Differential Diagnosis and Classification of Apathy

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This paper discusses the definition of apathy, reviews its differential diagnosis, and proposes a classification for the conditions that may produce it. Apathy is defined as diminished motivation not attributable to diminished level of consciousness, cognitive impairment, or emotional distress. In its differential diagnosis, abulia, akinesia and akinetic mutism, depression, dementia, delirium, despair, and demoralization must be ruled out. Classification of apathy is organized in terms of its adaptive and functional consequences, its relationship to personality or to sociocultural or environmental events, and its association with psychiatric, neurological, and medical disorders. An approach to assessment and treatment is proposed.

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Apathy is a familiar and salient feature of many psychiatric, neurological, and medical diagnoses. In addition, it has broader relevance to human functioning, which is evident in its occurrence in response to personal tragedy, natural catastrophe, social loss, environmental deprivation, and role change. Conceptually, apathy is closely linked to motivation and emotion. Perhaps because this conceptual significance has been rarely noted, little attention has been given to the theoretical or clinical aspects of apathy (1). Alternatively, the clinical utility of apathy may not have been considered previously because of difficulties in distinguishing it from other syndromes, such as depression, despair, and abulia. In the absence of a clear definition, it is understandable that apathy has not been the object of systematic investigation. This paper, which is part of an ongoing project evaluating the validity of a scale for the measurement of apathy (R.S. Marin, R. Biedrzycki, and S. Firinciogullari, unpublished manuscript, 1989), describes the differential diagnosis and classification of apathy and presents an approach to its evaluation and treatment based on this classification. The material is intended primarily for clinicians. However, many research questions are raised by the study of apathy; some of these are highlighted in the concluding section.

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DEFINITION AND DIFFERENTIAL DIAGNOSIS

Apathy, which is derived from the Greek *pathos*, or passions, is defined conventionally as absence or lack of feeling, emotions, interest, or concern. This definition is helpful for general purposes but has weaknesses when one is dealing with some of the common clinical disorders associated with apathy. For example, patients with frontal lobe injury may seem apathetic because they lack interest or motivation, but the fact that they may also be violent, irritable, or euphoric does not seem consistent with the notion that apathy denotes lack of emotion. Similarly, depressed patients may be described as apathetic, despite the fact that they are in great emotional pain rather than lacking in emotional expression. How can we define apathy for clinical purposes so as to account for these inconsistencies?

I suggest approaching the definition of apathy in the same way that we try to define other clinical terms. If we consider its clinical applications, it will be seen that apathy does indeed refer primarily to lack of motivation. Depressed patients *are* called apathetic because they profess loss of motivation. Similarly, frontal lobe syndromes are characterized by lack of interest or involvement in usual activities. However, if we simply define apathy as a state of diminished motivation, we confront the fact that it is but one of a number of amotivational states encountered in clinical practice. How, then, does the presence or absence of emotion enter into the definition of apathy? In the same way that we call patients aphasic only if their language is not disordered by an impairment of consciousness, attention, or general intellectual activity (2), apathy describes only those patients whose lack of motivation is not attributable to a diminished level of consciousness, an intellectual deficit, or emotional distress. Apathy is, therefore, a state of primary motivational impairment. For clinical purposes, individuals who show such primary motivational impairment may be regarded as having apathy syndromes (see appendix 1). Frontal lobe injuries are included among the states that may produce apathy syndromes because the lack of motivation of patients with these conditions is not attributable to emotional distress. In other instances, lack of motivation is a consequence of other problems (e.g., dysphoria) and is best regarded as a feature

or symptom of the syndrome in question (e.g., depression). It is these syndromes—delirium, dementia, depression, abulia, akinesia and akinetic mutism, and despair and demoralization—that constitute the differential diagnosis of apathy.

Delirium is a transient state of disordered consciousness in which patients show 1) impaired capacity to shift or maintain attention, 2) fluctuating levels of consciousness, 3) memory disturbance, 4) perceptual disturbances, 5) a variety of affective symptoms, including blunting or flattening of affect, and 6) behavioral changes, including agitation, withdrawal, and lack of interest. When lack of interest in the environment, lack of goal-directed behavior, and flat affect predominate, delirium resembles apathy. Lethargy, anergy, and drowsiness, which are seen in some delirious patients, are other features of delirium that may suggest apathy.

