

Interviews with Pioneers

Sir Martin ROTH

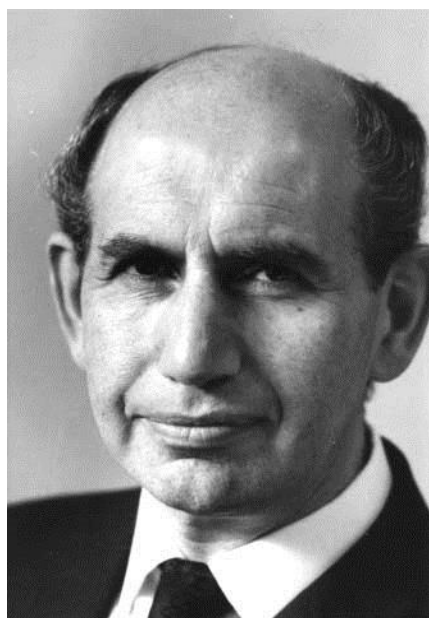
On the Differentiation of Depressive and Anxiety Disorders

Leonardo Tondo

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Biographic sketch



Sir Martin Roth (1917-2006), the son of a synagogue cantor, moved from Budapest to East End of London to escape anti-Semitism in Hungary. During his student years, he acquired a lasting love of literature and music, and rowing. As an adolescent, he contracted a serious illness and thought his life might be relatively short. This experience may have fueled his ambition. He married Constance Heller in 1945 and had three daughters.¹

He became interested in neurology and psychiatry. Following training in neurology, starting in 1943 with Lord Russell Brain² at Maida Vale Hospital, his interests shifted toward geriatric neuropsychiatry after training in psychiatry at the Institute of Psychiatry–Maudsley Hospital from 1945. There, he

worked with Sir Aubrey Lewis³, the first professor of Psychiatry there, and especially closely with his colleague and friend Eliot Slater,⁴ a pioneer in psychiatric genetics. Roth then moved to the Crichton Royal psychiatric hospital in Scotland to work with Wilhelm (“Willy”) Meyer-Gross⁵, who had moved from Germany in the 1930s from a professorship at the University of Heidelberg.

Roth became professor of psychological medicine at Newcastle (1956–1977) and later held the first chair in a new department of psychiatry at Cambridge University (1976). From the 1960s he studied disorders found in elderly patients who had been diagnosed with senile dementia. Instead, Roth found that many were suffering from mood disorders and, therefore, were more likely to respond to treatment. In Newcastle, he collaborated with neuropathologist Sir Bernard Tomlinson (1920–) and psychiatrist Robert Kendell,⁶ later professor of psychiatry in Edinburgh. This pioneering work was a founding contribution to the new specialty of geriatric psychiatry.

In addition to improving the treatment of elderly neuropsychiatric patients, he led development of a seminal diagnostic instrument, the *Camdex (Cambridge Mental Disorders of the Elderly Examination)*, first published in 1986.⁷ With Mayer-Gross and Eliot Slater, he wrote the influential textbook *Clinical Psychiatry (1954–1977)*,⁸ co-edited the five-volume *Handbook of Anxiety*⁹, and served on the editorial board of the *British Journal of Psychiatry* for 40 years. Although critical of the DSM-III (appeared in 1980), Roth was not against standardized diagnostic criteria, but he did not consider them a substitute for careful clinical interviews that included empathic exploration of a person’s mental life.

In 1971, Roth was elected president of the Royal College of Psychiatrists. He was awarded the Anna Monica Prize (1977), the Gold Medal of the Society for Biological Psychiatry (1981), the Sandoz Prize of the International Association of Gerontology (1985), the Kraepelin Gold Medal of the Max Planck Institute (1986), and the Camillo Golgi Medal (1995), in addition to receiving honorary doctorates from universities in UK and US.¹⁰ For his achievements in psychiatry, especially in the field of geriatric psychiatry, Roth became one of only three

psychiatrists to be elected Fellow of the Royal Society in modern times. The others were Sigmund Freud (1856–1939) in 1936, and Michael Rutter (1933–) in 1987.¹¹

About the Interview

The interview was conducted on January 24, 1990, in Pisa, Italy I met Martin Roth during a meeting on anxiety and affective disorders in Pisa in 1990. He was a witty gentleman and seemed pleased to give the following interview, which became much longer than expected. We recorded it during lunch and afterwards when I drove him and his very caring wife, Constance Heller, to the Pisa airport.

The interview

LT (Leonardo Tondo): You have been interested in the classification of affective disorders; how important would you consider this topic?

MR (Martin Roth): Yes, I think it's fundamental.

LT: Has it been fundamental only since the early steps of psychiatric classification, at the times of the first ICD or DSM?

MR: No, it goes back before that, I think it goes back to the time when I first came into contact with Lewis' unitary concept which was really influential in psychiatry. Lewis incorporated within the affective disorders, endogenous depression, neurotic depression and all forms of anxiety disorder and neurasthenia. So there was agitated depression and neurasthenia, then was endogenous depression and reactive depression. I cannot remember the precise titles he gave them but, in fact, it encompassed anxiety disorders for which he had no respect whatsoever and regarded those as nonexistent. The concept of all disturbances, mood and affect, as unitary and very common had a very wide influence in psychiatry. Early on, from my training at the Maudsley,¹² I was aware of the scientifically unprofitable nature of this concept and I was aware of Kraepelin's¹³ view that this was a fundamental misconception. In [the] Kraepelinian system

there was a fundamental line of demarcation between what he regarded as illnesses, psychoses—manic-depressive and schizophrenic. Endogenous and psychotic depressions were allied and, for [Kraepelin], were an illness. When it came to neuroses and psychopathies, for him, these were not illnesses at all. They were outside the scope of illness and this went deep in German psychiatry. Needless to say, that I do not agree with that: when you get outside psychosis you are dealing with problems in ordinary living. Schneider¹⁴ put this in a letter to an American psychiatrist in 1950, that in the neuroses and psychopathies we do not deal with illnesses but rather with variants of normal living, variants of normal life-adaptation. Neuroses do not require treatment [but rather] psychotherapy. So, in clinical practice it has been clear since the early stages of my psychiatric work that, first of all, endogenous and psychotic depressions were clearly defined categories in which one was dealing with conditions likely to be biologically determined. I was influenced at this time by Slater's work on the heredity of manic-depressive disorders.¹⁵ From my earliest days at Maudsley, depressions that were nonendogenous were dealt with something differently [and] were [considered to be] very closely related to the personality of the individual. Nonetheless, some phenomena were superimposed upon the abnormal adaptation patterns and characteristic forms of the primordial personality. I did not share the view of German psychiatry that psychopathy encompassed both neurosis and personality disorder and that they were all life-long phenomena. I could see that there were breaks in continuity of the adaptation of people with personality problems. I am talking here as if the reactive component was unimportant and I think this is how I viewed precipitating factors as making the condition understandable but not necessarily important. Anyway, the point is that I adopted the Kraepelinian position with regard to the separatedness of endogenous and psychotic depression from neurotic depressions. That was one Kraepelinian proposition. The second was that when we get outside the realm of psychosis we do not deal with illness but with a vague phenomenon that merges with the problems of daily living—problems that all people have, and which neurotic individuals have a little more and indeed, within the circumstances, are something that is not accepted [as illness]. My research activities in this sphere began in

Newcastle. While I took this problem with me from the Maudsley, where I finished my training, I listened to the teaching of Lewis in Birmingham: affective disorders were allowed no modification. If we look at what he described as affective disorders we find an enormous territory in psychotic depression. In the meantime, I had become interested in the anxiety conditions, anxiety and phobic states. During the course of my work I had observed anxiety disorders in which phobic symptoms and depersonalization were very prominent. I must be brief, I think; otherwise it will take a whole day. To cut a long story short, we embarked on this subject by the time I arrived in Newcastle in 1956. I was concentrated then on the anxiety states and particularly on phobic and depersonalization states.

