# 8

# Future research and clinical implications

In this chapter, some recommendations for future research will be given as well as some suggestions of possible implications for clinical practice.

## FUTURE RESEARCH

One important conclusion drawn in Chapter 7 was that the present study has not elucidated how neuroticism increases risk of depression. In that chapter we suggested that it might be necessary to measure other factors than the ones we did or to measure them in a different way. With regard to social cognition, for example, we suggested that priming tasks might be more suitable to detect biases in emotion perception associated with neuroticism. Studying other *kinds* of processing biases might also be an option. It might prove useful to investigate cognitive operations that require more effortful elaboration, like the storage and retrieval of emotional information. Neuroticism has thus far been associated most frequently with biases in memory processes, especially in the recall of information relating to the self (Martin, 1985). Depression also has been associated more consistently with problems in elaborate cognitive functions than with problems in the passive early stages of information processing (Williams, 1997).

We still think it makes sense to try to explicate neuroticism by means of depression-related factors that are more tangible than a self-report score. Self-report neuroticism scores are useful as a quick and potent risk indicator, but they do not explain *why* neurotics are at increased risk, so they also cannot yield clues with regard to prevention. It is therefore important that future researchers more often use observational, informant, interview, and laboratory-based methods alongside the traditional self-report measures of neuroticism (cf. Klein et al., 2002; Ormel et al., 2004).

Apart from trying to clarify the concept of neuroticism by relating it to more objective risk factors and mechanisms, it might also be useful to parse the concept itself. Neuroticism is a higher-order personality dimension, which means that it is an assemblage of several lower-order traits ("facets"). The concept therefore is rather broad and non-specific - a "container concept". The majority of studies have examined neuroticism at the higher-order level. It might be that studying the underlying facets will provide more or different insights. There is evidence that only particular facets of neuroticism play a role in the development of depression (Klein et al., 2002), and that the mechan-

isms by which the various facets increase risk of depression may differ (Zuroff et al., 2004). It might also be easier to find cognitive, behavioral, or physiological correlates of neuroticism when the concept is studied at the level of facets (cf. Claridge and Davis, 2001).

Above, we recommended the use of other measures than self-report ones. One problem with such measures is that they are laborious and expensive. This is especially true for ethological assessments, i.e. systematic observations of nonverbal behavior. The author of this thesis and her assistants have spent many hours in front of a TV screen to register the nonverbal behaviors of the participants and their interviewers meticulously. We do think this undertaking has been worthwhile. Nonverbal behavior is an essential element of human communication, an element neglected too often by psychiatric researchers and clinicians. Our study has shown that nonverbal communication is also relevant with respect to the occurrence of stressful life events and recurrence of depression. These findings can be considered even more telling in view of the fact that we could not assess nonverbal communication in all its subtleties. For example, we registered the frequency and the duration of gaze (one of the elements of our involvement factor), but we did not account for the fact that people can look at each other in many different ways. Presumably, there have been several of such nonverbal nuances that we could not grasp with our instruments.

More research is required to reveal the exact role of nonverbal aspects of communication in recurrence of depression. It would be a great help when technology develops further so that the laborious work of the behavioral observations can be automated. Some promising advances in this direction have been made in recent years (e.g., Noldus et al., 2001; Grammer et al., 2002). A next step would be to study everyday interactions of former depressives, especially those with "significant others" like partners or close friends. There is reason to believe that disturbances in interpersonal behavior come to the surface especially in interactions with such significant others (Schmaling and Becker, 1991).

With respect to the study of stressful life events, our findings suggest that a simple questionnaire can be an adequate measure. Of course, interview-based methods like the LEDS are preferable, as they can provide additional contextual information (Brown and Harris, 1989). Such methods, however, are much more elaborate. A self-report questionnaire can be administered more easily, making it more feasible to collect the relevant information prospecti-

vely (cf. Ch 7, p. 149). One direction for future research would be to investigate more everyday types of interpersonal stress. Life events are very important in the context of depression, but they occur relatively infrequently. Minor experiences of interpersonal stress occur far more often (in some people's lives they occur every other day). It would be interesting to study such minor stressors: to investigate how neuroticism is related to them; how they are related to recurrence of depression (cf. Monroe and Harkness, 2005); and whether problems in nonverbal communication do indeed contribute to their occurrence, as we have assumed. One difficulty with such research is how to assess such stressors adequately. This difficulty probably also explains why many researchers prefer to study life events; life events are relatively clear-cut incidents, and their occurrence is therefore easier to establish (but see, for instance, Myin-Germeys et al., 2003, for a clever alternative).