Dementia is an acquired syndrome of intellectual impairment sufficiently severe that social or occupational functioning is impaired (*DSM-III*). Patients with dementia often become apathetic, although the mechanisms of this apathy have not been studied. Recent evidence (3) suggests that in Alzheimer's disease, apathy tends to occur in the confusional stage of the disease. This apathy has been attributed to loss of the cognitive capacities needed to organize goal-directed behavior (3). However, psychological factors (e.g., perception of diminished capacities) and neurological factors (e.g., involvement of specific limbic brain regions, such as the frontal lobe, amygdala, and cingulate gyrus) provide other explanations. Similarly, in multi-infarct dementia, there are multiple possible psychosocial and neurological mechanisms for apathy (e.g., the location of infarction in a particular patient) (see the section on organic disorders later in this paper).

Depression is another syndrome in which apathy may appear. Many studies (1, 4–7) have documented the occurrence of apathy in depression, and, in fact, clinicians often regard depression as a model disorder for defining apathy. This is misleading, however, because there are a number of ways in which the apathy of depression, or what one might call depressive apathy, is distinguishable from other disorders (e.g., frontal lobe syndromes) in which apathy occurs as a syndrome per se. The description of depressed patients as apathetic is based on their inactivity, such as social inactivity, and their claims that they have lost interest in their usual activities. Paradoxically, there are a variety of ways in which depressed patients show features that are inconsistent with apathy. In comparison to apathetic patients, who are passive or compliant, depressed patients are generally quite deliberate and active in their avoidant behavior. For example, they may staunchly resist attempts to involve them in treatment or normal socialization. In the extreme, depressed patients are suicidal, which, clearly, does not reflect apathy but negativism and despair. This negativism is generally clearest in the thought content of depressed patients, who characteristically emphasize pessimism and hopelessness, often in association with self-deprecatory thoughts. These latter features contribute to the dysphoric affect that is virtually a sine qua non of depression and definitively distinguishes depression from true apathy, in which, by definition, one expects a lack of emotional distress.

Abulia, which is derived from the Greek *boul*, or will, is usually defined as a lack of will or motivation or an inability to decide. In clinical practice, the diagnosis is reserved for patients who are awake but otherwise severely impaired in their ability to communicate and to initiate and self-regulate purposeful behavior. Therefore, from a conceptual standpoint, abulia and apathy are on a continuum of motivational and emotional deficit, abulia representing the more severe portion of the continuum. This relationship is borne out by the fact that neurological dysfunction which causes apathy tends to produce abulia when the dysfunction is more severe, as in frontal lobe tumors.

Akinesia is usually defined as a disorder of movement, in contrast to apathy, which denotes loss of motivation. Akinetic patients show diminution or loss in the initiation of movement. In clinical practice the term is reserved for patients in whom the lack of movement is not attributable to elementary motor deficits, such as hemiplegia, or psychiatric states, such as catatonia. Thus, akinesia is primarily a motor disorder, usually attributed to basal ganglia dysfunction, and tends to be associated with other motor disturbances, including bradykinesia, rigidity, and abnormal movements such as tremor, chorea, and athetosis. It is of interest, however, that in practice akinesia often occurs with apathy; in fact, Rifkin et al. (8) have suggested that akinesia be considered a disorder of behavior in which apathy is a prominent feature (see the section on drugs and medical disorders later in this paper).

Despair and demoralization are psychological states occurring primarily in normal individuals in response to the experience of overwhelming stress (9). This may be contrasted to the previously discussed states, which refer to individuals who are ill. Both despair and demoralization share with apathy a loss of motivation. They differ from apathy, however, in that apathy denotes, as well, a lack of concern or emotional distress, whereas despair and demoralization are experienced as dysphoric, unpleasant states. In other words, it would be illogical to say that someone is *suffering* from apathy, whereas despair and demoralization are experientially painful psychological states. In addition, the concepts of despair and demoralization must be understood in terms of an individual's affective orientation to the future. In principle, apathy carries little or no connotation in this regard, whereas those suffering despair or demoralization express a loss of hopefulness or meaningfulness with respect to the future.