LT: Depersonalization seems to be an area of your specific interest.¹⁶

MR: Yes, [but] I never found the time to publish a lot of our material [on this subject]. I was describing agoraphobia but I did not describe what Westphal had described.¹⁷ This is why I gave it another name because Westphal described men who were afraid of open spaces and were so terrified and panic stricken that they would pick strangers from the street, even prostitutes, to accompany them home. Our phobics were women almost entirely. They were not afraid of open spaces; they were afraid of leaving home, even a few yards from home [and became] overwhelmed with terror when they were at a short distance from home. They were afraid of all sorts of situations: going into shops, shopping by themselves, entering queues. If they drove and were stuck at traffic lights, they became panic stricken as well as walking in the street with crowds around. Terror was not of open spaces; the other thing was that it was not just a cross-sectional phenomenon of people who were afraid of open spaces. We were dealing with a complex life historical phenomenon. Phobia [and] depersonalization occurred at a certain specified time of stress but these individuals were not absolutely normal before they got there. Their introversion and anxiety progressed from there and many other neurotic traits bore some resemblance to the neurotic symptoms that followed. The neurotic symptoms were a character to certain respects of what had been there before. In certain respects the neuroses presented new features that [could be] lumped with depersonalization. They were novel features, so there was a

real line of division between the agitation that preceded the disability that kept them housebound for years or decades. If you look at [our] paper¹⁸ [on that topic] you will find that I define it as pan-neurosis because these people were neurotic in so many different directions, they were also sometimes under possession of something, histrionic, and hysterical sometimes. So I was once again [left] with the problem of depression and anxiety.

Within a few years, I did publish [on this topic as] my partial entry into anxiety states.¹⁹ I was absolutely aware then of the problem of anxiety and depression and how they related to each other and how they separated from each other. Through the phobic anxiety syndrome I was aware that this problem was fundamentally important. Darwin²⁰ made the statement of two separate emotions: anxiety and depression, [which was accepted by] everybody who had been educated with me and not under the influence of Lewis. Lewis regarded anxiety states, even obsessional states, and endogenous depression as one condition.

I have left out my work at the Crichton General [Hospital],²¹ where, as I mentioned, I was under the influence of Mayer-Gross. I became very closely familiar with the Kraepelinian view of things and with German psychiatry. My perception of the psychotic-endogenous disorders as separate from the neurotic ones was deepened when I worked in Scotland for about three years. Then I left Crichton General [Hospital] for Greylingwell [Hospital]²² in 1950 and I brought the concept with me. There I was occupied with the problems of old age. I continued my interest in anxiety disorders which culminated in the 1959 publication, but by that year we had antidepressant drugs. In the Crichton Royal [Hospital] in Newcastle we were soon embarking upon clinical trials of imipramine. They were largely undertaken in my department there but Lesley Kiloh,²³ later professor in New South Wales, Australia, conducted a number of trials. I gave him very strong encouragement and was an author of one or two papers with him. The first trial,²⁴ one of the earliest trials was undertaken with him. [It] showed unequivocally that imipramine [Tofranil™], discovered in 1957 by Kuhn and collaborators,²⁵ was an effective substance and active antidepressant. It was significantly more effective in endogenous depression than in neurotic depression but was effective also in neurotic depressions. This was

surprising and made it clear one was dealing not just with some problem of living. As you know, if you give imipramine to an ordinary subject he feels awful. If you give it to severely neurotic depressives, they may achieve considerable improvement, and this was very important. Now Kiloh, Ball and Garside²⁶ [1962] in their early studies used multivarious statistical methods and I was already involved in using these methods for purposes of classification.²⁷ They did a factor analysis to try to differentiate between response patterns of endogenous and neurotic depression and also looked into their classification. Incidentally if I can bring here a point, Kiloh and Garside later were to make an historically very important analysis of Lewis' original observations in his M.D. thesis in the University of Adelaide.²⁸

They took what Lewis described in his cases in enormous detail and were able to do a principle component analysis on Lewis' clinical observations. They showed that on Lewis's own observations, endogenous depression [was] sharply distinct from nonendogenous depression. [After] this [finding] was sent to Lewis, it was published in the Australian Journal of Psychiatry.²⁹ [Lewis] responded by saying that multivariate statistic was an inappropriate method for studying patients; it was irrelevant and invalid to do it. Some statistical authorities have taken this view but the great majority have said [that Lewis' point] was quite incorrect. In fact, you should use these methods to separate [clinical groups]; everybody believed [that] you must *ipso facto* justify using them for classifying patients. In these analyses, you extract factors that summarize the distribution of variation within the pattern. When you plot factors, you plot along the axes; usually your first plot gives scores to each symptom, [which] may be very high or very low. When you use it to classify patients, [you] merely to add up the scores obtained with the symptoms and you plot that.

LT: I read that study.³⁰

MR: Yes, I think that was one of the most conclusive pieces of evidence [in the] paper published in the early 1960s. Later on we published a number of multivariate statistical studies. In 1965, Carney, Garside, and I published a study of the birth of classification of depression and the prediction of treatment response in the *British Journal of Psychiatry*.³¹ Briefly, it proved with

multivariate techniques that it is possible to get a bimodal solution, to get clear separation, that's all. And this was a special group of patients who had been selected for treatment with ECT, but they included both neurotic depressions and endogenous depressions so it was possible to investigate their differential response. [If] the concept of unitary psychosis were valid, there [should be] evidence that schizophrenia, manic-depressive disorders, [and] paranoid psychosis, were all one and the same. [If] we had unitary neurosis, people would say that psychosis and neurosis are useless terms, [and] unitary psychosis and neurosis [would] become one term. At the neurotic end there would be what all [of] German psychiatry says and also what Kendell says: that there is no distinction, no clear demarcation between neurotic phenomena and normal. So psychiatry is confronted with one enormous continuum [in] thinking of everything. [However,] this is a sterile concept because in these continua it is not clear what you are measuring. What are you to measure? How do you measure it? How do you devise a dimension to measure? What is it that you are measuring? What do you do with your measure? How do you advance the knowledge of treatment with these unitary concepts. We are back with Griesinger³² with this concept: one disease of the brain. This is, I think, the end of clinical psychiatry. I have published, for example, about the relation to mood disorders and affective disorders. Klerman³³ has often contributed something to my work; [I would not agree with] everything he says about the development [of psychiatric diagnosis] and the historical changes, but I think it is very interesting and worthwhile to look at.

