive disorder in the Research Diagnostic Criteria (Spitzer et al. 1978). The DSM-IV lists depressive episode with atypical features as a diagnostic subcategory, where hypersensitivity to rejection is a central aspect (American Psychiatric Association 1994).

Anger associated with depression: treatment response

Superior results were reported on treating anxious depressives with thioridazine and retarded depressives with imipramine, while hostile depressives responded equally well to either drug (Hollister et al. 1966). In another study, best efficacy was reported for amitriptyline in retarded depression, perphenazine in anxious depression and either of the two in hostile depression (Hollister et al. 1967). Treatment of depression with amitriptyline was found to improve hostility (Fava et al. 1986), while fluoxetine was reported to be useful in moderating anger that was part of the symptomatology of a number of axis I and II disorders (Rubey et al. 1996).

However, the use of specific serotonin reuptake inhibitors (SSRIs) in depressed patients manifesting anger-related psychopathology is controversial. Various case-control, healthy volunteer and meta-analytic studies suggest that SSRIs can induce agitation (Lane 1998; Besley et al. 1991; Tranter et al. 2002; Saletu et al. 1986), and this has been linked to SSRI-induced suicide by Healy (2003). However, the association of SSRI treatment with suicide remains questionable (Khan et al. 2003).

The presence of residual symptoms including anger has been strongly correlated with poor long-term outcome and future relapse (Fava 1999). The sequential treatment strategy based on the use of pharmacotherapy in the acute phase of depression and cognitive behavioural therapy in its residual phase focusing on residual symptoms (anger) has been found to decrease relapse rate in recurrent depression (Fava et al. 2003).

Anger attacks and depression

Fava et al. described anger attacks as a phenomenon in depression for the first time in 1990. Anger attacks improved with antidepressant treatment. Considering this response and the historical relationship between hostility, irritability and depression, they postulated that anger attacks were variants of major depression. Since then, most of the studies on anger attacks have been done in relation to depression.

Prevalence

The prevalence of anger attacks has been reported as 30 %–49 % in major depression (Fava et al. 1991, 1993b, 1993c, 1996; Sayar et al. 2000), 38 % in 'atypical' major depression, and 28 % in dysthymia, whereas no anger attacks were reported in normal controls (Fava et al. 1997).

Patients with major depression were twice as likely to report anger attacks as patients with panic disorder (Gould et al. 1996).

Clinical correlates

Depressed patients with and without anger attacks did not differ with regard to age and sex (Fava et al. 1991). No significant differences in rates of lifetime comorbid anxiety (including panic disorder) and eating and substance use disorders were found between depressed patients with and without anger attacks (Fava et al. 1991; Tedlow et al. 1997). However, the latter authors found that 8 % of depressed patients with anger attacks met criteria for current co-morbid panic disorder compared to 3 % of depressed patients without anger attacks, a finding that was significant at a trend level (Tedlow et al. 1997).

On dimensional measures (which are more sensitive), patients with anger attacks were reported to be significantly more depressed, anxious and hopeless compared to the patients without anger attacks. Severity of depression emerged as the strongest predictor of the presence of anger attacks (Sayar et al. 2000). Anger attacks have also been shown to be predictive of greater depression in patients with panic disorder and eating disorder (Gould et al. 1996; Fava et al. 1995). Despite having similar scores on the depression scale of the symptom questionnaire, depressed patients with anger attacks were reported to have higher scores on the anxiety, somatization, state and trait hostility and global psychological distress scales than depressed patients without anger attacks (Fava et al. 1993c). It was proposed that high scores on the anxiety scale in depression may be either due to a possible link between dysregulated anger and anxiety, or that it may be a reflection of autonomic symptoms experienced by depressed patients with anger attacks (Fava and Rosenbaum 1999).

When assessed on self-rated Personality Disorder Questionnaire-Revised, depressed patients with anger attacks were reported to be more likely to meet criteria for cluster B (histrionic, narcissistic, borderline, and antisocial) personality disorders in comparison to depressed patients without anger attacks (Fava et al. 1997). In another sample of 333 depressed outpatients where the clinician-rated SCID-II (Structured Clinical Interview For Personality Disorders) was the instrument for assessing personality disorders, it was found that depressed patients with anger attacks were significantly more likely to meet criteria for cluster C (dependent and avoidant) and cluster B (narcissistic, borderline, and antisocial) personality disorders than the depressed patients without anger attacks (Fava and Rosenbaum 1997).