CLASSIFICATION

As suggested by the foregoing review of apathy's differential diagnosis, apathy may be caused by diverse circumstances arising as part of normal development

or human experience as well as from a variety of medical, psychiatric, and neurological conditions. The following classification organizes the causes of apathy into three major areas on the basis of the answers to three questions.

Is Apathy a Characteristic or an Acquired Feature of Adult Personality?

It is common knowledge that among apparently normal individuals, there are some who are relatively apathetic and others who are highly motivated. Among individuals in whom apathy is characteristic of adult personality, there are some in whom the apathy is restricted to specific areas of psychosocial functioning and others in whom it is a pervasive characteristic. Those for whom the apathy is severe or pervasive enough to interfere with psychosocial functioning would meet the *DSM-III* criteria for personality disorder. For example, Neugarten et al. (10) described older adults with an apathetic pattern of normal aging characterized by lifelong characteristics of passivity, low role activity, low self-esteem, and low life satisfaction. A more common relationship to personality disorder is seen in those instances in which apathy is secondary to a recognized personality disorder, such as avoidant or schizoid personality, in which individuals seem uninterested or uninvolved because of their fears or inhibitions.

In contrast to the adaptive problems associated with pervasive apathy, it is common for normal individuals to be apathetic about some things. Thus, the apathy seen in normal individuals occurs in the context of an overall state of being normally concerned or motivated in many areas of psychosocial functioning. For this reason, apathy that is consistent with and characteristic of normal functioning may be called selective or relative apathy. Selective apathy is adaptive, and in most instances it simply reflects the fact that a person has not acquired or maintained interest in a particular activity. Selective apathy may serve defensive purposes as well (11). Last, one might view eccentric individuals who are interested in a narrow range of activity as showing an extreme form of selective apathy, although such restriction of range should not be viewed as characteristic of eccentric persons in general (12).

Does Apathy Represent a Response to Diminution in the Perceived Rewards or Incentives of the Person's Environment?

If apathy represents an acquired feature of adult personality, the first question to ask in classifying it further is whether it has developed in association with a decrease in available rewards or incentives. This category of apathy takes into account many otherwise diverse factors that disrupt normal emotional and motivational functioning. For clinical purposes it is useful to subdivide such factors into two groups: socioenvironmental and biological.

Socioenvironmental factors. Major changes in the social or physical environment may impair motivation by removing usual or expectable sources of reward or incentives. The loss of motivation and emotional responsiveness sometimes associated with institutionalization (e.g., in prisons, nursing homes, or chronic psychiatric facilities) is an example familiar to psychiatrists. When cultural or language differences interfere with the pursuit of values or goals (e.g., among immigrants or minorities segregated from the ambient and dominant culture), one sees a variety of motivational and emotional adaptations, of which apathy is one. Natural calamities such as floods, earthquakes, and tornadoes profoundly disrupt normal motivation, producing states of "psychic numbing" characterized by "apathy, withdrawal, depression and overall constriction in living" (13). In survivors of the Holocaust and the atom bomb attacks on Hiroshima and Nagasaki, similar reactions have been described (9).

In less severe cases of social disturbance, such as the loss of role function associated with retirement, the conclusion of child-rearing responsibilities for a homemaker, or other phase-of-life transitions, people commonly describe a purposelessness or lack of direction in the absence of emotional distress, that is, apathy. Elderly people may be particularly at risk for apathy arising from such psychosocial sources. In fact, some older individuals are influenced by the culturally derived but internalized expectations that one *should* become withdrawn or apathetic in later life (10). Simultaneously, the older person's social environment may no longer provide vocational, social, or financial opportunities for continued engagement in the activities that had defined optimal motivational functioning. Change of residence and, in particular, institutionalization are relatively extreme examples of environmental changes that may produce apathy in this way.

Biological factors. A variety of biological events, such as loss of peripheral sensory or musculoskeletal capacities, may produce diminution in the perception that there are sufficient rewards and incentives available in the environment to sustain behavior. (Central neurological dysfunction is discussed in the next section.) In elderly persons especially, loss of hearing and of visual ability may produce an insidious decrease in motivation. Misjudging the associated dysfunction as due to depression or early dementia may lead to errors in treatment or prognosis. Loss of motor effector systems, as in traumatic paraplegia, may produce apathy by essentially the same psychological mechanism.