I must try to be a bit more concise: I was very tired when I first met you, [and should] perhaps accelerate a little, take things more in outline. This issue of endogenous depression and neurotic depression dominated discussions of the classification of affective disorders in the 1960s and in the 1970s when depression was the leading theme in relation to mood disorders. To express an opinion, I believe that great many conditions were called depression and were called so because there were effective treatments for depression, so that individuals with any kind of disturbance of affect or mood received a diagnosis and treatment for depression. We also know that many anxiety disorders and phobic disorders were treated as depression because of so-called

“atypical” depression, [about which] there is quite a literature: Sargant and Dally wrote about it.³⁴ Then there was an American group, I think Prien was one of them, though I am not absolutely sure, [who] wrote about atypical depressions [which] were heavily loaded with such features as phobic symptoms, hypochondriacal symptoms, and unreality feelings.³⁵

LT: Do you think that the dichotomy between endogenous and neurotic depression became clearer due to the response to treatment?

MR: Well, I think it was. I believe that [our studies],³⁶ on the whole, showed that endogenous depressions had a better prognosis and I believe that the evidence showed this, but I suppose it is possible for critics to say that the difference was a quantitative, not a qualitative one. Some people believed it was a matter of severity, [in] that endogenous patients were more severe. [However,] in many cases of neurotic depressions I find [antidepressants to be] effective.³⁷ So [differences based on responses to] drug treatment could be viewed as a quantitative difference and not some difference of quality.

LT: If it is a quantitative difference, why did the first trials with imipramine show better response with people in endogenous depression?

MR: The same difference was shown in the studies of Kiloh³⁸ and the Newcastle trials. I do not think it is a quantitative difference because a neurotic depression can be very much more severe than an endogenous depression and an endogenous depression can be very quiet. One morning, [a patient] goes out and blows his brains out with a double-barreled shotgun, whereas a neurotic depression maybe very severe and an endogenous depression be quiet [and] not necessarily suicidal, but not by any measure of severity it would be less severe. So it cannot be a matter of severity that the partitions are on quite different grounds. However, that was the issue. We had begun already in the late 1960s to study the demarcation line between anxiety disorders including the phobic states, and depressive states we included the phobic states. By 1970 we published the first paper in relation to the classification of anxiety and depressive disorders in which we used multivariate techniques. We showed that we could separate anxiety

disorders and depressive states.³⁹ Now there were several lines of evidence that the [two types of conditions] were different. First of all the clinical phenomenology: when examined statistically, the clinical profiles of these patients were distinct and clearly separable. There were criticisms against this sort of separation of anxiety and depressive disorders because it was claimed that it was biased by the fact that we had begun by making the diagnosis, and were not entirely objective about the assessments and subsequent calculations based on analysis of symptomatology. I think that there is something in that view but it is [not] an entirely valid criticism. I do not want to enter into details, but [would] say is that if you start with a certain view that the two disorders are quite distinct and you have gotten a list of symptoms and then you submit the total matrix of symptoms to an analysis with these rather refined statistical techniques, it is quite possible for your view to be entirely refuted because you cannot possibly know in advance what weight, what score the computer will allot each one of 35 items, so the computer may decide that one item is [more] important than another and what you thought was important, virtually is not. So when you do get a bimodal distribution I think it means something. We had to use special techniques to show that there were two syndromes. We knew that such a result was tentative.

There were several other lines of evidence that showed that anxiety symptoms and anxiety disorders were different. I think we were the first people to do a follow-up investigation. Other people have looked at anxiety and depressive symptoms because benzodiazepines have come along in the meantime. [Nevertheless,] in a second line of evidence we showed in independent follow-up study with Kerr, Gurney and Schapira⁴⁰ that at every stage of the three-and-a-half to four-year follow-up investigation, depressions did better than the anxiety neuroses. A third line of evidence, now being contested by the people who talk of unitary neuroses, was that there was very little crossover. In other words, agoraphobic states did not change into depressions and depressions did not change into agoraphobic states. The last line of evidence was that the predictors which we developed [in our] the predictive indices or anxiety states and depressions were quite different from each other. In [such a] study, we included the endogenous

with the neurotic depressions. It could be held that the endogenous depressions served to pull the depressions away from the anxiety states. So, we did [another] study in which the endogenous depressions were excluded; that was the investigations I did with Mountjoy.⁴¹ Very much to my surprise, [we found] that even without the endogenous cases the neurotic depressions proved to be distinct from anxiety disorders. Here I come to the reemergence of the importance of the personality setting because since drugs have come with the emergence of the era of biological psychiatry, what was falsely called noise tended to be avoided. The view that the patient's symptoms are the disease, [led to] the disappearance of historical-developmental [and] dynamic personality factors [had led] to the impoverishment of psychiatry.

LT: Probably the personality is not really suited for science.

MR: That's right partly, but you see one very distinguished biological psychiatrist, a very intelligent person (I would not mention her name) said that a biological psychiatrist of the future will be very terse in his examination. He will not conduct detailed investigations into life situation, development, interpersonal relationships, relationships with parents, childhood, adolescence, sexual life in the developmental sense. He will ask about sleep, energy, appetite, weight, mood, physical symptoms and sexual function and that will [be] quite enough. I believe that people who believe that are going to be the coffin-bearers of psychiatry who would bear psychiatry into its graveyard [chuckles].

So perhaps I should emphasize here my own attitude to these things. Somebody in a *festschrift* [suggested] that I am repeatedly referred to as a neokraepelinian, [though] I am not a neokraepelinian. I accept that clinical subdivision in the psychoses, in organic disorders are great but the whole of the Kraepelinian and the German school, their attitude that neuroses are identical with personality disorders and [that] both have nothing to do with illness [but are] version of normal mental life is totally remote, totally unacceptable to me; not for 35 years has [this view] been a part of my outlook. In fact, I do not think I have ever accepted that view in psychiatry, even in the psychoses. I [also do not accept] the Scandinavian concept of psychogenic psychosis, even psychogenic endogenous depression. Not that I accept that life-

event [are] the whole cause. [Instead], I think you are looking at some personality problem. It had never been acceptable to me that the neuroses and personality disorders were outside the realm of psychiatry or could I even accept that even in the psychoses. You could look just at the symptoms [as] the disease, and nothing else in relation to personality method ... I am rambling a bit ... I come back to the question of personality factors. I would like to mention the work of Caetano, [who] worked with me for about five years and published a doctoral thesis in Cambridge.

LT: Who was this person?

MR: Caetano Dorjival, a Brazilian student who did a very fine study of all kinds of depression versus anxiety.⁴² The important point [is that] he used the *16 Personality Factors Questionnaire* (16PF),⁴³ and the *Maudsley Personality Inventory* (MPI),⁴⁴ to study a very large material of patients from a consecutive sample; the other important thing is that his patients were examined with the PSE.⁴⁵ He showed that, in a group of patients who had achieved remission from their illness, using the two personality tests alone he could allocate more than 80% of the patients [to a] most confident diagnosis. Special statistical methods [used involved removing] a middle group where there is ambiguity, and you are uncertain of the diagnosis [so as to] have two clean groups. [In this way, Dorjival] was able to allocate more than 80% with the personality tests alone to the correct anxiety or depressive groups.

LT: Sometimes personality tests actually evaluate symptoms.