To examine the emotional and behavioural characteristics of the offspring of depressed parents with and without anger attacks, Alpert et al. (2003) examined 43 parents who met the criteria for major depressive disorder and completed the Achenbach Child Behavior Checklist – Parent Report Version for each of their children. They found that parents with anger attacks had a significantly younger age of onset of depression. Offspring of depressed patients with anger attacks were found to have significantly lower social and school competency scale scores and higher scores for deliquency, attention problems, aggressive behaviour and global psychopathology.

Anger attacks and subtypes of depression

Findings on the association of anger attacks with subtypes of depression have been inconsistent. Anger attacks were found to be more prevalent among patients with atypical depression and dysthymia in comparison to normal subjects in one study (Fava et al. 1997), but not in another (Fava et al. 1993c).

Anger attacks have been suggested to indicate a bipolar depressive episode in adults (Fava and Rosenbaum 1997). However, Jain et al. (1997) found that anger attacks were reported by 34 % of the unipolar depressed patients, but none of the bipolar depressed patients. Also, switches into mania or hypomania were reported to be no more frequent in unipolar patients with anger attacks than in unipolar patients without anger attacks (Tedlow et al. 1997).

Biological studies

Studies suggest that patients of major depression with anger attacks may have a relatively greater serotonergic dysregulation than those without such attacks. Compared to depressed patients without anger attacks, depressed patients with anger attacks have been found to have a blunted prolactin response to thyrotropin releasing hormone stimulation which normalized after 8 weeks of 20 mg/day fluoxetine treatment (Rosenbaum et al. 1993). Also, a blunted prolactin response to fenfluramine challenge in depressed patients with anger attacks was reported, while no such blunting was noted in depressed patients without anger attacks (Fava et al. 2000). Mischoulon et al. (2003) examined the ability of dopamine (D_1) and serotonin ($5HT_2$) receptor binding potential on positron emission tomography to predict treatment (nefazodone) response in depressed patients with anger attacks. About half of these patients responded to the treatment of depressive symptoms with disappearance of anger attacks. Improvement in anger attacks was associated with significant percentage de-

crease in $5HT_2$ binding potential in right mesial frontal and left parietal regions, but no significant change was observed in D_1 binding potential in any region after 6 weeks of treatment.

Treatment response

Fava et al. (1991) found that depressed patients with anger attacks improved to a greater extent in comparison to those without anger attacks when both groups were treated with fluoxetine (Fava et al. 1991). They suggested that large placebo controlled studies comparing the serotonin specific reuptake inhibitors (SSRIs) with relatively noradrenergic tricyclic antidepressants might help in determining whether depressed patients with anger attacks show a distinct response to specific drug treatment. Although such trials have not been conducted, evidence from other studies has not supported a pharmacological cleavage between depression with anger attacks and depression without anger attacks. Anger attacks disappeared in 53 %–71 % of depressed outpatients treated with SSRIs (fluoxetine or sertraline) or a tricyclic antidepressant (imipramine) (Fava et al. 1993c, 1996, 1997). Also, a similar number of patients who failed to meet the full criteria for anger attacks before antidepressant treatment did so after treatment with various antidepressants (fluoxetine 6 %–7 %, sertraline 8 %, imipramine 10 %). However, these anger attacks cannot be attributed to antidepressants as 20 % of those treated with placebo also developed anger attacks (Fava et al. 1997).

Conclusion

This review suggests that anger, an important dimension of emotion, is yet to be explored fully in psychiatric research. Also, though the concept of melancholia has been replaced successively by endogenous depression and major depression, agitation, excitement and anger remain important parts of the spectrum of depression. The study of anger attacks is only a recent focus of research, but it has thrown up some intriguing findings. The subgroup of depressed patients with anger attacks appears to be distinct from the subgroup of depressed patients without anger attacks in terms of clinical correlates, personality features and biological characteristics, though not in terms of treatment response.

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