Is Apathy a Feature of Some Identifiable Psychiatric, Neurological, or Medical Disorder?

Psychotic and affective disorders. The conceptual relationship of apathy to depression has already been discussed. The association of apathy with adult depressive disorders has been documented in multiple factor analytic studies of patients with depression (1, 4–7). Spitz's description of anaclitic depression in infants

(14) included a stage of withdrawal and diminished responsiveness to the environment. Apathy is also frequent in adolescent depression (15). In comparison to younger adults, elderly depressed patients are less likely to show depressed mood, whereas they more frequently show apathy, anergy, pessimism, somatic complaints, and cognitive dysfunction (16). Illustrating the complexity and importance of differentiating the causes of apathy in the elderly is the following comment of Raskin and Sathananthan (17): "One has to be careful to separate out the apathy and withdrawal that is often seen in aged persons from the apathy specific to depression in this age group. One also needs to distinguish the apathy seen in depressed elderly from the motor retardation and emotional withdrawal that occurs in other psychiatric conditions such as schizophrenia."

An extensive literature addresses the changes in emotional and motivational state accompanying chronic schizophrenia. A variety of terms have been used to describe the same phenomena, including "changes in affectivity" (18), "flat affect" (19), "amotivational syndrome" (20), "emotional blunting" (21), "negative symptoms" (22), and "type II schizophrenia" (23). Apathy in schizophrenia is of particular interest because it is a recognized clinical state that is not simply a symptom of some other clinical syndrome but, instead, strongly characterizes the clinical picture. This is evident in the following vivid portrait written by Bleuler (18): "Many schizophrenics . . . sit about the institutions to which they are confined with expressionless faces, hunched up, the image of indifference. They permit themselves to be dressed and undressed like automatons, to be led from their customary place of inactivity to the messhall, and back again without expressing any sign of satisfaction or dissatisfaction. They do not even seem to react to injuries inflicted on them by other patients" (p. 40).

Currently, these characteristics of schizophrenia are receiving renewed interest (22–25). Their clinical importance was underscored by Ullman and Krasner (26), who stated that "apathy" or "lack of interest in the environment . . . [is] . . . probably the major treatment problem when working with chronic schizophrenic patients" (p. 400).

Postpsychotic depression refers to a depression occurring in the wake of a period of schizophrenic or other psychotic disorder. Although the term implies similarity to depressive disorders, it is questionable whether the phenomenology of the disorder always justifies the comparison. Some reports (27) have documented elevated depression ratings in patients with postpsychotic depression. However, Floru et al. (28) stated that the condition is "seldom expressed by genuine deep melancholy or depressive contents but by apathy." Other terms used to describe patients with postpsychotic depression, including "lack of vital impulse," "lack of desire" (28), "wooden" demeanor (29), lack of initiative (30), and paucity of spontaneous speech (31), also suggest a similarity to apathy rather than to depression. These observations suggest that in some patients, postpsychotic depression is more accurately described as a syndrome of apathy than of depression. The inconsistencies in the literature may have to do with the fact that depression scales do not permit discrimination of depression and apathy when scores are given as total scores. For example, a patient who is primarily apathetic might endorse items for decreased energy, interest, libido, and psychomotor speed and not endorse items specific to depression, such as depressed mood, guilt, suicidal ideation, and sleep disturbance.

Organic disorders. As indicated, both delirium and dementia may produce apathy. Delirious patients who are agitated and emotionally aroused are usually not considered apathetic. Apathy is more likely to be thought present in cases of delirium characterized by drowsiness, sedation, or hypoactivity. In such hypoaroused delirious states, the sedation results in failure to initiate behavior. The mechanism may be interference with the ascending reticular activating system by medical illness (e.g., renal or hepatic failure), by drugs (e.g., sedative-hypnotics), or by a structural lesion (e.g., a brain tumor or subdural hematoma) that compromises these critical brainstem regions. Given the large number of agents and conditions that may produce toxic-metabolic encephalopathies (32), it is clear that numerous medical illnesses need to be considered in the etiological evaluation of patients with apathy.