MR: [Dorjival] did [his study] in the phase of remission [or] recovery, and with very simple items which we excavated from the study I did with Mountjoy.⁴⁶ At the time, we were not interested in studying personality; we used the MPI because it had been part of the protocol used by Gurney originally.⁴⁷ But we went back and looked at this personality issue. It has become important, and just about four years ago I said, 'Let us dig out all the items we have about historical development and personality, childhood history and so on.' First, we did the discriminant function analysis to see whether we could separate anxiety and depression. In other

words, with the personality data we had showed that patients with anxiety and depressive disorders were distinct groups. At first doing all the patients, the separation was not very impressive. Then I suggested that we should do the men separate from the women. Now this was very interesting. First of all the [diagnostic] separation in the women was far more clear than in the men. Secondly, the indices which separated anxiety from depressive states were very different in the women from what they were in the men. I think far too little attention had been paid to this [sex effect]: when we talk of anxiety disorders or phobic disorders, men are a rather different group from women. The main point was that the view of the symptoms of the entire disease is not validated and I think that people are now looking more and more into personality dimensions. Now, along comes DSM-III.

LT: When did the interest in differentiation between endogenous and nonendogenous depression start?

MR: Well, Kraepelin assumed that they were different psychogenic disorders – as he called them – that were different from the psychoses. There were great debates in the 1920s between Aubrey Lewis and the distinguished psychologist Robert Gillespie.⁴⁸ Lewis was a unitarian, he was not a good clinical psychiatrist.

LT: Was also Meyer a unitarian psychiatrist?

MR: Yes, Adolf Meyer believed in reaction types, not in diseases. Anybody could get any disorder, so scientifically his heritage was rather impoverished, scanty, and sparse. It is a good thing you mentioned [him] because English psychiatry had been heavily influenced by Meyer. Lewis went to Johns Hopkins⁴⁹ and became inspired by Adolf Meyer with his rather nebulous conception. Desmond Curran,⁵⁰ a famous English psychiatrist worked with Meyer in Baltimore, [as did] David Henderson.⁵¹ They all came back to England with the Meyerian view which looked rather at reaction types and showed very little interest in taxonomy. Mind you, Meyer had the virtue of introducing the human being onto the stage and encouraging a new kind of dynamics; something that departed from Freudian dynamics [but fostering] an examination of the

life history of every patient and insisting that this was the clue: the life history of the individual. The trouble is that if you concentrate attention on individual patients and ignore classification, you cannot get anywhere. Looking at an individual you can do nothing but gaze at him in ineffable wonder and you cannot expect any truth from, unless there is knowledge about groups. How do you dig out any facts? How do you separate signals from noise looking at the individual? So it was a worthy objective but it could not be carried into realistic effect or in actual [clinical] practice in the absence of head-headed look at classification. On the other hand, in reaction against psychoanalysis, American psychiatry came in with what they call the new Kraepelinian view [represented by] DSM-III which I [will] not go [into] too much ... It threw neurosis out of the window and it ignored the concept of psychosis.

LT: What do you mean by that statement?

MR: Well, I mean that the distinction between neurosis and psychosis does not figure [in DSM – III]: they are two entities, two groups of disorders, each with a separate little pigeonhole to be put in—a general concept without any general conceptual structure. Another important fact about the DSM-III is that it introduced a number of axes, so in a sense you could claim that it was multidimensional. But, if you read any research clinical publication that matters you will not see many descriptions of axis-II diagnoses figuring as criteria of admission to a given study; axis II sat there in the wings waiting to be called in what was [a] cross-sectional classification. One can understand that approach to psychiatric [diagnosis], but it ruled that anxiety disorders and affective disorders were separate, quite distinct conditions; anxiety disorders suddenly began to be explored [after] 1980. Shortly afterwards there came panic and panic-agoraphobic disorder and this is where interest was taken in my original description of phobic anxiety and depersonalization because there is nothing [is] identical with agoraphobia in its acute stage.

LT: Regarding this particular issue, do you think that the inclusion of obsessive-compulsive disorder in the anxiety group of DSM-III disorders was justified?

MR: No, I don't think so. I believe it was not strictly in accordance with facts because, if there one condition which stands out as being distinctively recognizable, having a course of its own, having commanding and very high measure of inter-observer agreement in diagnosis, you would choose obsessive-compulsive psychoneuroses. But there are elements of justification for it; certainly obsessive-compulsive patients are very anxious, so like many other conditions, [including] psychotic disorders, which are not in the anxiety group. Obsessive-compulsive neurosis [has] an enormous repertoire of symptoms, like one day fearing that lightning will strike you down, next day fearing that a meteor might drop out of the sky [or that] they would suffer from contamination [and need] to wash hundreds of times: that's classical of obsessive-compulsive neurosis. But [in] general anxiety disorder, it is very common to find one obsessional thought, one fear. Although the doctors cannot find any evidence of cancer, the person may have cancer; these are not depressions, usually they are anxiety disorders in obsessive-compulsive personality setting. The answer to your question is: no, I do not think that obsessive-compulsive neurosis belong to the anxiety disorder but I believe that agoraphobia does and that cases of social phobia do.

LT: Would you consider personality as an important background in terms of further development to a clear-cut psychiatric disorder; does a special personality develop into a particular kind of disorder, or you think that personality and disorders are independent?

MR: Very interesting and astute question, if I may say. I am sure that personality *factors* matter, but first our measures [of these] are rather crude and I am not at sure that [such] measures give us the right answer. I believe that there are mysteries about which we do not know very much. I am certain, for example, that anorexia nervosa – which I think one has to accept as a neurosis – occurs in many different kinds of personality; and agoraphobia, which I know very well, also is not confined to one type of personality dimension or profile. I believe there is something like a mystery here that needs more light to be shed on it. What I am certain of are two things: that if psychiatry develops along the line in which it is concerned with presenting symptoms and signs alone, it will become impoverished and will die of inanition. The other thing I am certain of is

[that] to study the historical and developmental aspects of psychiatric patients and to try to understand the individual is indispensable for psychiatry. The term ‘understanding’ is very unfashionable; it is regarded with skepticism, even with a certain contempt [as a] totally unscientific activity; there is a very fine passage in Kraepelin which reflects Kraepelin’s thought about understanding. He said that in ordinary social life, understanding is indispensable; we cannot live without trying to understand those we meet [or] relate to, trying to work out what they like and entering into a relationship with them. In real disease, it is very open to self-deception and, except for the cases of psychopaths, by that [Kraepelin] meant neurotic and personality disorders, which he did not regard as illnesses, [in which] understanding is best avoided. I disbelieve that and I disbelieve also that understanding is fundamentally at variance with the scientific approach in psychiatry, because the concept of understanding others by studying their behavior, their language, their facial expression does not come from me or even from Jaspers;⁵² it comes from Charles Darwin. You find a very good description of this in Darwin’s *Expressions of Emotions in Man and Animals*. When I spoke of personality as being important it is not that I know that personalities are the specific antecedents of different forms of psychiatric illness. Studies by von Zerssen⁵³ showed no distinctive personality setting in [a broad] variety of illness except [for] endogenous depression.

LT: Speaking of von Zerssen, what do you think of the concept of temperament and how it is different from personality?