One of our findings was that a positive association between cortisol levels and negative emotion perception was related to recurrence of depression. We interpreted this finding with reference to the notion of the hypersensitive fear circuit (Ch 7, pp.154-156). This finding definitely should be investigated more thoroughly. At any rate, our way of establishing it was rather indirect and not very elegant. A direction for future research may be to identify factors that can serve as a more direct measure for the degree to which the fear circuit is sensitized. It would also be interesting to do more research on the positive side of the sensitization coin; to investigate how such phenomena can be prevented or counteracted. Animal research has yielded some remarkable results in this respect. For example, whereas early, chronic, or repeated stress is known to result in long-lasting hypersensitivity of the HPA axis, increased maternal caregiving, induced by neonatal handling of rat pups, has been found to lead to a *decrease* in HPA-axis excitability. Rat pups reared in this way are less sensitive to stress and less fearful later in life (Weinstock, 1997; Heim and Nemeroff, 2001). In a similar vein, social housing of adult rats has been found to counteract the neuroendocrine effects of chronic stress exposure, especially in females (Westenbroek, 2004).

## CLINICAL IMPLICATIONS

Of course, it would be naive to think that the results of the study can be translated directly into a clinical treatment strategy or a prevention program.

The distance between fundamental research and clinical practice is long. Moreover, one should be cautious when making causal inferences. One cannot be sure whether the risk factors identified in the present study are also *causal* factors. Establishing the causal influence of a factor on an outcome would imply to show that by manipulating the factor one could alter the outcome (Kraemer et al., 1997). We did not do so. Moreover, our results have to be replicated.

Nevertheless, the study does indicate some points of potential clinical importance. First, the findings suggest that some problems of individuals at risk of recurrence may only appear in the interplay between these individuals and others. This points to the relevance of an integrated treatment approach that focuses not only on the remitted patient but also on his or her social environment. This may especially be relevant in recurrent depression. When individuals become depressed over and over again, a great burden is also placed on families, partners, and friends. The result may be a progressive worsening of the interpersonal circumstances of the affected individuals (see Ch 7, p. 158). Interpersonal psychotherapy may do some good in this respect, as this type of therapy is specifically directed at improving the interpersonal problems of (former) depressives (Klerman and Weissmann, 1987; Frank et al., 1990).

Another point which the study hints at is the importance of nonverbal signals in interpersonal interactions. Clinical practitioners may benefit from paying more attention to nonverbal aspects of communication (Bouhuys, 2003; Philippot et al., 2003). For example, nonverbal cues may provide information of which clients are unaware, or information which they are unwilling or unable to report. Further, nonverbal communication is an important element in the creation and maintenance of the therapeutic relationship. Processes of nonverbal matching and synchronization like the one we studied are particularly relevant in this respect. Congruent body movements and mirror-imaged postures have been found to be linked to perceptions of affiliation and increased verbal disclosure (Cappella, 1981). Clinicians who are nonverbally "in tune" with their clients are more likely to induce feelings of rapport and relatedness in their clients and are more often perceived as being warm and understanding, which has been shown to contribute to the success of the therapeutic interaction (e.g., Davis and Hadiks, 1994; Van Os et al., 2005; Lambert and Barley, 2002). Nonverbal behavior may also be an explicit focus of therapy (Segrin, 2000; Philippot et al., 2003). Although nonverbal communi-

cation occurs largely unconsciously, it can be brought under conscious control. Training can help to increase patients' awareness of nonverbal signals and to teach them how to employ nonverbal behaviors in a more favorable way (e.g., Kinseth, 1989; Bellack et al., 1996). Such training has been found to be effective in the treatment of depression (Bellack et al., 1981; Hersen, 1984; Dow, 1994). It might also be useful in therapies aimed at preventing recurrence.