Dementia and organic amnestic disorders are two other syndromes of cognitive impairment that have been associated with apathy. The production of apathy by Alzheimer's disease was mentioned in the discussion of differential diagnosis. Several causes of dementia involving primarily basal ganglia pathology have been referred to collectively as "subcortical dementias," in part on the basis of similarities in several of their neuropsychiatric features, including forgetfulness, slowness of thought processes, impaired problem-solving capacities, and, finally, personality change in which apathy, depression, euphoria, or irritability may occur (33). The term "subcortical dementia" encompasses Parkinson's disease, Huntington's disease, and progressive supranuclear palsy. Marsden and Parkes (34) stated that in some Parkinson's disease patients, one sees "blunting of interest and drive, amounting to apathy, a limitation in intellectual activity, and an apparent slowing of thought process and memory." In their review of the literature on progressive supranuclear palsy, Albert et al. (35) found that apathy and depression were more common personality disturbances than irritability and euphoria. Caine et al. (36) observed that in Huntington's disease patients, apathy arises primarily from lack of initiative, not lack of affect or persistence. The coexistence of apathy with subcortical pathology and cognitive impairment is also seen in patients with multiple vascular insults to paramedian diencephalic structures (37).

With regard to organic amnestic disorders, it is of interest that for Korsakoff's syndrome, which is gen-

erally characterized in terms of the amnesia that accompanies it, there is a lengthy literature emphasizing loss of motivation (38). It should be noted that the pathology of Korsakoff's syndrome primarily involves diencephalic structures, particularly the mammillary bodies and medial dorsal thalamus. Korsakoff patients generally have the capacity for normal emotional display, but their initiative and emotional response to important events are decreased.

A separate group of apathetic patients are those demented individuals in whom there is profound loss of behavioral, cognitive, and emotional capacities, producing states of mutism or abulia. Akinetic mutism refers to a syndrome in which there is virtual absence of movement and communication by patients who are fully awake and do not have paralysis (39). The syndrome occurs as a result of bilateral damage to one or more of the following areas: cingulate gyri, septal region, frontal poles, thalamus, or hypothalamus (39). In cases of unilateral cingulate involvement, the diminution in the capacity to express and experience emotion is less severe, producing an apathetic, rather than an abulic, state. Damasio and Van Hoesen (40) described a patient who suffered infarction involving the cingulate gyrus, supplementary motor area, and mesial motor area. In addition to weakness of the contralateral lower extremity, the patient showed what "could best be described as akinesia and mutism, but might as well be designated as a state of aspontaneity and nonlateralized neglect of most stimuli," since she reported that prior to recovery she had had " 'nothing to say.' Her mind was 'empty.' 'Nothing mattered.' She apparently was able to follow our conversations even during the early period of illness, but felt no 'will' to reply to our questions. In the period after discharge she continued to note a feeling of tranquility and relative lack of concern."

There are many reports in the literature which document the fact that patients with right hemisphere stroke may develop what was originally called by Babinski (41) the indifference reaction. Babinski and more recent workers (42–44) have variously described such patients as showing lack of emotional concern, lack of emotional expression, inappropriate cheerfulness, or apathy. Robinson et al. (44) found apathy more associated with lesions in the anterior part of the right hemisphere. Other personality changes in such patients include irritability and angry outbursts. Confirming the motivational significance of the indifference reaction are reports of slower recovery of social and motoric function in patients with right, as compared to left, hemisphere damage (45).

Destructive neurological lesions that affect the amygdala and anterior temporal lobes bilaterally may produce a syndrome of "blunted affect, apathy, and pet-like compliance" (46). Such patients are thought to represent human cases of the Kluver-Bucy syndrome, originally described in monkeys who had undergone bilateral temporal lobectomy (47). Human cases of the Kluver-Bucy syndrome have been caused by almost every category of neurological disorder, including trauma, surgery, tumor, vascular lesions, and degenerative diseases.