MR: These are rather bad terms. Temperament refers to the emotional characteristics of the individual; the old theory of the temperaments in terms of the old Greek concept of the humors. Personality is wider and it refers not just to mood but [also] to a wide range of other things; the term relates to terms that psychologists nowadays use in their frame-dimension. You could use such things as motivation, a novelty seeking, dependency reward—in other words, [an entire] range of dimensions other than those which relate to temperament. What about character: did you ask me that or did I ask myself that? Character refers more to those aspects of personality which relate to the system of aspiration, values, self-disciplinary strategies and techniques, and

the manner in which these are expressed in relationship with others. I think they are related concepts; temperament relates to mood, [but] personality is wider.

LT: In patients with panic disorder and agoraphobia we have seen traits characterized by hyperthymic temperament, over-controlling of emotions, especially among high-achievers.

MR: 'Hyperthymic' refers to individuals with elated states, [as] you find in Akiskal.⁵⁴ However, that is interesting. I think this is a difficult area which needs much research. I believe that two things stand out for me from that background; the first is that these are individuals who may show a drive toward high achievement, may show apparently actual achievement as well as high drive toward it, but fundamentally these are compensatory activities; and emotional dependence on others is a central characteristic. It is seen in the characteristic form in the individual who is housebound, who cannot get out of the home without feeling panic and being overwhelmed, unless she is accompanied by somebody rather close to her, [perhaps] a husband. You see that this a complete negation of any physiological theory alone; here is a phenomenon where you have an individual in a state of panic with heart pounding at 160 but give her a friend and she can go away, to the end of the earth. I think this does not come on, does not commence with agoraphobia; it has been there as a personality trait long before. I have said all these things far better in many other places, I am a great supporter of biological psychiatry ... [There are] genetical discoveries in relation to schizophrenia and manic-depressive disorder, [and] recently about panic disorder. They claim to have mapped the gene for panic disorder as major locus, [possibly] on chromosome-7.⁵⁵ I am a great believer in this [approach]; biological psychiatry perhaps is at a growing point. [Its] reductionism is very powerful but it is not to be regarded as the answer to all the problems of psychiatry. I don't believe that it is likely to be able to arrive at the biological language which eliminates the language of clinical and psychodynamic observations, and certainly I don't have answer to the problem of making a scientific discipline out of the definition of personality profiles and their relation to illness.

LT: In many patients with panic disorder I have seen also over-controlling parents, mainly mothers with a lot of anxiety and very concerned that something may happen to their children.

MR: You also see under-controlling ones; that is the trouble.

LT: Dealing with power in the relationship between mothers and children; also you mentioned that mother-child separation is the first moment of agoraphobia, supporting the idea that you depend on somebody. On the same line there is the issue of early and recent losses in patients with panic disorder and depression. What do you think?

MR: Klein⁵⁶ claimed that separation anxiety occurs in high proportion of people and he has related this to [a] Bowlbian concept. I think this is a very controversial field for two reasons: first of all in the recent investigations including those by Klein himself he has not succeeded in demonstrating that a significant excess of patients with agoraphobia had had separation experiences.⁵⁷ In fact, he introduced some ad hoc explanation why [such patients have had] very controlling parents who have never let them experience separation; I don't think a great deal of that, saving your hypothesis from extinction. [Also], child psychiatrists who have published follow-ups on people who had school phobia have not confirmed [that] those who have suffered with school phobia, with the exception of a small minority who begin phobias after the age of eleven, are especially liable to neurotic disorder in later life. [That is,] follow-up of school-phobic patients does not provide very good confirmation for this theory. [Concerning] loss of a parent, George Brown's⁵⁸ work [finding that early] loss is a consistent or major causal agent in depression during adult life has been replicated by some but rebutted by more people. I have not looked at the recent research but I was familiar [with it] until three [or] four years ago. I don't think the evidence for [an association between early loss and later depression] is very good nor peculiarly productive. Of course, if you lose a mother, you suffer a disadvantage without any question, but how much this contributes and to what disorder is another matter. I don't think that Brown's notion is very well substantiated. I suppose that Bowlby's⁵⁹ idea that agoraphobia [arises from] separation anxiety is an attractive idea. One can see that [agoraphobia] is indeed the fear of being separated from home [and from] people who belong there, but it is hard to expect that some separation which occurred in childhood may lead to an [adult] illness. I do not think it has been proven.

Can I just mention [a] very important issue here which has brought back the old question of separation of anxiety and depression? [Regarding] the phenomenon of comorbidity, certainly there is quite often a depressive coloring to agoraphobic disorder, but people failed to differentiate between depression as a symptom and depression as a syndrome. Anxiety and depression are constantly working in association, but the presence of one depressive symptom does not mean a comorbidity of depressive illness with panic disorder. If an anxiety symptom in depression which does not lead to the diagnosis of a depressive illness, an anxiety symptom in a depressive illness does not lead to a diagnosis of depression [either]. In addition, depressive symptoms, one or two, which tend in any case to be transient in anxiety or phobic disorder, do not lead you to vary the diagnosis issue. What I would say is this: when you study agoraphobics for years you will find from time to time they become depressed and sometimes very depressed so that they may have to go to a hospital with the depression superimposed on their agoraphobia. [Nevertheless,] there is a refractory-resistant core that survives year after year, the agoraphobia. This is the explanation of the fact that you will get some patients with agoraphobia [even] 10, 15, and 20 years [after presenting] for the first time. The same is true of social phobia. Evidence has been advanced recently that suggests that phobia, panic disorder, agoraphobia, and depression have some common foundation in etiology. I do not think [it] is very well founded [or is of] sufficient depth [regarding] the phenomenology, course, and outcome.

LT: People who agree with the idea of comorbidity claim that the effectiveness of antidepressants for both depression and anxiety could be one of the elements supporting the association.

MR: Having a treatment that is successful in several diseases does not mean the diseases are the same; if that were the case, if you use the effect of corticoids as a principle of classification in medicine you would have a very peculiar picture. In relation to depression and anxiety disorder what is certain is that there is a treatment that sharply discriminates between them: we are talking of the rediscovery of ECT. ECT in severe depressive disorder with suicide symptoms and with typical endogenous symptoms can be a life-saving procedure. I do not know of any evidence

that ECT is an effective treatment for anxiety disorder. In fact, if you give ECT to [anxious] patients, you are likely to make them worse; frequently they may switch on to an attack of depersonalization that lasts for months or years. Have you seen this?

LT: Not in my patients because I have no access to ECT in Sardinia.

MR: No ECT in Sardinia: not allowed?

LT: Because there no facilities where to administer it.⁶⁰

MR: It is incredible.

LT: I know patients who have been treated with ECT in whom the indication probably was not 100% correct, who experienced depersonalization.