Our finding that a positive association between HPA-axis hyperactivity and negative emotion perception was related to recurrence of depression also requires some clinical considerations. The idea behind this finding was that the usual link between these systems may have become sensitized as a result of previous episodes of depression or of early or chronic stress exposure, in a way as proposed by stress-sensitization and cognitive kindling models of depression (Segal et al., 1996; Post and Weiss, 1998). Such sensitization processes do not have to be irredeemable. Above, we noted that animal research has shown the potential of some conditions (care, support) to prevent or counteract stress-induced alterations of the HPA axis. In humans, it has been shown that hypercortisolemia can be reduced by antiglucocorticoid treatment (Wolkowitz et al., 2001). Behavioral approaches aimed at decreasing stress and arousal (e.g., relaxation techniques and stress management therapies) have also been found to be effective in lowering cortisol levels (Wolkowitz et al., 2001). Such behavioral methods seem to be more favorable in the long run, as they increase the flexibility and adaptability of the stress system rather than "clamping" hormonal activity at a certain level (Wolkowitz et al., 2001). Cognitive kindling phenomena also are not necessarily irreversible. Cognitive therapy has proven quite successful in the treatment of depression as well as in preventing depression relapse and recurrence (Beck et al., 1985; Scott, 1996; Fava et al., 2003). It may also prove useful in adjusting biases in emotion perception like the ones found in our study. A combined approach, targeting both stress physiology and social cognition, might prove most effective in this respect.

## REFERENCES


Beck AT, Rush AJ, Shaw BF, Emery G (1985) *Cognitive therapy of depression*. New York, NY: Guilford Press.

Bellack A, Hersen M, Himmelhoch J (1981) Social skills training compared with pharmacotherapy and psychotherapy in the treatment of unipolar depression. *American Journal of Psychiatry* 138, 1562-1567.

Bellack A, Hersen M, Himmelhoch J (1996) Social skills training for depression: A treatment manual. In *Sourcebook of psychological treatment manuals for adult disorders*, pp. 179-200. Eds V Van Hasselt and M Hersen. New York, NY: Plenum Press.

Bouhuys AL (2003) Ethology and depression. In *Nonverbal behavior in clinical settings*, pp. 233-262. Eds P Philippot, EJ Coats, and RS Feldman. London: Oxford University Press.

Brown GW, Harris TO (1989) *Life events and illness*. New York, NY: Guilford Press.

Cappella JN (1981) Mutual influence in expressive behavior: adult-adult and infant-adult dyadic interaction. *Psychological Bulletin* 89, 101-132.

Claridge G, Davis C (2001) What's the use of neuroticism? *Personality and Individual Differences* 31, 383-400.

Davis M, Hadiks D (1994) Nonverbal aspects of therapist attunement. *Journal of Clinical Psychology* 50, 393-405.

Dow M (1994) Social inadequacy and social skill. In *Cognitive and behavioral interventions: An empirical approach to mental health problems*, pp. 123-140. Eds L Craighead and WE Craighead. Needham Heights, MA: Allyn & Bacon.

Fava G, Ruini C, Sonino N (2003) Treatment of recurrent depression: A sequential psychotherapeutic and psychopharmacological approach. *CNS Drugs* 17(15), 1109-1117.

Frank E, Kupfer DJ, Perel JM, Cornes C, Jarrett DB, Mallinger AG, Thase ME, McEachran AB, Grochocinski VJ (1990) Three-year outcomes for maintenance therapies in recurrent depression. *Archives of General Psychiatry* 47, 1093-1099.

Grammer K, Fink B, Renninger L (2002) Dynamic systems and inferential information processing in human communication. *Neuroendocrinology Letters* 23 Suppl 4, 15-22.

Heim C, Nemeroff CB (2001) The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. *Biological Psychiatry* 49, 1023-1039.

Hersen M, Bellack A, Himmelhoch J, Thase M (1984) Effects of social skill training, amitriptyline, and psychotherapy in unipolar depressed women. *Behavior Therapy* 15, 21-40.

Kinseth L (1989) Nonverbal training for psychotherapy: Overcoming barriers to clinical work with client nonverbal behavior. *Clinical Supervisor* 7, 5-25.