Finally, mention should be made of what is perhaps the best-known cause of apathy arising from neurological damage, the so-called frontal lobe syndromes. The complex clinical picture presented by patients with these syndromes and our developing, albeit limited, understanding of the neurobehavioral relationships seen in such patients suggest that the term itself is too general (48). Blumer and Benson (49) distinguished among frontal lobe patients according to the region of the frontal lobes involved. They suggested that "slowness, indifference and apathy" may predominate in patients with convexity lesions, whereas loss of social graces, impulsive anger, violence, inappropriate sexual behavior, and inappropriate wit are more typical of patients with orbitofrontal lesions. Nevertheless, it has been frequently reported that victims of frontal lobe brain damage show an impairment in initiating and carrying out behavioral tasks. A general lack of concern and interest accompanies these behavioral changes, while affective alterations in the direction of superficiality and impulsivity are commonly seen. Euphoria, silliness, or inappropriate anger and, occasionally, rage occur (40, 48, 50). Even patients who show such marked emotional expressions frequently show "an underlying background of abulia and apathy" (50).

Drugs and medical disorders. The discussion of delirium highlighted the fact that there are numerous medical conditions which may produce apathy as a component of delirium. It is also well-known that elderly patients who develop hyperthyroidism sometimes appear apathetic, which is a paradoxical presentation in view of the hypermetabolic state produced by thyroid hyperactivity (51). Bachman and Albert (52) reviewed evidence that hypoparathyroidism and pseudohypoparathyroidism may present with behavioral abnormalities similar to those seen in individuals with frontal lobe injuries, an especially interesting similarity in view of other evidence suggesting that the features of both conditions may be mediated by abnormalities of central dopaminergic systems (52).

Drugs of several sorts may be responsible for apathetic states. Perhaps best-known is the reported association of chronic marijuana use with an amotivational syndrome (53), although the question of whether the apathy of these individuals represents a physiological or a psychosocial consequence of marijuana abuse has not been resolved. The occurrence of apathy in association with neuroleptic drugs is of particular interest. Akinesia, which is generally defined as a disorder of movement, has been shown to include prominent changes in affect, including apathy (8). In fact, Rifkin et al. (8) defined akinesia as a "behavioral state of diminished spontaneity characterized by few gestures, unspontaneous speech, and, particularly, apathy and difficulty with initiating usual activities." Their report suggested that patients who take antipsychotic drugs

are frequently at risk for apathy occurring in association with the motor changes which usually define akinesia. Apathetic states also occur in the wake of cocaine or amphetamine discontinuation by chronic abusers. In cocaine addicts (54) these symptoms include anergy, depression, decreased sexual interest, and psychomotor retardation. Some of their symptoms (e.g., hypersomnia, hyperphagia, and decreased concentration), however, are not part of an amotivational picture per se.

ASSESSMENT

The following guidelines for assessment of apathy are based on the foregoing discussion of the differential diagnosis and classification of the syndrome. A careful psychosocial history, incorporating information from family members, if possible, is needed in order to evaluate whether apathy has been present throughout adult life or whether it represents a change in personality. For those in whom apathy is a feature of adult personality, it is important to ascertain whether the apathy is deviant or normative for the individual's society or subculture. The evaluation of personality and sociocultural environment will also clarify whether the apathy is a pervasive feature of personality or whether it is selective. Identification of individuals' skills, accomplishments, and social relationships will distinguish between persons in whom apathy is adaptive and selective and those in whom it is defensive or pervasive.

When apathy is an acquired feature of adult personality, it is important to evaluate the possible contributions of multiple socioenvironmental and biomedical factors. Natural or personal catastrophes can usually be identified easily. Less severe stressors, such as retirement, change of residence, loss of a job, divorce, and role change, also produce diminution in motivation. Loss of motor capacities is usually identified easily by history and physical examination. However, cognitive impairment and sensory loss may develop insidiously. In this situation, patients' perceptions of environmental reward or incentives may change with little or no awareness on their part. Thus, evaluation for mild degrees of sensory or cognitive loss is important in such patients. Elderly persons are at higher risk for apathy because of the prevalence of many of these psychological, sociocultural, and biomedical causes of apathy in their lives.