MR: I would be interested if you send me a few case histories. I think the difference [in the effect of antidepressants] is decisive. Obviously, if you find that antidepressants work in panic disorder – and I am not so sure they work in the long term in agoraphobia – I think we have a few follow-up studies of the effects of drugs in agoraphobia; if they work in panic disorder and also in depression, [there] must be some common factors, but it does not mean that they are the same disease. They may have one connecting thread: for neurotic disorder as a whole that there are threads in common between neuroses, but it would be very distractive to go from that to the inference that agoraphobia, social phobia, hysterical or conversion disorders, obsessive-compulsive states, hypochondriacal disorder, anorexia nervosa, post-traumatic stress disorder are all one condition. I do not think that [by] continuing to draw a line across distinct disorders to show by means of some matching symptom scores, you can demonstrate no visible break in the curve that connects the symptom scores of all these conditions. [This,] to me, is an empty exercise; that there is no difference it is not acceptable. Many excellent investigators argue, in principle, in favor of unity of neuroses. What they are saying is that same genes [are associated with] different syndromes. You asked about differentiation. I think that in relation to psychopharmacology there is something rather specific about the effects of clomipramine in obsessive-compulsive states; I believe that there is a lot of evidence that it is effective in a

substantial proportion [of such cases], and there is a recent review paper by Murphy.⁶¹ There [also] is evidence social phobic states tend to benefit from monoamineoxidase inhibitors. I don't think we have yet any treatment for anorexia nervosa unless you can tell me one. Do you think we can take a five-minute break? [that was a euphemism to mean that the time was over].⁶²

Notable comments

Several of comments made by Dr. Roth during my 1990 interview with him were particularly noteworthy:

The trouble is that if you concentrate attention on individual patients and ignore classification, you can't get anywhere. Looking at an individual you can do nothing but gaze at him in ineffable wonder and you can't expect any truth from unless there is knowledge about groups.

I am certain, for example, that anorexia nervosa, which I think one has to accept as a neurosis, occurs in many different kinds of personality.

If psychiatry develops along the line in which it is concerned with presenting symptoms, it will become impoverished and will die of inanition. ... To study the historical and developmental aspects of psychiatric patients and to try to understand the individual is indispensable for psychiatry.

Many [who] show a drive toward high achievement may show apparently actual achievement, ... but fundamentally the central characteristic is that these are compensatory activities and emotional dependence on others.

I don't have an answer to the problem of making a scientific discipline out of the definition of personality profiles and their relation to illness.

The phenomenon of co-morbidity ... Certainly there is quite often a depressive coloring to agoraphobic disorder but people fail to differentiate between depression as a symptom and depression as a syndrome; of course anxiety and depression are constantly working in association, but the presence of one depressive symptom does not mean a comorbidity of depressive illness.

In reaction against psychoanalysis, American psychiatry came in with what they call the new Kraepelinian view of DSM-III ... It threw neurosis out of the window and it ignored the concept of psychosis.

[The] biological psychiatrist of the future will be very terse in his examination. He will not conduct detailed investigations into life situation and development, and relationships with parents; childhood, adulthood, sexual life. He will ask about sleep, energy, appetite, weight, mood, physical symptoms and sexual function and that will give him quite enough. Well I

believe people who believe that are going to be the coffin-bearers of psychiatry ... into its graveyard [That future is now].

Endnotes

¹ Photo from: Sir Martin Roth, an appreciation (Kerr TA, Kay D. Sir Martin Roth, FRS. An appreciation. *Br J Psychiatry* 2007; 190: 375–378.) The article includes more biographical notes. An even more detailed autobiography is included in a publication by the CINP (Ban et al 2000) and other notes are included in some newspaper articles: (Anonymous. Obituary: Sir Martin Roth. *Bull RCP* 2006; 10: 95; Anonymous. Obituary: Professor Sir Martin Roth. *The Daily Telegraph*, 13 October 2006; Kay D. Obituary: Sir Martin Roth. *The Guardian*, 27 October 2006; and Wischik CM. Professor Sir Martin Roth. *The Independent*, 19 October 2006.

² Walter Russell Brain, 1st Baron Brain (1895–1966), British neurologist, author of *Brain's Diseases of the Nervous System* and editor of the homonymous neurological medical journal aptly titled *Brain*.

³ Sir Aubrey Julian Lewis, (1900–1975) was born in Australia. In 1946, he became the first Professor of Psychiatry at the Institute of Psychiatry in London. He was a great supporter of the unitarian view of depression following Adolf Meyer's ideas. Lewis was pragmatic in his approach to diagnosis: "if clinical differences did not make a difference in practice, then there was no difference". Roth, instead, was a divider who emphasized psychopathology: "if clinical syndromes could be shown to be different in phenomenology, then they are different" (Ghaemi NS. The heterogeneity of depression: an old debate renewed: *Acta Psychiat Scand* 2011; 124: 497.)

⁴ Eliot Trevor Oakeshott Slater (1904–1983), British psychiatrist, co-editor of *Clinical Psychiatry*, the leading textbook for psychiatric trainees. He had polyhedric interests, including chess, music, poetry, painting, statistical study of literature, and euthanasia.

⁵ Wilhelm Mayer-Gross (1889–1961), German psychiatrist, worked in Heidelberg and was important in the field of phenomenologic psychiatry. He moved to England in 1933, first in London and then in Birmingham, where he became very influential in British psychiatry.

⁶ Robert Evan Kendell (1935–2002), a Welsh psychiatrist trained under Sir Aubrey Lewis, chair of psychiatry in Edinburgh. Roth and Kendell argued a lot about differences between anxiety disorders and depression. Kendell claimed that, together, they formed an undifferentiated spectrum of emotional disorder, too often found together to be able to distinguish them (see: Kendell RE. Clinical Validity. *Psychol Med* 1989; 19: 45–55). Roth favored two distinct biological entities, with different clinical features, different genetics and different natural history. From the diagnostic point of view, and also based on modern molecular genetics, Roth's concept won and is included in DSM and ICD. Nevertheless, from a therapeutic perspective, there remains a large overlap between the two groups of disorders (see: Wischik CM. Professor Sir Martin Roth. *The Independent*, 19 October 2006.)

⁷ Roth M, Tym E, Mountjoy CQ, Huppert FA, Hendrie H, Verma S, Goddard R. CAMDEX: a standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. *Br J Psychiatry* 1986; 149: 698–709.

⁸ The third edition was published in 1966 and the partial edition of 1977 was prepared by Roth and Slater since Mayer-Gross died in 1961 in Birmingham on the night before he was due to return to Germany. A fourth edition was in preparation for years but never published (Ban 2000).

⁹ Roth M. Categorical subtypes and dimensions of illness in the anxiety and related disorders. In: Noyes R, Roth M, Burrows GD, editors. *Handbook of Anxiety, vol. 2*. New York: Elsevier; 1988a. pp. 53–79.

¹⁰ Ban T, Healy D, Shorter E. *The history of psychopharmacology and the CINP as told in autobiography*. Budapest, Animula. 2000, pp. 238–249.

¹¹ Previously, other psychiatrists became Fellows of the Royal Society: William Battle (1704–1776) in 1742, Sir John Charles Bucknill (1817–1897) in 1866, and William Halse Rivers (1864–1922) in 1908.

¹² The Maudsley Hospital in South London and is the largest mental health training institution in the UK; it is partnered with the Institute of Psychiatry of King's College. It was founded in 1907 when the Victorian psychiatrist Henry Maudsley offered London County Council the sum of £30,000 to help found a new mental hospital that would be exclusively for early and acute cases

rather than chronic cases, have an outpatient clinic, and provide for teaching and research (Wikipedia 2015).