Klein DN, Durbin CE, Shankman SA, Santiago NJ (2002) Depression and personality. In

*Handbook of depression*, pp. 115-140. Eds IH Gotlib and CL Hammen. New York, NY: Guilford Press.

Klerman GL, Weissmann MM (1987) Interpersonal psychotherapy (IPT) and drugs in the treatment of depression. *Pharmacopsychiatry* 20, 3-7.

Kraemer HC, Kazdin AE, Offord DR, Kessler RC, Jensen PS, Kupfer DJ (1997) Coming to terms with the terms of risk. *Archives of General Psychiatry* 54, 337-343.

Lambert M, Barley D (2002) Research summary on the therapeutic relationship and psychotherapy outcome. In *Psychotherapy relationships that work: Therapist contributions and responsiveness to patients*, pp. 17-32. Ed. J Norcross. London: Oxford University Press.

Martin M (1985). Neuroticism as predisposition toward depression: a cognitive mechanism. *Personality and Individual Differences* 6, 353-65.

Myin-Germeys I, Peeters F, Havermans R, Nicolson NA, DeVries MW, Delespaul P, Van Os J (2003) Emotional reactivity to daily life stress in psychosis and affective disorder: an experience sampling study. *Acta Psychiatrica Scandinavica* 107, 124-131.

Monroe SM, Harkness KL (2005) Life stress, the "kindling" hypothesis, and the recurrence of depression: considerations from a life stress perspective. *Psychological Review* 112, 417-445.

Noldus LP, Spink AJ, Tegelenbosch RA (2001) EthoVision: a versatile video tracking system for automation of behavioral experiments. *Behavior Research Methods, Instruments, and Computers* 33, 398-414.

Ormel J, Rosmalen J, Farmer A (2004) Neuroticism: a non-informative marker of vulnerability to psychopathology. *Social Psychiatry and Psychiatric Epidemiology* 39, 906-912.

Philippot P, Feldman RS, Coats EJ (2003) The role of nonverbal behavior in clinical settings: introduction and overview. In *Nonverbal behavior in clinical settings*, pp. 3-13. Eds P Philippot, EJ Coats, and RS Feldman. London: Oxford University Press.

Post RM, Weiss SRB (1998) Sensitization and kindling phenomena in mood, anxiety, and obsessive-compulsive disorders: the role of serotonergic mechanisms in illness progression. *Biological Psychiatry* 44, 193-206.

Schmaling K, Becker J (1991) Empirical studies of the interpersonal relations of adult depressives. In *Psychosocial aspects of depression*, pp. 169-185. Eds J Becker and A Kleinman. Hillsdale, NJ: Lawrence Erlbaum Associates.

Scott J (1996) Cognitive therapy of affective disorders: a review. *Journal of Affective Disorders* 37, 1-11.

Segal ZV, Williams JM, Teasdale JD, Gemar M (1996) A cognitive science perspective on kindling and episode sensitization in recurrent affective disorder. *Psychological Medicine* 26, 371-380.

Segrin C (2000) Social skills deficits associated with depression. *Clinical Psychology Review* 20, 379-403.

Van Os TWDP, Van den Brink RH, Tiemens BG, Jenner JA, Van der Meer K, Ormel J (2005) Communicative skills of general practitioners augment the effectiveness of guideline-based depression treatment. *Journal of Affective Disorders* 84, 43-51.

Weinstock M (1997) Does prenatal stress impair coping and regulation of hypothalamic-pituitary-adrenal axis? *Neuroscience and Biobehavioral Reviews* 21, 1-10.

Westenbroek C (2004) *Influence of gender and social environment in an animal model of affective disorders. Evidence for 'social support' in rats?* (Thesis). Groningen: University of Groningen.

Williams JMG, Watts FN, MacLeod C, Mathews A (1997). *Cognitive psychology and emotional disorders*. Chichester: Wiley.

Wolkowitz OM, Epel ES, Reus VI (2001) Stress hormone-related psychopathology: pathophysiological and treatment implications. *World Journal of Biological Psychiatry* 2, 115-143.

Zuroff DC, Mongrain M, Santor DA (2004) Conceptualizing and measuring personality vulnerability to depression: comment on Coyne and Whiffen (1995). *Psychological Bulletin* 130, 489-511.