With respect to the psychiatric, neurological, and medical conditions that enter into the differential diagnosis of apathy, a comprehensive psychiatric and neuromedical assessment is called for. It is important to look for a history of psychosis in order to determine whether apathy represents residual or negative symptoms of schizophrenia. In such cases the apathy is likely to have been long-standing. A recent episode of psychosis may be a clue to postpsychotic depression, in which apathy may be prominent. Recent psychosis may also be a clue to psychotomimetic abuse. Finally, psychosis may also be linked to apathy because psychotic patients often receive neuroleptics, which may produce akinesia and apathy.

In general, apathy resulting from depression is diagnosed by the fact that the patient is, paradoxically, not truly apathetic. With some exceptions, depression is a dysphoric state, so that depressed patients who claim to be uninterested or unmotivated will also report low self-esteem, self-deprecatory thoughts, anxiety, depressed mood, hopelessness, etc. Also, they are likely to have vegetative signs of depression. On the other hand, depression in the elderly is sometimes distinguished by apathy in the absence of emotional disturbance and depressive thought content. Previous history of depression, thoughts of futility or hopelessness, somatization, and other physiological changes of depression may help in establishing the diagnosis in these cases.

A complete neuromedical evaluation will lead to a clarification of multiple possible etiological factors. Evaluation of thyroid function is, of course, pertinent in evaluating apathetic patients for the possibility of "apathetic" hyperthyroidism (51). Delirium, which may be produced by numerous toxic or medical disorders, may produce apathy. Therefore, the evaluation of patients with apathy may require consideration of a large number of toxic-metabolic conditions (32). The presence of elementary sensorimotor abnormalities is helpful in clarifying this differential diagnosis. In the elderly it is especially important to evaluate hearing, vision, and cognitive ability. When cognitive impairment occurs in association with dementia, one is naturally lead to consider Alzheimer's disease, multi-infarct dementia, and subcortical dementing diseases.

Sometimes, however, apathy or other evidence of personality change may be the first indication of illness. Discovering the cause of apathy is more difficult in such situations. As a general principle, it is important to keep in mind that change in personality is very unusual in adulthood. While some individuals may make changes in their life style—for example, as part of the so-called midlife crisis or in response to the financial or environmental restrictions of retirement—persistent changes in motivational or emotional behavior are warning signs that a clinical problem is present (55). When there is suspicion of such clinically significant behavioral change, the patient should undergo full medical and neurological evaluation. In addition to a brain-imaging procedure and EEG, lumbar puncture and neuropsychological testing should be considered. Right hemisphere lesions may produce apathy or indifference with few elementary sensory or motor abnormalities. The diagnosis will be supported by a history of left-side sensorimotor symptoms or by neuropsychological evaluation that shows denial of illness (anosognosia), difficulty in getting dressed, visuospatial impairments, or neglect of the left side of space (56).

More difficult to recognize are syndromes of personality change associated with frontal lobe disease. Ap-

athy in association with euphoria, irritability, impulsivity, and loss of social graces suggests frontal lobe disease. Specific neuropsychological testing for frontal lobe capacities, frontal release signs, and evidence of olfactory or visual field abnormalities may be helpful (40, 56). It is important not to rely unduly on brain-imaging procedures, since inflammatory conditions, such as syphilis, acquired immune deficiency syndrome, and granulomatous diseases, may affect the frontal lobe without producing detectable structural changes.

TREATMENT AND RESEARCH IMPLICATIONS

The causes of apathy have been classified here as psychosocial, environmental, and biomedical. A rational approach to the treatment of apathy is based in part upon this classification. In addition, when apathy is secondary to a diagnosable disorder, treatment is built around diagnosis of that disorder. In such cases the heuristic value of apathy lies in its ability to facilitate accurate assessment. In practice the two approaches are complementary.

When apathy represents a response to stable but inadequate rewards or incentives, interventions can be directed at the social or physical environment. In some instances, such as social loss or deprivation, social or political initiatives are called for. These cases, therefore, are not conventionally seen as part of the clinician's responsibility to the patient. On the other hand, it is evident that when there are such concerns, ethical issues need to be considered in defining the extent of clinicians' responsibilities. In a more restricted sense, however, apathy as a response to social deprivation certainly calls on clinicians to initiate involvement of the available community resources. Cases of neglect of children or elderly persons represent fairly common instances in which such social management is an important part of care. They illustrate an important way in which the recognition of apathy as a sign of dysfunction may have heuristic value.