¹³ Emil Kraepelin (1856–1926) was a German psychiatrist considered the founder of the modern scientific psychiatry. His major work, *Compendium der Psychiatrie: Zum Gebrauche für Studierende und Aertze* (*Compendium of Psychiatry: For the Use of Students and Physicians*), was first published in 1883 and was expanded in subsequent editions (total of 9) as *Ein Lehrbuch der Psychiatrie* (*A Textbook of Psychiatry*) until 1927. His major contribution to psychiatry was the description of a dichotomy between *dementia præcox* (later termed schizophrenia) and manic-depressive psychosis (later, bipolar disorder and recurrent major depression).

¹⁴ Kurt Schneider (1887–1967) was a German psychiatrist whose main interest was the study of schizophrenia, personality disorders, and psychopathic personalities.

¹⁵ a. Slater E, Tsuang Ming–Tso. J. Abnormality on paternal and maternal sides: Observations in schizophrenia and manic-depression. *J Med Genet* 1968; 5: 197–199.

b. Slater E, Maxwell J, Price JS. Distribution of ancestral secondary cases in bipolar affective disorders. *Br J Psychiatry* 1971; 188: 215–218.

¹⁶ a. Roth M. The phobic anxiety-depersonalisation syndrome. *Proc R Soc Med* 1959; 52: 587–596.

b. Roth M. Phobic anxiety-depersonalization syndrome and some general aetiological problems in psychiatry. *J Neuropsychiatry* 1960a; 1: 293–306.

c. Roth M. Depressive states and their borderlands: classification, diagnosis and treatment. *Compr Psychiatry* 1960b; 1: 135–155.

d. Harper M, Roth M. Temporal lobe epilepsy and the phobic anxiety-depersonalization syndrome: a comparative study. *Compr Psychiatry* 1962; 3: 129–151.

e. Roth M, Harper M. Temporal lobe epilepsy and the phobic anxiety-depersonalization syndrome: practical and theoretical considerations. *Compr Psychiatry* 1962; 3: 215–226.

f. Cassano GB, Petracca A, Perugi G, Toni C, Tundo A, Roth M. Derealization and panic attacks: clinical evaluation on 150 patients with panic disorder-agoraphobia. *Compr Psychiatry*

1989; 30: 5–12.

g. Toni C, Cassano GB, Perugi G, Murri L, Mancino M, Petracca A, Akiskal H, Roth SM.

Psychosensorial and related phenomena in panic disorder and in temporal lobe epilepsy. *Compr Psychiatry* 1996; 37: 125–133.

¹⁷ Karl Friedrich Otto Westphal (1833–1890), German psychiatrist from Berlin coined the term ‘agoraphobia’, after the observation of three men with anxiety and feelings of dread associated with being in public areas. In: Westphal C. *Die Agoraphobie: eine neuropatische Erscheinung*. *Archs Psychiatr Nervenkr* 1871; 3: 138–161.

¹⁸ Roth M, Argyle N. Anxiety, panic and phobic disorders: an overview. *J Psychiatr Res* 1988; 22(Suppl 1): 33–54.

¹⁹ See note 11a.

b. Roth M. Anxiety neuroses and phobic states. I. Clinical features. *BMJ* 1969; 1: 489–492.

²⁰ Charles Darwin (1809–1882). His most famous book was *On the Origin of Species* (1859) in which he claimed that all living beings descend from common ancestors introducing the concept of natural selection and the survival of the fittest. In 1871 he published *The Descent of Man, and Selection in Relation to Sex*, followed by *The Expression of the Emotions in Man and Animals* (1872) which represents an important contribution to psychology.

²¹ The Crichton Royal Hospital is the largest Scotland’s psychiatric hospital. It was founded in Dumfries in 1838 by Elizabeth Crichton (1779–1862), a wealthy local widow. She persuaded the phrenologist William A. F. Browne (1805–1885) to become medical superintendent and to implement his innovative ideas of occupational therapy (Wikipedia).

²² Graylingwell Hospital (formerly The West Sussex County Lunatic Asylum) was a psychiatric hospital in Chichester, West Sussex. It was completed in 1897. It closed in 2001, due to the decline of the number of patients having moved away from long stays in psychiatric wards to community-based care (Wikipedia).

²³ Leslie Kiloh (1917–1997), Australian psychiatrist who studied medicine at the London University and King’s College Hospital. In 1961, he coined the term *pseudodementia* to indicate

a syndrome of the elderly with symptoms consistent with dementia which, instead, is a depressive syndrome.

²⁴ Ball JR, Kiloh LG. A controlled trial of imipramine in treatment of depressive states. *Br Med J* 1959; 2: 1052–1055.

²⁵ a. Kuhn R. Über die Behandlung Depressiver Zustände mit einem Iminodibenzylderivat (G 22355). *Schweiz Med Wochenschr* 1957; 87: 1135.

b. Tondo L. Closer Looks. Roland Kuhn. *Clinical Neuropsychiatry* 2012; 9: 138–154.

²⁶ Kiloh LG, Ball JR, Garside RF. Prognostic factors in treatment of depressive states with imipramine. *BMJ* 1962; 1: 1225–1227.

²⁷ Garside RF, Roth M. Multivariate statistical methods and problems of classification in psychiatry. *Br J Psychiatry* 1978; 133: 53–67.

²⁸ Kiloh LG, Garside RF. Depression: a multivariate study of Sir Aubrey Lewis's data on melancholia. *Aust N Z J Psychiatry* 1977; 11: 149–156.

²⁹ See note 24.

³⁰ Roth M. Depressive and manic psychoses and allied disorders. *Curr Med Drugs* 1964; 4: 3–18.

The topic was further discussed in a subsequent paper: Roth M. Problems in the classification of affective disorders. *Acta Psychiatr Scand (Suppl)* 1981; 290: 42–51.

³¹ Carney MW, Roth M, Garside RF. The diagnosis of depressive syndromes and prediction of ECT response. *Br J Psychiatry* 1965; 111: 659–674.

³² Wilhelm Griesinger (1817–1868), German neurologist and psychiatrist who studied at the University of Zürich and in Paris. He worked in Württemberg), Stuttgart, Tübingen, and Kiel. He was also the director of the Medical School in Cairo where he became the personal doctor of the King Abbas I. In 1845, he published *Die pathologie und therapie der psychischen Krankheiten (The Pathology and Treatment of Psychic Diseases)*. His major claims were that in order to understand a psychic symptom it is important to localize it in the brain and that all psychic illnesses were caused by a pathological alteration of the brain.

³³ Gerald L. Klerman (1928–1992), American psychiatrist and researcher who developed interpersonal psychotherapy, who directed the NIMH in 1977–1980. He was an expert of psychopharmacological treatments of depression and anxiety disorders.

³⁴ a. Sargant W. The treatment of anxiety states and depressions by the monoamine oxidase inhibitor drugs. *J Neuropsychiatry* 1962; 3: 96–103.

b. West ED, Dally PJ. Effects of iproniazid in depressive syndromes. *Br Med J* 1959; 1: 1491–1494.

³⁵ No reference was found on atypical depression by Robert F. Prien. The first account of atypical depression in PubMed is by Anchersen (Anchersen P. Atypical endogenous depressions. *Acta Psychiatr Scand* 1961; 37(Suppl): 233–239), and the concept was reviewed by Pae et al. (Pae CU, Tharwani H, Marks DM, Masand PS, Patkar AA. Atypical depression: comprehensive review. *CNS Drugs* 2009; 23: 1023–1027.) Atypical depression refers to the depressive group meeting DSM-IV criteria for major depression or dysthymia, with significant mood reactivity, and two of the four associated symptoms: hyperphagia, hypersomnia, leaden paralysis, and rejection sensitivity.