When apathy, despair, or demoralization occurs in the wake of personal or natural catastrophe, there are many individual and social interventions that may be considered (57). In general, they entail marshaling help from external resources and responding to the individual, family, or community sense of powerlessness, loss, and anger.

Treatment of apathy arising from cognitive, perceptual, or sensorimotor impairment entails two aspects: first, ensuring optimal treatment of the patient's hearing, visual, or elementary sensorimotor problems and, second, taking steps to match the patients' social and physical environment to any residual impairments. Supportive individual therapy can be useful. It is important to pay attention to family or other caregivers. Inactivity, which is often the cardinal sign of apathy, may be mistakenly judged as unchangeable when there are physical deficits that can explain it. As a consequence, reversible sensory or cognitive loss may be overlooked. Caregivers may also invoke psychological explanations that interfere with care and interpersonal relationships. For example, sometimes apathy will be viewed as willful, in which case the caregiver may become angry with the patient. A variation of this is projecting one's own anger onto the patient and then viewing the inactivity as the patient's way of showing anger, a problem particularly likely to occur when the patient has expressed anger indirectly in the past. More generally, when apathy results from an otherwise unrecognized medical problem (e.g., apathetic hyperthyroidism), evaluation will lead to specific medical treatment. When it results from some irreversible medical or neurological disease, the ability to label apathetic behavior as such will help patients or family members to understand and cope more effectively with the ambiguities or frustrations that arise from seeing previously competent individuals fail to initiate new goals or persevere at their previous activities.

Currently, the treatment for apathy secondary to major psychiatric disorders usually entails treatment directed at the primary diagnosis. However, in the case of schizophrenia, research targeting negative symptoms represents a specific attempt to treat apathetic states pharmacologically (24, 25). The use of methylphenidate to treat apathy in demented elderly patients (58) and the evaluation of motivational change in Parkinson's disease patients treated with dopamine agonists (52) may also be viewed as attempts to manipulate neural subsystems involved in producing apathy. In effect, these approaches suggest the possibility that apathy is a dimension of behavior having its own neurobiological substrates which may be modified for clinical purposes. If this is the case, treatments found effective for apathy in some conditions might be generalized to other disorders capable of producing apathetic states by similar mechanisms. Viewing apathy as a dimension of behavior having its own mechanisms also raises the possibility that when it occurs as a symptom in association with other syndromes, such as depression or akinesia, apathy may represent a behavioral feature having specific implications regarding mechanism or treatment.

The study of apathy may have additional value for clinical research and treatment. Apathy serves as a heuristic concept to help us examine the mechanisms by which actual or perceived changes in the physical or social environment lead to motivational impairment. Most of the disorders accompanied by apathy involve neural systems known to be important in the elaboration and control of emotion and motivation, such as the midbrain, diencephalic, frontal, and temporal subsystems that constitute the limbic system. In biochemical terms, many of the conditions that produce apathy affect catecholamines. In particular, hypofunction of dopaminergic systems has been postulated to play a central role in many of the conditions discussed (e.g., postpsychotic depression, depression, Parkinson's disease, frontal lobe syndrome, type II schizophrenia,

pseudohypoparathyroidism, neuroleptic-induced akinesia, and amphetamine or cocaine withdrawal). These neurobehavioral and biochemical correlations are consistent with the concept that apathy is a state of primary motivational impairment. They suggest that the study of apathetic states may contribute to our understanding of the neurobiology of motivation. Conversely, information about the socioenvironmental, psychological, or neural controls on motivation may help us develop effective treatments for apathetic states.

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APPENDIX 1. Psychological and Clinical States That May Produce Apathy Syndromes

Schizophrenia (type II or negative symptoms)
Frontal lobe injury
Postpsychotic depression
Frontoparietal right hemisphere infarction
Cingulate gyrus/supplementary motor area infarction
Amphetamine or cocaine withdrawal
Other states of catecholamine hypoactivity, especially dopaminergic hypoactivity, e.g., neuroleptic-induced akinesia
Loss of environmental incentive or reward, as in role loss, institutionalization, and other states of environmental deficiency
Loss of elementary sensory or motor capacity, including hearing or vision
"Apathetic" hyperthyroidism