³⁶ a. see note 11c.

b. Gurney C, Roth M, Garside RF. Use of statistical techniques in classification of affective disorders. *Proc R Soc Med* 1970; 63: 232–235.

c. see note 23.

d. Roth M. Classification of affective disorders. *Pharmakopsychiatr Neuropsychopharmakol* 1978; 11: 27–42.

e. Roth M, Garside RF, Gurney C, Kerr TA. Psychotic and neurotic depression: a reply on method. *Br J Psychiatry* 1979; 135: 94–96.

³⁷ a. Marshall EF, Mountjoy CQ, Campbell IC, Garside RF, Leitch IM, Roth M. Influence of acetylator phenotype on the outcome of treatment with phenelzine, in a clinical trial. *Br J Clin Pharmacol* 1978; 6247–254.

b. Mountjoy CQ, Marshall EF, Campbell IC, Garside RF, Roth M. Prediction of response to treatment with phenelzine in neurotic patients. *Prog Neuropsychopharmacol* 1980; 4: 303–308.

³⁸ See notes 20 and 22.

³⁹ See notes 23 and 33b. Also: Roth M, Gurney C, Garside F, Kerr TA. Studies in the classification of affective disorders: relationship between anxiety states and depression illness. *Br J Psychiat* 1972; 121: 147–162.

⁴⁰ a. Kerr TA, Gurney C, Schapira K, Roth M. Measurement and prediction of outcome in affective disorders. *Proc R Soc Med* 1970; 63: 235–238.

b. Kerr TA, Schapira K, Roth M, Garside RF. The relationship between the Maudsley Personality Inventory and the course of affective disorders. *Br J Psychiatry* 1970; 116: 11–19.

c. Schapira K, Kerr TA, Roth M. Phobias and affective illness. *Br J Psychiatry* 1970; 117: 25–32.

⁴¹ Roth M, Mountjoy CQ, Caetano D. Further investigations into the relationship between depressive disorders and anxiety state. *Pharmacopsychiatria* 1982; 15: 135–141.

⁴² See note 38.

⁴³ Cattell RB, Eber HW, Tatsuoka MM. Champaign (IL): IPAT; 1970.

⁴⁴ Eysenck HJ. *The Manual of the Maudsley Personality Inventory*. London: University of London Press; 1959.

⁴⁵ *Present State Examination* developed by John Wing and collaborators at the Maudsley in 1967 (Wing JK, Birley JLT, Cooper JE, Graham P, Isaacs AD. Reliability of a procedure for measuring and classifying "Present Psychiatric State". *Br J Psychiatry* 1967; 113: 499–515.) Since version-10, it has been called the *Schedules for Clinical Assessment in Neuropsychiatry* (SCAN). It encompasses a set of diagnostic items able to measure mental disorders in adult persons.

⁴⁶ See note 38

⁴⁷ See note 33b and 37a.

⁴⁸ Robert D. Gillespie (1884–1965), psychologist, coauthored with David Henders on the textbook, *Henderson and Gillespie's Textbook of Psychiatry for Students and Practitioners*; Oxford University Press, 1927, and later worked at Cambridge.

⁴⁹ Johns Hopkins Hospital, Baltimore (MD).

⁵⁰ Desmond Curran (1903–1985), British psychiatrist, emeritus professor at the University of London. In the postwar years, he ran the weekly psychiatric case demonstrations at Hyde Park Corner (along with Sir Paul Mallinson and 'Bird' Partridge) which became nationally and internationally famous providing teaching to postgraduate students. His clinical skills were legendary and came to be regarded as an infallible prognostician (Anonymous 1986).

⁵¹ Sir David Kennedy Henderson (1884–1965), a distinguished Scottish psychiatrist, knighted in 1947, president of the Edinburgh's Royal College of Physicians in 1949, and co-author with Robert Gillespie on a 1927 textbook of psychiatry.

⁵² Karl Theodor Jaspers (1883–1969), a German psychiatrist and philosopher, a major exponent of existentialism. His major contribution to psychiatry was the book *General Psychopathology* (1913).

⁵³ Detlev von Zerssen (1926–), German psychiatrist, who studied depressive disorders, typological characters, circadian rhythms, and temperaments. See: von Zerssen D, Koeller DM, Rey ER. [The premorbid personality of patients with endogenous depression. A cross-validation of the results of an earlier investigation (German)]. *Confin Psychiatr* 1970; 13: 156–179.

⁵⁴ Hagop Souren Akiskal (1944–), Armenian-American psychiatrist best known for his research on temperament and bipolar disorder.

⁵⁵ Initial research showed inconclusive evidence of linkage of panic disorder to the alpha-haptoglobin locus on chromosome 16q22 (Crowe RR. Panic disorder: genetic considerations. *J Psychiatr Res* 1990; 24[Suppl 2]: 129–134.)

⁵⁶ Donald Franklin Klein (1928–), New York psychiatrist who discovered the effect of imipramine in panic attacks, (Klein DF. Anxiety reconceptualized: gleaning from pharmacological dissection—early experience with imipramine and anxiety. *Mod Probl Pharmacopsychiatry* 1987; 22: 1–35,) and in childhood anxiety disorders (Rabiner CJ, Klein DF.

Imipramine treatment of school phobia. *Compr Psychiatry* 1969; 10: 387–390.) Most of his research was carried out with his wife, Rachel Gittelman-Klein, a child-psychiatrist.

⁵⁷ a. Gittelman R, Klein DF. Relationship between separation anxiety and panic and agoraphobic disorders. *Psychopathology* 1984; 17(Suppl 1): 56–65.

b. Gittelman-Klein R, Klein DF. School phobia: diagnostic considerations in the light of imipramine effects. *J Nerv Ment Dis* 1973; 156:199–215.

⁵⁸ George Brown (1930–), a British sociologist and psychologist, who investigated several social factors and life events associated with the origin of depression. See: Brown GW, Harris T. *The Social Origins of Depression: A Study of Psychiatric Disorder in Women*. London: Tavistock Publications; 1978.

⁵⁹ Edward John Mostyn Bowlby (1907–1990), a British psychologist, psychiatrist, and psychoanalyst, famous for his interest in child development and for his work in attachment theory (see: Tondo L. Closer Looks. *John Bowlby*. *Clinical Neuropsychiatry* 2011; 8: 159–171.)

⁶⁰ Since the year 1995, there has been a facility for ECT at the San Martino Hospital in Oristano (Sardinia) thanks to the efforts of Dr. Gian Paolo Minnai.

⁶¹ a. Murphy DL, Pigott TA. A comparative examination of a role for serotonin in obsessive compulsive disorder, panic disorder, and anxiety. *J Clin Psychiatry* 1990; 51 (Suppl53–8): 59–60.

b. Murphy DL, Zohar J, Benkelfat C, Pato MT, Pigott TA, Insel TR. Obsessive-compulsive disorder as a 5-HT subsystem-related behavioural disorder. *Br J Psychiatry Suppl* 1989; Dec: 15–24

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